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Changing the Mix of Healthcare Providers: Impact on Price, Efficiency and Quality

A Thesis Submitted for the Degree of Doctor of Philosophy

August 2015

Padhraig G. Ryan B.Sc.(Pharm.) M.Sc.(PH) PG Dip.(Stat)
Centre for Health Policy and Management
School of Medicine
University of Dublin
Supervisor: Professor Charles Normand

Declaration

I declare that this thesis has not been submitted as an exercise for a degree at this or any other university.

This thesis is my own work, however it includes the published and unpublished work of others. The published work of others is acknowledged in the text and included in a bibliography. The unpublished work of others is duly acknowledged in the text where relevant.

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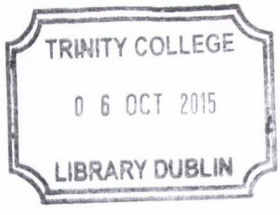

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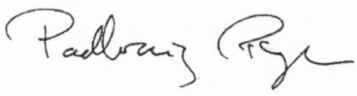

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Contents

Abstract

Service providers, the personnel and organisations that deliver care, are the foundation of any health care system. The personnel include not only doctors, but pharmacists, nurses, and an array of allied health professions, while the organisations include hospitals, pharmacies, and ambulatory surgery centres. The configuration of providers influences dimensions of performance such as access, clinical quality, and value.

In health systems around the world there are challenges in assuring high quality and compassionate care, equitable access to services, and prudent use of resources. A key policy instrument is reconfiguration of skill mix and provider organisations. Yet there is limited evidence on the effects of such changes. This thesis generates evidence to improve our understanding.

The first of three papers examines skill mix arrangements in the context of chronic warfarin therapy in the United States (USA). In one warfarin management centre, pharmacists are the primary caregivers and patients do not attend the clinic in person. The second site is nurse-led and also operates remotely. In the remaining two sites, nurses care for patients through face-to-face consultations.

The surrogate clinical outcome is the "time in the therapeutic range" (TTR), and I measured elements of patient experience, such as satisfaction and comprehension of clinical instructions, using surveys such as the Duke Anticoagulation Satisfaction Scale. The EQ-5D instrument measured health-related quality of life.

For the TTR calculations I collected 7,678 patient years of observation, and a total of 854 patients responded to the survey. According to multivariate linear regression analysis, TTR was positively associated with older age, male gender, an indication of atrial fibrillation, and a proxy marker of lower poverty levels.

Quality of care in each site was comparable to recent clinical trials. There were no significant differences in TTR between sites after adjusting for potential confounding variables. Survey responses were comparable between sites for most items, but significant differences emerged with regard to communication standards and convenience of care.

The results suggest that provider organisations can utilise a variety of skill mix arrangements to achieve high quality warfarin care, if underpinned by rigorous training, performance measurement, and a culture of continuous improvement.

Since 2010, pharmacists in Ireland have administered vaccinations to prevent influenza. The second paper models the effectiveness and cost-effectiveness of this change in skill mix. This paper did not uncover evidence of a significant increase in vaccination rates due to provision by pharmacists.

Dynamic models of infectious disease transmission resulted in estimates of cost-effectiveness falling within generally acceptable ranges. A range of sensitivity analyses tested the robustness of the results under different assumptions, such as varying vaccine effectiveness. Results suggest that pharmacist provision of vaccination is cost-effective under many assumptions, but oversight is needed to assure effective training and to avoid care fragmentation.

The traditional setting for surgery is the hospital, but in recent decades much surgery in the USA has shifted to ambulatory surgery centres (ASCs). These providers specialise in day surgery and may compete against hospitals. Proponents argue that ASCs enable clinicians to meet the needs of patients more effectively, and may leverage the benefits of multidisciplinary, team-based health care. The third paper deploys fixed effects models, a tool of econometrics designed to minimise bias in longitudinal observational studies, to analyse the effects of ASCs on price and volume.

For the base case model, market entry of ASCs was associated with a significant reduction in price for five of twelve surgical procedures, while none had a significant increase in price. The reduction in price ranged from $27.99 to $82.25 for a net increase of one ASC per 100,000 population. ASC market structure was not associated with a significant change in volume. Results suggest that ASCs may lower the price of surgery without resulting in supplier-induced demand, but further evidence is needed to validate this.

Collectively, these studies suggest that reconfiguration of service providers may facilitate the attainment of high quality, equitable and affordable health care in some circumstances, but this is dependent on effective planning and change management.

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Part I
Introduction and Background

Chapter 1

Introduction

1.1 Providers of healthcare

The foundation of any health care system is the personnel and organisations that deliver care, collectively termed providers. The personnel include not only doctors, but also pharmacists, nurses, a broad array of medical technicians, and even health care administrators. The organisations include hospitals, primary care centres, ambulatory surgery centres, and pharmacies. Policies that shape the number, distribution, and behaviour of these providers determine the performance of the system, by influencing dimensions such as access, quality, and cost.

The heterogeneous mix of providers across different health systems arises due to a combination of policy intervention and idiosyncratic factors such as market dynamics and culture. Policy makers can control the range of medical services offered by each form of provider, using tools such as regulation, organisational restructuring, and the crafting of financial incentives. In order to control the supply of providers, policy makers use tools such as licensing of clinicians (determining who is permitted to practice) and credentialing of organisations. These policy instruments are important mechanisms to influence performance.

There is limited evidence on the consequences of changing the mix of providers. The purpose of this thesis is to mitigate this gap in the evidence base. This thesis investigates changes to the provider mix in three clinical areas: anticoagulation management, influenza vaccination, and ambulatory surgery. Each clinical area is

the focus of a separate research paper. The first two papers consider heterogeneity in the mix of clinical personnel, and the third considers heterogeneity in the organisational form of providers. Each paper shall involve quantitative data analysis to ascertain the consequences of changes in the provider mix on key dimensions of performance.

A number of definitions bear emphasis. This thesis refers to two terms, "skill mix" and "provider mix", that have overlapping but distinct meanings. "Skill mix" refers to the blend of skills of clinical personnel who provide care. In the context of this thesis, skill mix is demarcated by professional qualifications, such as advanced nurse practitioner, physician or pharmacist. In some areas of the literature, the term skill mix may reflect different skills within a professional cohort. For example, levels of clinical sophistication, communication skills and enthusiasm may differ widely within cohorts of nurses or pharmacists, despite homogeneous professional qualifications. In this thesis, changes to skill mix do not necessarily imply a change in the absolute number of personnel, but may reflect reallocation of roles and responsibilities among different professional cohorts.

The second key term is "provider mix". As noted, this is broader than skill mix, as it refers to the institutions and clinical personnel that deliver care. In this thesis, the institutional form of provider is of interest partly as a tool to facilitate modification of skill mix. For example, ambulatory surgery centres may be more agile than hospitals in aligning the skills of nurses with the needs of patients, and this may underlie some performance differences between institutions. In observational research, however, it is not possible to isolate a single variable as a causative agent in performance changes, and I elaborate on this challenge later in this section.

The remainder of this chapter outlines major problems in the current system of health care delivery, and then discusses the rationale for adopting the tools of health services research, in particular the quantitative techniques of economics, to analyse this topic. This is followed by a comparison of health care delivery systems in Ireland and the United States of America (USA), the two health systems forming the context for this thesis. Chapter 2 initially explores commonalities and differences between the three clinical areas, followed by an elaboration on the background to each of these clinical areas in Sections 2.2 to 2.4. Chapters 3 to

11 contain three academic papers which present the empirical analysis for each clinical area. Chapters 3 to 5 constitute the anticoagulation study, Chapters 6 to 8 the influenza study, and Chapters 9 to 11 the ambulatory surgery study. A concluding chapter draws some general inferences from the three papers.

1.2 Why is change necessary?

All health systems experience common problems in the delivery of care. In this section I focus on three problems of relevance to this thesis: uneven clinical quality, changing patterns of demand for services, and wasteful spending. Each of these issues is potentially impacted by changes in skill mix and the mix of provider organisations.

The first problem is unwarranted variation in the clinical quality of care. This occurs within and between organisations, regions and countries [1–3]. The performance spectrum has been conceptualised as a bell curve, with some providers delivering markedly sub-standard care, a few achieving notably superior outcomes, and a majority clustered around the median performance level. The level of quality is linked to the standard of teamwork, as multidisciplinary teams are often required to meet the needs of patients [4].

Whilst some centres of excellence have substantially reduced the level of iatrogenic harm and improved clinical effectiveness, a significant amount of health care provision appears to be characterised by frequent lapses in quality. Hospitals in Michigan have dramatically cut the rate of central line associated bloodstream infections, a complication that may impose a direct economic cost of $2 Billion per year and may kill up to 20,000 patients in the USA each year. A key factor in this success was the leadership of nurses, and a tempering of the steep authority gradient that occurs frequently in health care and that may inhibit effective teamwork [5, 6]. But this has rarely been emulated in health systems in other parts of the USA or in Europe, including Ireland. The tale of quality improvement appears to be one of modest, incremental gains punctuated by occasional dramatic success such as the Michigan case [7].

In terms of chronic disease management, there are perceived successes such as the efforts of Kaiser Permanente to manage hypertension in its population of

diabetic patients. This programme leverages multidisciplinary teamwork to meet the disparate needs of patients [8]. But the management of chronic conditions in much of Ireland and the USA exhibits sub-optimal levels of interprofessional coordination, adherence to evidence-based medicine, and systematic auditing and enhancement of outcomes.

A second problem in most developed countries is that demographic changes are increasing the level of clinical need. The proportion of the population aged over 65 years is increasing in Ireland and the USA, and this will increase the number of patients requiring careful management of complex co-morbidities [9]. The economic impact may not be the "apocalyptic" scenario predicted by some commentators [10], because health care costs appear often to be concentrated in the relatively brief period preceding death, as opposed to a more linear increase with age. Accordingly, increased longevity may postpone a significant proportion of the cost of medical care, rather than resulting in a substantial increase in healthcare spending per annum [11, 12].

Nonetheless, these demographic changes shall pose challenges for clinicians. For instance, there will be greater numbers of individuals requiring management of chronic interventions such as warfarin therapy, and this will require the development of additional institutional infrastructure and clinical expertise. The number of high-risk patients requiring influenza vaccination is predicted to rise, and this will pose challenges in ensuring appropriate levels of uptake. In addition, the need for surgery is correlated with age, and demand for surgery is projected to increase. Consequently there will be increasing challenges in the management of preventive, chronic and acute care. This will require astute management of skill mix and the mix of provider organisations.

The epidemiology of disease is changing in other ways that will pose challenges for care delivery. The increased prevalence of a sedentary lifestyle elevates the rate of chronic illness. Reductions in the rate of smoking may reduce the age-standardised burden of cardiovascular disease, chronic respiratory disease, and lung cancer, but may also increase longevity and the associated burden of chronic illness. This will impact the level of need for each clinical area under consideration in this thesis, which in turn will influence the required number and configuration of providers.

The shifting patterns of clinical need are illustrated by the specialty of paediatric care. According to one study, the number of patients per pediatrician in the USA will have dropped by one third by 2020 because of a fall in clinical need. To sustain the average workload, pediatricians must provide an expanded range of services and/or expand their patient population [13]. But this is subject to significant uncertainty and other factors could exert countervailing effects on the level of need. More generally, the level of demand shall increase for specific services and decrease for others. The patterns of need are changing for the three clinical areas assessed in this thesis. Challenges of this nature pose a major challenge to health services globally, and shall require careful and nimble management of skill mix in order to assure high quality, efficient care.

The third fundamental problem in care delivery is waste of resources. Many interventions in modern health care are not supported by rigorous evidence, for instance, and collectively these comprise a significant portion of health care spending [14,15]. As new and unproven interventions become embedded in clinical practice, the utilisation of ineffective services may grow. For example, knee arthroscopy appears to offer no additional clinical benefit compared to a sham (fake) operation for certain indications. Yet it appears that this procedure is frequently conducted on an unwarranted basis [16], and is one of the most commonly performed procedures in ambulatory surgery centres. Some analysts argue that certain forms of provider organisation, such as ambulatory surgery centres and office-based surgeries, are associated with stronger incentives for supplier-induced demand. The impact of the mix of provider organisations on surgery is the subject of Chapters 9 to 11.

Poor quality care may lead to an increase in costs in some circumstances. The iatrogenic complications of health care can lead to a need for additional interventions. An example is sub-optimal management of warfarin therapy, which increases the likelihood of hospitalisation for adverse events such as gastrointestinal and cerebral haemorrhage. These adverse events instil upward pressure on spending. Changes in skill mix may impact clinical quality and utilisation rates, and this may impact on spending levels.

Setting aside the issue of clinical quality, changes to the provider mix may impact on efficiency in other ways. Task delegation from primary care physicians to

non-physician team members may influence the number of patients that a primary care team can care for. One analysis suggested that the number of patients which a primary care team could manage ranged from 1,947 to 1,387, based on assumptions that 77% and 50% of preventive care would be delegated respectively, and 47% and 25% of chronic care delegated respectively [17]. Another study found that a primary care physician would require around 18 hours per day in order to provide all recommended chronic and preventive care to a panel of 2,500 patients, without including the time needed for acute care and care coordination [18]. In light of the current supply of physicians and the economic constraints associated with expanding this supply, the use of non-physicians is needed to provide care in an efficient manner.

There is likely to be complex interaction between the mix of providers, clinical quality, appropriateness of care, and costs. Policy instruments that successfully mitigate these problems can improve population health and facilitate a more efficient allocation of societal resources. Yet there is incomplete evidence on the optimal mechanisms to mitigate these problems. For this reason, it is important to generate rigorous evidence on the impact of changes in the mix of clinical personnel and provider organisations.

1.3 The delivery of health care in Ireland and America

The Irish health system has a number of distinctive features. The Irish social model has been conceptualised as "between Boston and Berlin" [19]. In health care this manifests as tension between the role of private, voluntary health insurance, and the public system of financing and provision founded on principles of progressivity and social solidarity. Most citizens must pay sizeable out-of-pocket payments to visit a primary care physician (around €50 per visit). Enrollees in private health insurance (almost 50% of the population) are entitled to gain faster access to some essential clinical services. This inequity is important as waiting lists for care are often lengthy [20, 21].

Physicians in the primary care sector undertake six years of medical school

training and four years of primary care training [22]. Yet systematic efforts to improve the quality of primary care in Ireland have been limited, and the health service appears to exhibit major systemic problems. These problems include capacity constraints [23], fragmented care pathways, inadequate inter-professional communication, and uneven quality of care [24, 25]. Evidence suggests there may be significant underdiagnosis of conditions such as hypertension and osteoporosis among people aged over sixty [26].

Changes in the mix of provider personnel and organisations have been a feature of health policy in Ireland, but official intent has not always culminated in substantive change. The government proposes to create multidisciplinary primary care teams (PCTs) across Ireland coupled with compulsory enrolment for all citizens. In the 2001 Primary Care Strategy, the incumbent government set out to establish between 600 and 1,000 PCTs, but by 2009 only 222 had been established [27]. Many of these teams are "virtual", as they are not co-located in a base primary care centre (PCC), and there may be a limited degree of care coordination. The newly elected government, after the election of 2011, committed to increasing the number of PCTs [28].

A quite recent increase in the number of annual GP training places may facilitate an increased number of PCTs [29]. In addition, growing numbers of multipartner physician practices [22] may prove a useful building block for assembling PCTs. According to the 2001 Primary Care Strategy, each PCC would include multiple GPs and nurse/midwives, allied health professionals such as physiotherapists, occupational therapists, health care assistants, social workers, and home help workers. This core team would be complemented by a wider "primary care network" incorporating pharmacists, psychologists, dieticians, and speech and language therapists [24]. In reality, there is some fluidity around the configuration of PCCs, for example "network" members such as dieticians and pharmacists are now based in some PCCs and the team composition is variable.

The American health care system is also distinctive in a number of ways. Key characteristics of care delivery include decentralisation, an historic focus on specialist care rather than generalist care, a strong role for private provision, and fragmentation of clinical services across provider organisations. The system incorporates a plethora of diverse provider systems, and across 50 states there are

significant differences in financing, organisational structure, credentialling, and regulatory norms. Comparative analyses of international health systems have criticised the standard of care in the USA. Commonly cited problems include limited access to care for the uninsured portion of the population [30], spending levels that may threaten the nation's fiscal viability [31], and a large burden of iatrogenic harm [1].

The clinical outcomes appear comparable to other countries for certain conditions, including certain forms of cancer, although these comparisons are vulnerable to a range of biases. By contrast, outcomes for conditions such as asthma in the USA appear inferior to other developed countries. This may reflect a historic lack of investment in primary care services, a problem addressed by elements of the Patient Protection and Affordable Care Act, enacted by the administration of President Barack Obama [30].

The role of the primary care "medical home" model in the USA is increasingly prominent. This seeks to achieve an accessible primary care model of team-based care, continuity of care, a comprehensive range of services, and high quality [32]. A key tool is multidisciplinary teamwork. This exemplifies the policy approach of founding a primary care service on the disparate skills of different team members, and it is supported by innovative reimbursement models. While there have been evaluations of pilot projects, the impact of this model in addressing quality and efficiency on a large scale has yet to be demonstrated.

Although criticism of the health system in the USA may be justified, the diversity of healthcare in the USA means that positive as well as negative lessons can be learned. For instance the Chronic Care Model, developed by clinicians and researchers linked to the Group Health Cooperative in Washington State, has been an influential pillar of primary care improvement in many countries. The techniques of shared decision making, a key component of patient-centred care, were advanced significantly by clinicians in organisations such as Massachusetts General Hospital and Dartmouth Hitchcock Medical Centre. Despite its perceived weaknesses, the system in the USA warrants careful scrutiny to derive generalisable lessons for performance improvement. This thesis shall examine patterns of care in both Ireland and the USA.

1.3.1 A note on the methods of analysis

A variety of methodological approaches can be deployed to address the topic of the provider mix. This thesis deploys the tools of health services research. Health services research is not a discipline, but rather it uses empirical methods from a variety of disciplines to investigate the performance of health professionals and systems. Health services research incorporates both quantitative and qualitative empirical methods. In general, it seeks to examine the confluence of cultural factors, organisational design and operations, financial incentives, technology, and individual behaviour, and the impact of these factors on access to services, utilisation rates, clinical quality, cost, and the outcomes of patients such as health and wellbeing [33–35]. In keeping with the practice of health services research, this thesis uses a blend of disciplines to investigate the impact of provider mix, including economics and biostatistics, while some measurement tools derive from the science of clinical medicine and psychology.

The principal discipline used in this thesis is health economics. This is a useful lens through which to analyse the impact of changes in provider mix for a number of reasons. First, the quantitative techniques of economics offer rigour in dealing with quasi-experimental and other forms of observational data. Second, health systems consist of multiple interlinked markets comprising supply and demand. Interdependencies exist between the markets for inpatient acute services, outpatient services, and the markets for medical equipment and clinical personnel to deliver these services. The interdependent nature of these markets can be conceptualised and investigated through economic analysis. Third, financial and intrinsic incentives influence the behaviour of health professionals and systems in many circumstances, potentially influencing the utilisation rates of surgery for example. Fourth, there is sizeable waste of economic resources in care delivery, and due to the finite nature of these resources and the high levels of need for health services, this leads to the inability to provide care to all individuals who need it. Reconfiguration of providers may alleviate this problem. Each of these factors interacts with the question of skill mix, and accordingly health economics offers a useful body of tools to address the issue of skill mix.

Health economics comprises a number of distinct sub-disciplines, one of which

is economic evaluation. Economic evaluation seeks to compare the value for money of alternative courses of action. These alternatives can include implementation of different health technologies and behavioural interventions. In Chapters 6 to 8, I use economic evaluation to investigate the impact of the provision of influenza vaccination by pharmacists, following implementation of a policy change in Ireland. Another area of health economics is the use of econometric techniques to investigate market dynamics. Chapters 9 to 11 use a number of econometric tools, notably fixed effects and random effects models, to interrogate panel data on price and volume. These tools have been developed to minimise the risk of bias in observational studies. In this instance I use them to ascertain the impact of alternative organisational models of ambulatory surgery in the USA.

Another discipline used in this thesis is biostatistics, for example the paper on the topic of anticoagulation therapy (Chapters 3 to 5) uses techniques such as ordinary least squares regression and chi-squared tests, while the paper on the topic of influenza vaccination uses techniques such as poisson regression and Student's t-tests.

There is increasing overlap between the fields of biostatistics and econometrics, and each field has influenced the other. Tools such as instrumental variables analysis were developed by econometricians, but have more recently been used commonly in health services research. The tool of randomisation has been prominent in health research in the past fifty years, whereas econometrics has had a traditional reliance on observational data analysis. More recently, econometricians have implemented increasing numbers of randomised controlled trials. In the context of this thesis, it was not feasible to conduct a randomised controlled trial, therefore this thesis deploys state of the art tools to control for bias and confounding where possible.

The impact of changes to skill mix is mediated and influenced by organisational context, and it is difficult to disentangle these factors. A randomised controlled trial would seek to distribute evenly across study groups any potentially confounding variables, to isolate the effect of the variable (intervention) of interest. By contrast, in observational analysis, it is not possible to isolate the effect of a single variable such as skill mix changes, and a number of organisational confounders may influence the outcomes of interest. This thesis examines large-scale policy changes

using observational data, and a randomised design is infeasible in the constraints of this project. In each paper, consideration is given to organisational and administrative factors that can modulate the impact of skill mix changes. This reflects the complexity in improving service delivery, as policy makers require improved understanding of the conditions that facilitate effective changes in skill mix.

An issue under consideration in this thesis is the experience of patients in receiving care. I investigate this issue in the area of anticoagulation management, by administering surveys to patients via the internet and telephone. This survey assesses patients' views on the burdens, hassles and limitations of chronic anticoagulation therapy, which can impact on adherence to medicines and clinical outcomes. Furthermore, to measure the clinical quality of anticoagulation services provided by different categories of clinicians, this paper draws on scientific research regarding performance measurement in anticoagulation. Consequently, I have used this thesis to develop skills in a number of disciplines. In addition, I have carefully selected research methods to address the research question and available data in a thorough and valid manner.

Chapter 2

Clinical areas under consideration

2.1 Commonalities and differences

This thesis shall focus on three clinical areas: anticoagulation management, influenza vaccination, and ambulatory surgery. These areas share notable similarities and important differences.

One similarity is that each clinical area is amenable to protocolisation. Influenza vaccination requires relatively little training, and clinicians can follow protocols to determine if a patient is eligible for vaccination. For example, vaccination is contraindicated for patients with a severe allergy to eggs, but is recommended for patients with mild to moderate allergy as the benefits are perceived to outweigh the risks [36]. Information such as this can be codified into protocols.

The management of warfarin involves more clinical judgement but is still highly amenable to protocolisation. As shown in Chapter 3 of this thesis, it appears that a significant fraction of variability in clinical control between centres can be explained by the degree of adherence to a simple dosing algorithm. Similarly, whilst the provision of ambulatory surgery requires significant clinical skill, protocols and checklists play an important role in promoting effectiveness and safety. This is demonstrated by the World Health Organisation's safe surgery checklist [37], and the use of bundled interventions for surgical site infections [1]. The existence of detailed protocols can facilitate reconfiguration of skill mix.

Another commonality is that in each of these clinical areas there is significant

interaction between clinical quality and costs. Investment in influenza vaccination may be offset by prevention of costly hospitalisations and reduced absenteeism from employment. For certain subpopulations this may result in net savings. The price of warfarin medication is low relative to newer anticoagulants, but its clinical management imposes significant costs in terms of periodic blood testing and patient counselling. Investment in quality improvement for warfarin services may yield net savings through the prevention of costly adverse events such as intracranial and gastrointestinal hemorrhage, and innovation in skill mix arrangements can play an important role in improvement. Similarly, ambulatory surgery may result in costly complications, some of which are preventable by quality improvement. I elaborate upon this relationship for ambulatory surgery in Chapter 9.

Another commonality is that each clinical area will be impacted by changing demographics. These changes are increasing gradually the need for each of these three forms of care. Individuals aged over 65 years are at elevated risk of complications from influenza illness, which increases the importance of vaccination against seasonal illness. The risk of developing atrial fibrillation and venous thromboembolism, two common indications for anticoagulants such as warfarin, also increase with age. As regards ambulatory surgery, elderly individuals are much more likely to require common interventions such as cataract surgery and joint arthroscopy, although certain forms of ambulatory surgery such as tympanostomy are largely confined to younger patients.

Finally, patients' values and preferences play a significant role in determining appropriate care in each clinical area. For influenza vaccination many benefits are external to the vaccinated individual (by prevention of viral transmission), and mandatory vaccination has been encouraged for certain subpopulations such as staff in clinical facilities. Nonetheless it is generally appropriate for clinicians to discuss the rationale for vaccination with patients and to respect the preferences of patients in deciding whether to vaccinate.

Patient preferences can also guide aspects of anticoagulation therapy. For example, many patients can decide between using warfarin, whose safety profile is well-established, or a newer anticoagulant agent. These newer agents do not require intensive monitoring via laboratory tests. Patients taking warfarin may choose whether to self-monitor the effects of warfarin at home using a medical de-

vice, or to attend a laboratory for periodic testing. In addition, patient preferences are important for many forms of ambulatory surgery. Studies show that when patients are informed of the evidence base underpinning many surgical interventions, the demand for interventions drops by 20%. Elucidating and respecting the preferences of informed patients, a process known as shared decision making, may mitigate the potential for supplier induced demand in ambulatory surgery. The blend of skill mix and organisational providers may impact the degree to which patients' preferences are integrated into decision-making.

Despite these similarities, there are important differences between these clinical areas. Consequently, this thesis offers insight into the role of changes in the provider mix across disparate forms of clinical care. First, warfarin management is a chronic intervention for many patients. Whilst certain subpopulations, such as patients who have undergone orthopedic surgery, take warfarin for a short duration, many patients require warfarin over many years. This poses challenges for care coordination and continuity. This is particularly challenging given the large number of drug-drug and drug-food interactions that may precipitate treatment failure.

Influenza vaccination, by contrast, is typically administered only once a year. There is no requirement for follow-up of patients except in the case of side effects, or treatment failure when a vaccinated patient contracts influenza. The need for patient counselling is modest compared to warfarin therapy. In ambulatory surgery, interventions are typically once-off events, although they may be targeted at chronic conditions such as osteoarthritis and cataracts. Patients often require follow-up care, or even follow-up surgery in the case of perioperative complications, but the timeframe for ambulatory surgery is short compared to warfarin management.

Another area of divergence is the goal of therapy. Influenza vaccination is conceptualised as a form of primary prevention against influenza (although in patients with conditions such as chronic obstructive pulmonary disease, it may be viewed as secondary prevention of complications). Vaccination is typically administered to a large proportion of the population, in order to enhance population health through herd immunity. Warfarin therapy, by contrast, is targeted at a narrow subset of patients in whom one or more clinical indications are present. Around

1.5% of the population may be prescribed warfarin at a given time. Ambulatory surgery is often a form of tertiary prevention, as it may address an established disease process in order to improve a patient's quality of life.

In addition, credentialing and accreditation requirements differ between these clinical areas. Of note, these requirements may also vary between jurisdictions. The mechanics of influenza vaccination are relatively straightforward, and the training programme for pharmacists in Ireland is of short duration [38]. The effective management of warfarin, by contrast, requires detailed understanding of pharmacokinetics and pharmacodynamics (i.e. drug metabolism and the drug's effects on the human body, respectively). Warfarin care is simplified by the existence of dosing algorithms which can guide clinical decisions, but the credentialing process in some settings is more elaborate than for influenza vaccination [39].

The practice of ambulatory surgery requires significant skill and teamwork, and incorporates a variety of support staff such as nurses and anesthesiologists. The accreditation requirements for ambulatory surgery centres can be extensive, although credentialing is not mandatory in all states in the USA. There may be significant barriers to entry in the form of infrastructure costs, as well as certificate of need legislation to limit the construction of new facilities (see Chapter 9).

2.2 Anticoagulation

Epidemiologists have observed that as countries become industrialised and enhance the standard of living, an epidemiological transition tends to occur. The burden of disease and mortality shifts from acute, infectious illness to chronic, non-communicable illness. Therefore in industrialised nations such as Ireland and the USA, a sizeable portion of health care resources is used in the care of patients with chronic illness. Chronic illness is commonly cited as accounting for around 80% of health care spending, but this estimate varies widely depending on the selected definitions of chronic and acute illness. The evidence base unambiguously shows that successful management of chronic illness poses a major challenge for clinicians and is a major strain on resources.

Changes to skill mix are a key instrument to facilitate high quality chronic disease management, but there is uncertainty regarding the optimal blend of skill

mix in provider organisations. Even though a set of guiding principles is set out by the Chronic Care Model, including coordination across team members and the use of health information technology, there is much flexibility for providers to adapt skill mix in a tailored manner.

One area in which changes in skill mix may enhance quality is in the management of anticoagulation therapy. Warfarin reduces the risk of embolic stroke by two-thirds in patients with atrial fibrillation, the most common indication for warfarin [40]. The first paper in this thesis addresses the effects of changes in skill mix on quality for patients on anticoagulation therapy (see Chapters 3 to 5). Four provider organisations are under scrutiny, in which care is provided by different blends of pharmacists, nurses and physicians, with varying degrees of autonomy for non-physician team members. This paper draws heavily on routinely collected performance data to compare quality of care across providers. In Subsection 2.2.1, I describe some advantages and limitations of this type of non-randomised, routinely collected data as a tool to assess changes in the provider mix.

2.2.1 Performance measurement to assess changes in the provider mix

Performance measurement is an important tool to illuminate unwarranted practice variation [41]. Quality of care is a complex, multifaceted concept incorporating subjective as well as objective aspects, and performance metrics encompass structural features, processes, and outcomes of care. The impact of skill mix on quality warrants scrutiny.

In assessing the impact of changes in the provider mix, each metric should be underpinned by a strong evidence base [41], but this is lacking in many clinical areas [42]. Performance measurement is particularly challenging when patients suffer from a range of co-morbidities, because providers often must deviate from guidelines in order to meet their needs [43].

There are numerous factors that influence clinical outcomes, some of which lie beyond the direct control of providers. For instance, the rate of hemorrhage among warfarin patients rises with age, while patients' cognitive abilities, socioeconomic status, and co-morbidities may also systematically influence outcomes. Therefore

judging clinical performance on the basis of outcomes may be misleading. Clinicians who treat a relatively high proportion of poorer, older and sicker patients may be mistakenly perceived to provide low-quality care. A statistical technique to adjust for this is risk-adjustment, however this is technically challenging and necessitates quite rich data. An alternative approach is to exclude certain patient subgroups from the estimation of a performance metric [43]. The first paper in this thesis adopts a blend of these approaches to assess the impact of different blends of skill mix on clinical quality.

The management of warfarin is an example of the fruitful application of performance measurement in health care. A standard surrogate outcome measure is the "time in the therapeutic range" (TTR)[1]. This serves as a useful prognostic marker and a benchmark of clinical quality [44]. A surrogate outcome measure should be easy to calculate, should occur frequently, be reliably associated with more definitive outcomes, and should be a valid reflection of provider quality rather than the characteristics of the patient population [45]. Arguably the TTR fulfills the first three preconditions, but efforts to develop risk adjust algorithms for TTR have been scant, therefore there is scope to enhance TTR as a measure of provider quality [46–48].

Nonetheless, the association between the TTR and clinical outcomes has been demonstrated in observational studies and trials, both at the level of individual patients and health centres. Greater TTR is associated with superior clinical outcomes [49–54], including a reduction in stroke and systemic embolism, major hemorrhage, and all-cause mortality. Comparable associations have been observed for patients with venous thromboembolism [55] and mechanical heart valve replacement [56].

2.2.2 Patient centred care

The foremost objective of health care is to enhance quality of life and longevity. But a complementary challenge is to meet the psychosocial needs of patients, and this is increasingly recognised in the literature on quality improvement. These psychosocial needs include dignity, autonomy, respect for patients' preferences, and

[1] All acronyms are listed in Appendix A

informed decision-making. These are intimately linked with clinical outcomes and can influence medicines adherence, the degree of relief from physical symptoms, satisfaction of patients and clinicians, and costs. Health care that holistically fulfills these psychosocial needs is termed "patient-centred care" [57].

For example, a key determinant of successful treatment of chronic conditions is the level of adherence to medicines. Sub-optimal adherence to Warfarin may increase the likelihood of debilitating, resource intensive events such as cerebral embolism. A large body of evidence demonstrates that adherence to medication for chronic conditions is far from optimal. One systematic review found that patients "typically take less than half" of prescribed medicines, and argued that improved medicines adherence could exert a much larger impact on health than any novel treatment [58]. In the USA, approximately 89,000 premature deaths [59] and over $100 Billion in spending on avoidable hospitalisations [60] are attributed to medication non-adherence each year. Substantial health gains may be achieved by systematically enhancing medicines adherence for medications such as warfarin.

Overcoming non-adherence poses particular challenges in Ireland and the USA due to perceived under-capacity in primary care services, and the limited extent of training for clinicians in communication skills and shared decision making. The reasons for non-adherence can be classified as intentional or unintentional. Clinicians in anticoagulation management services must be vigilant in identifying and managing each of these forms. Intentional non-adherence may relate to inadequate understanding of medicines or the disease process [61], or to real or anticipated side-effects. Unintentional non-adherence relates to forgetting to take medicines or to fill a prescription in a timely manner.

Evidence suggests that a good relationship between physician and patient can enhance adherence [62–64]. Clinicians should nurture these bonds. There may be differences in the ability of different categories of clinicians to achieve this. Therefore it is important to measure and understand the experience of patients during the clinical encounter. In this thesis I capture critical elements of patients' experience of care using surveys, and compare this across sites employing different clinical professions, in conjunction with a comparison of clinical quality based on TTR.

2.2.3 The management of Warfarin in Ireland

In Ireland there is little systematic monitoring or external scrutiny of the quality of warfarin management. Given the lack of concerted effort to improve quality, it appears unlikely that management is of uniform high quality. Much care is administered by nurses in warfarin management centres associated with hospitals, while primary care clinicians also play a role.

In the primary care sector, one centre has publicised its quality improvement efforts as a retrospective audit from 2002 to 2009 [65]. Quality was measured in a number of ways, firstly using the TTR, calculated by linear interpolation using the Rosendaal method, and secondly by the point prevalence method which is the cross-sectional fraction of "INR" values within the target range. Of note, INR refers to the international normalised ratio, a measure to track the propensity of blood to clot, and a measure of the effectiveness of warfarin. The centre had managed a total of 167 patients until 2010, and was managing the warfarin therapy of 57 patients at the time of analysis in 2010.

The clinicians adopted an INR target range of 2 to 3 for patients with atrial fibrillation and 3 to 4 for patients whose indication was heart valve replacement. According to the lead clinicians, clinical control was within 5 per cent of target INRs for each method, but the precise TTR was not published.

The centre did not use decision support software, and the authors suggested this software could be a way to enhance quality in future. A number of studies suggest that computerised dosing support is superior to dosing by experienced anticoagulation clinicians in terms of TTR, although evidence of improved outcomes such as stroke and mortality rates is less clear [66–70].

Another recent study in Ireland compared usual, hospital-based warfarin management against pharmacist-led patient self-testing. The investigators used a crossover, randomised controlled trial over six months. The incremental cost per patient was €59.08, and the TTR was significantly higher in the intervention arm (72% versus 59%). The aggregate cost per patient was €226.45 in the intervention arm. The authors concluded that the pharmacist-led intervention "provides significant increases in anti-coagulation control for a minimal increase in cost" [71].

2.2.4 International evidence on the quality of warfarin management

There is wide variation in the quality of warfarin management. In some centres perhaps as few as 30% of patients are within the INR target range at a given time [72]. By contrast, in some recent trials the corresponding proportion of patients is 64 to 87% [73–78]. In the USA, TTR has been higher in dedicated anticoagulation clinics than in standard community care [79].

One meta-analysis included 47 studies of anticoagulation for patients with atrial fibrillation, and found that TTR in randomised controlled trials (RCTs) was superior to retrospective, observational studies (TTR of 64.9 and 56.4% respectively) [80]. In the RE-LY trial, which compared warfarin versus dabigatran, the mean TTR was 64% [81]. The high TTR in trials is not widely generalisable for reasons such as strict adherence to clinical protocols, patient selection, and motivation and monitoring of patients.

Sweden is perhaps an exception, as its routine anticoagulant care appears to be of high quality. One study analyzed the TTR of 18,391 patients across 67 different centres. The number of patients treated with warfarin in Sweden is around 150,000, which is 1.5% of the population [82]. The principal indications for treatment were atrial fibrillation (64%), VTE (19%), and heart valve dysfunction (13%). The mean TTR for all patients was 76.2%. Age was inversely associated with mean weekly dosage and positively associated with TTR. The rates of major hemorrhage and venous or arterial thromboembolism were only assessed for patients in two centres (n = 4,273). The rates were 2.6% and 1.7% per treatment year, respectively, and for the subset of patients with atrial fibrillation, 2.6% and 1.4% per year. The TTR in this population was higher than in most RCTs of warfarin treatment, and the rate of complications was low. The authors claim that this was not due to patient selection issues [44], but there may be systematic differences in the complexity of patients across settings [83].

A multifaceted strategy has culminated in this successful management of warfarin in Sweden. One element is Auricula, a national registry of patients with atrial fibrillation established in 2006 to enhance anticoagulation care. This incorporates a web-based algorithm which suggests a dosage of warfarin based on the previous

two INR values. The rate of complications is quantified via routine, follow-up telephone calls.

More generally, quality improvement efforts in routine care can significantly improve the TTR. As noted, TTR is inversely correlated with the rate of bleeding and thromboembolic complications [80]. Quality improvement is important, and performance measurement can serve as a cornerstone of these initiatives. A systematic review found that more frequent monitoring of INR levels was associated with better TTR [72]. On the other hand, good control of INR generally leads to less frequent laboratory testing for each patient [46]. TTR was found to be higher for experienced anticoagulation patients compared to treatment-naive patients [72].

2.2.5 Evidence on skill mix in warfarin management

A number of trials have examined the role of skill mix arrangements in warfarin management. The improvement in TTR associated with pharmacist-led patient self-management in the Irish context has already been noted (see sub-section 2.2.3).

In Australia, one RCT assessed the impact of an enhanced role for pharmacists in the management of newly anticoagulated patients after hospital discharge. The sample size was 128 patients. The project pharmacist visited the intervention group patients at home on four occasions, compared to one home visit from a general practitioner for the control group. Clinicians conducted INR testing during each home visit. The median duration of each pharmacist home visit was 24 minutes [84].

On discharge, 42% of the intervention group and 45% of the comparator group had an INR reading in the target range. By day eight, this had changed to 67% and 42% respectively ($P < 0.002$). At three months after discharge, 15% of intervention group patients had experienced a bleeding event compared to 36% of the comparator group [84].

A limitation of this trial was its open-label design. Care intensity was greater within the intervention group (four visits versus one), therefore it is unclear whether it was the altered skill mix (i.e. the medicines expertise of the pharmacy profession) or the greater frequency of visits that enhanced care [84].

Of note, evidence suggests that earlier discharge of patients from hospitals can increase the burden on warfarin management services in primary care. In Australia, prior to 2002, around two thirds of hospitalised patients had INR values within the target range at the time of discharge. But by 2002 this had fallen to less than half of patients. The trend toward reduced length of stay may have contributed to this change. This increases the need for effective management of skill mix in primary care to safeguard access to high quality services.

In one of the centres involved in this thesis, pharmacists deliver care remotely via telephone. Similarly, researchers in a Veterans Affairs hospital compared their standard AMS to an "interim telephone model" in a randomised controlled trial. The intervention comprised fewer face-to-face visits and greater telephone contact than usual care. The goal was to enhance efficiency without compromising therapeutic outcomes. The trial ran for 36 months (24 month intervention and a 12 month follow-up extension) and included 192 patients.

In the trial, the primary outcome was the TTR, and the secondary outcome was the rate of adverse events. There were no significant differences in outcomes between groups (TTR equalled 57.8% for the intervention group, 55.1% for the comparator; $P = 0.28$). At a subgroup level there were modestly significant differences, as patients in the intervention group with higher INR targets (2.5 to 3.5) had superior INR control ($P = 0.04$) and fewer complications. However, the intervention group reported a higher rate of minor bleeding events, mostly among those with lower INR target levels (2.0 to 3.0).

This study only included patients with a long-term indication for warfarin therapy, who had been stable on warfarin for at least three months. The intervention group undertook a limited amount of self-management, as well as brief face-to-face consultations with nursing staff during every encounter and with a pharmacist every three months. Each clinic appointment was followed by telephone contact [85].

In an observational study in the USA, the implementation of a pharmacist-led, telephone-based anticoagulation management service was associated with a reduced risk of complications. Pharmacists delivered care mainly by telephone and mail, and there were no face to face consultations with patients [86].

Collectively these studies imply that skill mix changes and alternative models of care, such as remote management, may have an effective role to play in warfarin

management. But further evidence is required on their impact on clinical control of anticoagulation and elements of patient experience.

2.3 Ambulatory Surgery Centres

The organisational landscape of health care is dynamic, and major advances in technology have facilitated altered service configuration in a number of ways. This process of change is exemplified by the dramatic transition from inpatient to outpatient care over the last decade [87]. There have been new treatment modalities such as minimally invasive surgery, and the use of others such as lithotripsy has diminished. As novel medical interventions arise and evidence on their effectiveness accumulates, the need for specific services can rise or fall, with implications for the setting in which care is provided. In the USA, total spending by Medicare and beneficiaries on hospital outpatient services grew by 112% between 2002 and 2012 [87].

The shift to outpatient surgery has occurred in numerous countries, in some instances linked to political impetus to lower bed capacity. Since 1990, the reported bed numbers per capita have dropped by around 10% - 20% in most Western European countries, with 45% and 47% drops in Sweden and Finland respectively. The Netherlands underwent modest reductions in bed numbers, but bed occupancy fell substantially. In some settings such as Denmark, Ireland, and the United Kingdom, where patients have encountered waiting lists for hospital admission, the reductions may have been excessive (See Figure E.4 in Appendix E [88]).

It is difficult to compare bed numbers between countries as there is no standard definition of a "hospital bed". For instance, the number of "acute care beds" may or may not include beds for patients undergoing ambulatory surgery, while chairs for patients undergoing dialysis are counted as beds in certain settings. Nonetheless, it is clear that the trend toward reduced beds per capita and increased ambulatory surgery is significant [89].

Alternative models of care delivery have emerged outside of the hospital setting. In the USA, provider organisations that exclusively provide ambulatory surgery are known as "ambulatory surgery centres" (ASCs). In the UK the comparable organisation is the "independent sector treatment centre" [90,91], and this

organisational form is common also in countries such as the Netherlands and Germany [92]. Ambulatory surgery can also be provided in physician offices, which possess less infrastructure than an ASC. Ambulatory surgery requires interprofessional teamwork, and the ASC setting may be more amenable to this than the traditional hospital setting. On the other hand, this institutional setting may increase incentives for supplier induced demand. The focus of Chapters 9 - 11 is the trend toward increased rates of ambulatory surgery and the consequences of the ASC organisational form.

2.3.1 Market and regulatory approaches to ASC distribution

Proponents argue that ASCs offer clinicians greater flexibility to streamline care processes, and to design care to enhance efficiency and quality. This could enable clinicians to meet the clinical and psychosocial needs of patients more effectively [93]. Of note, there is a relationship between the quality and cost of surgery. For instance, to limit avoidable perioperative complications, clinicians in the Geisinger health system identified 40 integral process steps for effective, patient-centred execution of coronary artery bypass grafting. Clinicians are compelled to provide a valid reason for the omission of any step. This bundle was predicted to improve outcomes and to lower the cost of complications over 90 days by 50%. Multidisciplinary teamwork has played a key role in improvements in clinical care in Geisinger [94–96].

The growth of ASCs is relatively unfettered in some states such as Florida, where there are few regulatory hurdles to prevent new market entrants. Consequently the number and distribution of ASCs is dictated predominantly by market forces. ASCs have proliferated in some of these settings. By contrast, in states such as New Hampshire the number of ASCs is small, related in part to regulatory barriers to entry. I shall exploit variation in the number of ASCs per capita in Chapters 10 and 11 of this thesis, to assess the consequences of ASC market entry on price and utilisation.

The following paragraphs discuss the rationale for divergent regulatory approaches regarding ASC market entry, through the lens of economics. In market

oriented systems, provider supply is a function of the demand for services and the cost structure of firms (or labor supply of personnel). Economic models assume that in a competitive market, firms (such as hospitals or pharmacies) have an optimal, efficient scale of production. In a state of equilibrium, firms would produce at this level and charge a price equal to the average (and marginal) cost. There would be few barriers to entry, therefore firms would enter the market in order to meet demand. This arises via market signals without external intervention. When too few firms are present, prices increase which induces entry, whereas when the market contains excessive firms prices fall and some firms must close. Such a system is flexible, responding relatively quickly to changes to demand.

But the reality of health systems is markedly different from this theoretical construct. One general class of market failures arises from market power. In competitive markets prices are driven down to the marginal cost of production. However this requires a sufficient number of firms, and there are various reasons why this may not be the case in health care. In industries in which firms have high fixed costs (such as the hospital sector), the minimum efficient scale may be high relative to demand. In the extreme, only one firm may fit in the market, becoming a natural monopoly. This leads to excessively high prices and low volume. Some components of the hospital industry may theoretically possess sufficient firms for competition, such as the market for ambulatory surgery, but this is less likely in the market for tertiary care services such as organ transplants.

Various theoretical models of industry behaviour predict outcomes between the perfectly competitive and monopoly outcomes. For instance, collusion or oligopoly creates prices exceeding the competitive ideal. In the health care sector some peculiar market failures arise. Patients are largely insulated from the price of services, and therefore patients' sensitivity to price is often negligible. In addition, patients generally lack the ability to assess the quality of care on offer, which limits the scope for competition on the basis of quality.

In the ambulatory surgery sector, there is concern in relation to supplier induced demand. Patients are often reliant on the opinion of physicians to guide their medical decisions. In many health care systems, providers benefit financially from higher utilisation rates and thus have an incentive to encourage patients to use more care. As most ASCs are partly or fully owned by physicians, a physi-

cian may benefit financially from increased demand. This may render patients susceptible to induced demand.

There are a number of variants of the supplier induced demand hypothesis. One posits that market entry of providers reduces the level of demand per provider, and providers react by inducing demand to offset this effect [97]. The other posits that as payers reduce fees, providers increase volume to offset the financial impact.

But many studies assessing supplier induced demand are difficult to interpret because of reverse causality. It is unclear if greater physician supply results in higher volume or higher demand results in greater physician supply. For example, Fuchs deploys instrumental variables techniques to assess demand inducement, and found that each 10% increase in surgeon numbers per capita was associated with an increase in utilisation by 3% [98].

However, Dranove and Wehner apply similar quantitative methods to Fuchs and find a positive correlation between the supply of gynecologists and the rate of childbirth, consistent with the assumptions of the supplier induced demand hypothesis. They argue this is implausible, and conclude that the assumptions underpinning much of the econometric literature testing the presence of induced demand are flawed [99]. Such econometric studies have been poorly equipped to address administrative and organisational factors, such as management oversight, utilisation management programmes, and financial incentives, that may impact induced demand. The following two paragraphs describe analytic approaches that may be more fruitful.

There is evidence of a link between reductions in physician fees and the volume of services [99–105]. For example, in an analysis of provider behaviour in reaction to Medicare fee cuts for coronary artery bypass grafting surgery, it appeared that providers increased volume for Medicare and other (non-Medicare) patients as the magnitude of fees diminished [105].

In addition, evidence shows that pervasive asymmetries of information render patients vulnerable to supplier induced demand. In one study 88% of patients who underwent angioplasty believed it would reduce their risk of heart attack, but only 37% of the cardiologists conducting the intervention held this incorrect view. But even in cases where physicians believed angioplasty offered no clinical benefit, 43% stated they would nonetheless carry out the procedure [106].

A fully informed patient may choose to forgo such interventions. However the process of informed consent often occurs immediately before a procedure when patients have already made their decision, and risks and benefits are not typically presented in an easily understood format [107]. Therefore there is a risk of over-supply of services in provider settings such as ASCs, and further evidence is required on this phenomenon. This is an important feature associated with the configuration and incentives of clinical personnel and provider organisations.

Policy responses to excessive supply

Policy makers have sought to curb growth in provider supply through numerous strategies, mostly in clinical areas considered to be over served. Some states in the USA have placed moratoriums on the construction of new ASCs. Many states have implemented another strategy, the Certificate of Need (CON) programme, which requires providers to obtain regulatory approval in order to expand facilities or provide certain high tech services. CON programmes are administered at the state level, frequently by independent boards. For instance, in New Hampshire a CON is needed to construct or modify a provider ASC reaching the following statutory threshold:

- $2,031,454 for any ambulatory surgical facility project;
- $865,916 for any ambulatory surgical facility located within the service area of a hospital containing less than 70 licensed beds [108]

Although the foregoing is a solitary example, this is characteristic of a process similar in other states with CON rules. The variation in regulatory processes between states results in significant variation in the number of ASCs per capita, which forms the subject of Chapters 9 - 11 of this thesis.

2.4 Influenza

The influenza virus is marked by versatility, a long-term, persistent threat, and a major potential for harm [109]. In Ireland, typically around 5-15% of the population contracts seasonal influenza each year [110]. Most patients experience a few

days of symptoms including fever, headache, nausea and malaise, and then return to full health without complications. But certain segments of the population are at elevated risk of severe complications, such as exacerbation of underlying respiratory disease, adverse cardiovascular events, or secondary bacterial pneumonia [111].

The bulk of morbidity and mortality arises in the older population, and within this cohort the morbidity rate increases almost exponentially with age, probably due to immunosenescence [112]. In the USA, elderly people account for around 90% of all influenza-related deaths, and around 70% of pneumonia and influenza related hospitalisations each year [112], and this appears comparable to Ireland and other European countries. However, vaccination of younger adults and children is important, from an economic perspective as a significant proportion of influenza associated costs are indirect productivity losses, and from a clinical standpoint as younger individuals are disproportionately responsible for transmission of influenza, and the vaccination of this subpopulation can lead to herd immunity.

2.4.1 Influenza vaccination in Ireland

Most influenza vaccination in Ireland is carried out in primary care centres by general practitioners (GPs) or nurses, during home visits, or in occupational health centres (in workplaces or healthcare facilities). During the 2010-2011 influenza season, vaccination took place in pharmacies for the first time. However, this was confined to a single pharmacy chain. Numerous additional pharmacies carried out vaccination during the 2011-2012 season, following the introduction of authorising legislation in October 2011 [113]. This role for pharmacists is comparable to care delivery in many states in the USA, where pharmacists have been authorised to administer vaccines for a longer time [111, 114, 115].

The list of subpopulations for whom vaccination was strongly indicated in Ireland for the 2013/14 season is as follows:

- those aged 65 years and over
- those aged from 6 months to 65 years
  - with a long term medical condition such as diabetes. heart, kidney, lung or neurological disease

  - who are immunocompromised due to disease or treatment
  - whose Body Mass Index exceeds 40
- residents of nursing homes and other long stay institutions
- pregnant women at any stage of pregnancy
- healthcare professionals
- carers
- those with regular close contact with poultry, water fowl or pigs

GPs provide a number of special services to public sector patients in addition to the standard General Medical Services (GMS) contract, of which influenza vaccination is the most costly. In Ireland in 2011 there were 401,614 influenza vaccination claims by GPs at a total cost of €15,940,542, based on figures from the Primary Care Reimbursement Service [116]. But there is evidence of under-vaccination of at-risk subpopulations. Evidence is needed on the ability of alternative skill mix arrangements to facilitate increased vaccination coverage.

2.4.2 Policy Issues in Influenza Vaccination

Vaccination imposes direct costs on the health system and on patients, including the cost of personnel, the vaccine itself, training, and equipment. Vaccination also imposes indirect costs on society (productivity losses arising from patients taking time from work to undergo vaccination). These costs must be balanced against any productivity gains and drop in direct costs of influenza illness arising from influenza vaccination.

The cost of vaccination is influenced by the delivery model. Internationally, there is evidence that administration in mass vaccination clinics can be less costly than in physician offices [117]. Since 2011 the PCRS has paid pharmacists a fee of €15 for influenza vaccination. In 2011 the mean payment to GPs per influenza vaccination claim was €39.69, compared to €42.74 in 2010, but by 2014 the fee to GPs for influenza vaccination had fallen to match this at €15 [118,119]. There is no

good evidence on whether competition from a pharmacy delivery model facilitated the lowering of GP fees to this level.

The province of Ontario in Canada was the first major region to implement a universal programme of influenza vaccination. In July 2000 it began providing vaccination to the entire population aged six months or older, free of charge. The cost was around double that of a targeted programme, but it reduced the rate of influenza and mortality by 61% and 28% respectively, and could save around 1,134 quality adjusted life years (QALYs) per season. The incremental cost per QALY gained was estimated at Can$10,797. Whilst most cost savings arose from prevention of hospitalisations, the results were most sensitive to the cost of vaccination and to the number of mortalities averted [120].

Another study estimated the number of people across 25 European Union countries for whom vaccination is indicated, based on the prevailing guideline recommendations. Vaccination was recommended for as much as 49.1% of the population (223.4 million people). On average however, around 35.4% of at-risk individuals were vaccinated each year, an apparent shortfall of around 144.4 million people. However, this is probably an overestimate of the number of people for whom vaccination is indicated, as many patients who have co-morbidities were double-counted [121]. Modeling studies suggest that to contain even a pandemic of moderate severity, very high levels of vaccination, treatment, and matching of the vaccine to circulating strains will be required [122].

The vaccination of every at-risk individual across the EU-25 would avert an estimated 7.22 million cases of influenza, 1.96 million visits to primary care physicians for influenza treatment, 796,743 hospitalisations, and 68,537 influenza-related mortalities. In the five EU countries for which sufficient data were available, the implementation cost would be around €1.52 billion, and this may save around €39.4 million via reduced primary care visits, and €1.59 billion via reduced hospitalisations (in France, Germany, Italy, Spain, and the United Kingdom). This is the first attempt to estimate the size of the at risk population group across the whole of the EU-25 countries [121].

However, these estimates of savings may be overstated, firstly as GPs are salaried in many countries, therefore payments to GPs may be unaffected by a reduction in influenza related illness. Second, even if GPs are paid by fee-for-

service (activity based payment), any reduction in fees may be partly or wholly offset by an increase in utilisation related to other conditions. For example, GPs may react to a reduction in demand by attending to previously unmet need, or by inducing clinically inappropriate demand. The estimates of hospital cost savings may also experience a similar offsetting [123].

The incubation period for influenza is a mean of two days, ranging from one to four days [111]. However, manufacturers have a period of seven months from the time the World Health Organisation (WHO) identifies the seasonal influenza strains for inclusion in a vaccine, to the time the vaccine must be provided to patients [124]. The predominant manufacturing method is egg-based, which typically takes around five to six months from the specification of vaccine strains until completion of the first vaccine doses. This falls within the seven month timeframe. Accordingly, more rapid production methods may offer scant improvement for managing seasonal influenza outbreaks. However, for pandemic influenza outbreaks there is need for more urgent production of vaccines.

Cell-based vaccine technologies, which are faster than egg-based production methods, could offer an advantage in dealing with influenza pandemics [124]. Cell-based technologies offer trivalent protection, and their efficacy is equivalent to egg-based vaccines, but they are significantly more expensive to produce. There is competition also from quite recently approved quadrivalent vaccines, which contain an additional influenza B strain (two A strains and two B strains) and may offer superior protection [125].

A recent study found that the incremental cost-effectiveness ratio (ICER) for a quadrivalent vaccine as compared to a trivalent vaccine was £27,378 per QALY, at a list price of £9.94 and £5.85 respectively. The authors concluded that the ICER fell with an acceptable range of cost-effectiveness at this price. If the price was £6.72, 15% higher than the trivalent price, the estimated ICER was £5,299 per QALY [126]. Other promising new strategies for improved influenza vaccination are high dose vaccines, and vaccines containing adjuvants to enhance efficacy [124, 127, 128]. There has been scant investigation of the impact of different skill mix arrangements on vaccine uptake and cost-effectiveness, in the context of novel vaccine technologies. It is possible that the optimisation of influenza vaccination will require changes to skill mix in combination with technological changes in

vaccination. Detailed assessment of this issue is beyond the scope of this thesis.

2.5 The linkage between these studies

It is evident that several issues underlie the question of new models of care. Some issues relate to the ways that professional skills are developed and maintained, others to professionalism and quality of care, others to the feasibility of change, and others relate to efficiency and cost. An important consideration is whether new models of care can demonstrably improve clinical outcomes, patient experience or value.

These issues raise a number of important requirements in the evidence base. This thesis addresses a set of changes in service delivery to investigate some of these requirements, in particular around extended roles of professionals, changes in skill mix and professional mix, and changes in the configuration of service providers. The outcome measures include the impact on access to care, some proxies and measures of clinical and patient-reported outcomes, and measures of the efficiency implications of changes in market structure and the availability of potentially more efficient providers. A vast number of studies must be conducted in order to proceed with major and effective reforms of service delivery, but this thesis has presented an opportunity to develop this area of work with some opportunistic but relevant studies. These studies investigate important issues about the feasibility and outcomes of such changes to the provider mix, and also on some of the challenges that arise.

The three studies in this thesis are reflective of these wider issues in healthcare delivery. Parts II and III deal with the need to assure quality and professionalism, and the building and maintenance of skills. The impact of changes in skill mix on costs of care and access to care is explored also in Part III. In addition, these papers consider the dynamic and often ad-hoc nature of changes to the provider mix, arising from a confluence of local initiative, market incentives, and formal policy.

As noted in the foregoing, the quality of anticoagulation management varies widely across provider sites. Much of this variation appears to be explained by the degree of adherence to established quality standards, such as periodic follow-up of

patients to improve adherence to medicines, and education of patients regarding pharmacokinetic and drug-drug interactions. The level of quality may be impacted by changes to the mix of professionals who provide care. There are many patients for whom anticoagulation therapy is indicated but are not prescribed warfarin. Access to appropriate services may be enhanced by expanding the mix of clinicians eligible to manage warfarin care.

Anticoagulation management exemplifies the need to actively develop and maintain clinical skills. Each site participating in this study enrols clinical staff in training programmes to bolster prescribing skills and patient counselling ability. Training is ongoing rather than once-off. The impact of this training in the USA offers important lessons for other contexts, such as Ireland, where there is a need to align the requirements of patients with the skills of clinicians.

Officially, the implementation of pharmacist-led anticoagulation management was enabled by the implementation of Collaborative Drug Therapy Management (CDTM) legislation in Massachusetts. However, in practice this legislation may have exerted minimal impact on working arrangements in the pharmacist-led centre, as pharmacists were already actively managing patients. CDTM appears to have established a legal basis for care that was already taking place.

The administration of influenza vaccination also raises broader issues regarding health system performance. Pharmacists are generally not co-located with primary care physicians in Ireland, and there are issues around teamwork and inter-professional communication. The expanded role of pharmacists in administering influenza vaccines in Ireland was opposed by a number of physicians on the basis that it would further fragment primary care services [129]. The HSE sought to mitigate this problem by establishing a centralised notification system for each administration of influenza vaccines in pharmacies.

Influenza vaccination raises issues around building and maintaining professional skills. The training programme for pharmacists in Ireland was critiqued by an advisory body after some pharmacists administered an incorrect dosage to patients, and the training programme was redesigned to prevent reoccurrence of this mistake. This lapse in clinical quality was relatively conspicuous and easily detected, and was the subject of corrective action by policy makers [130]. By contrast, lapses in other areas of healthcare may be less visible to policy makers, therefore some

consequences of changes in skill mix may be more difficult to detect. The interaction between the mix of providers and clinical quality is an issue common to all health care systems.

Changes to skill mix for influenza vaccination exert immediate as well as downstream economic consequences. In Ireland, there were immediate consequences for the cost of vaccination from the perspectives of patients and the health system. The downstream effects arise due to changes in the vaccination rate and herd immunity effects, which may reduce the cost of influenza illness, medical complications, and the indirect costs of productivity losses.

Implementation of influenza vaccination by pharmacists illustrates how a multi-stakeholder initiative involving policy makers and clinicians can lead to systemic change in skill mix arrangements. This change in skill mix was supported by government bodies, and appears to have been motivated by evidence of sub-optimal vaccination rates of at-risk individuals, as well as the cost imposed by influenza vaccination by GPs.

In contrast to the systematic, government-backed policy of influenza vaccination in Irish pharmacies, the growth of ASCs in the USA has been ad-hoc and market-driven. The growth in ambulatory surgery was facilitated by financial incentives for surgery that do not vary to reflect length of stay, as discussed in Chapter 9. Other factors contributing to this growth are market dynamics and the dynamism of physicians seeking to bolster control over their practice conditions and potentially improve their financial revenues.

Ambulatory surgery poses challenges in relation to teamwork, for example a cohesive team incorporating a mild authority gradient may be more likely to implement evidence-based checklists reliably for patient safety [1]. Nurses should adopt an active role in each perioperative stage. The organisational setting may impact the extent to which this teamwork occurs [131].

The emergence of ASCs impacts on costs of care, as procedure prices are generally lower and operating times may be shorter in ASCs (see Chapter 9). This may be due to the increased flexibility of physicians to streamline processes and engage in multidisciplinary teams (i.e. efficiency gains), but also due to the absence of cross-subsidisation of less profitable clinical areas such as emergency care.

In summary, the configuration of service providers is a pivotal dimension of

health services, and major variability exists in configuration both within and between countries. The provider mix can exert an important impact on performance. This thesis conducts a number of relevant and opportunistic studies in clinical areas that characterise key issues relating to the provider mix. This adds to our understanding of the consequences of changes to the provider mix and the challenges that must be overcome to assure high quality and efficient health care.

Part II

The impact of structural features of anticoagulation management on patient experience and time in the therapeutic range [2]

[2]Professor Charles Normand contributed to the design and revision of this paper. Discussions with a number of individuals contributed to the design of this study including Jean Connors, John Fanikos, William Churchill, and Thomas Lee

Chapter 3

Background to Anticoagulation Services

Warfarin, an anticoagulant medication, is indicated for the prevention of stroke in a number of patient subpopulations, such as those with atrial fibrillation and venous thromboembolism [132]. But although warfarin is efficacious, its management is characterised by uneven quality of care. The evidence base indicates that a significant proportion of patients receive care that deviates from the best available evidence, is poorly coordinated, and achieves sub-optimal outcomes.

The management of warfarin poses peculiar challenges for clinicians. The values, preferences and level of engagement of patients are often crucial, as effective management necessitates adherence not only to dosing regimens that can be complex and subject to frequent modification, but to lifestyle habits such as an appropriate diet and alcohol intake. Moreover, as the metabolism of warfarin is modulated by a range of medicines such as aspirin, patients must be vigilant to avoid potentially dangerous pharmacodynamic interactions.

In light of these issues, it is important to configure warfarin services for high quality care. This can involve changes to skill mix, and it is important to improve our understanding of the impact of skill mix adjustment. Reconfiguration of skill mix may impact on the appropriateness of warfarin dosing, the degree of patient adherence, and features of care such as the follow-up of patients who fail to undergo monitoring of warfarin effectiveness in a timely manner. Skill mix changes not only

impact the treatment of patients when they present to a clinician, but may impact the ability to manage a population of patients over time, with implications for clinical quality, patient-centredness, and cost-effectiveness.

A traditional model of skill mix is care by generalist clinicians, such as primary care physicians and "hospitalists" in the United States of America (USA) [6, 45]. However, the evidence base demonstrates that this arrangement tends not to optimise quality. The evidence suggests that dedicated anticoagulation centres are required for optimal quality. These are predominantly staffed by clinicians who specialise in warfarin therapy, based on a comprehensive implementation framework such as that specified by the Joint Commission [133]. But such a framework leaves significant flexibility over skill mix arrangements. There is scope for varying roles and levels of responsibility for physicians, nurses, pharmacists and other allied health professionals.

Further evidence is needed to illuminate the potential role of skill mix changes in improving quality. This study mitigates this gap in the evidence base, by conducting a comparison of clinical performance and patient experience across four warfarin management centres. These centres adopt different approaches to skill mix, with varying roles for nurses, pharmacists and physicians. There are also differences in a number of other features, such as the number of face to face consultations with patients, the mode of remote communication with patients, and the co-location of laboratory services with the anticoagulation management centre.

Each centre has undertaken significant quality improvement efforts and is likely to be a high-performing site, relative to the clinical performance of providers in numerous other studies. But there is limited understanding of the relative performance of skill mix arrangements in these centres. The primary objective of this study is to compare these sites using the time in the therapeutic range (TTR) as the surrogate clinical outcome, and to compare patient experience across dimensions such as satisfaction and the perception of clinicians' communication standards. The secondary aim is to test the power of patient experience and quality of life survey measures as predictors of TTR.

This study constitutes observational research into existing models of care. Accordingly, it is not possible to isolate the effect of a single variable, such as skill mix arrangements, on performance. In addition to skill mix, numerous contextual

features impact on quality, and these features include the design of financial incentives, continuing professional development, managerial oversight, adoption of information technology, and elements of leadership culture such as an the organisational authority gradient.

The aim of this study is to explore the effect of skill mix on performance, rather than to isolate and quantify its impact unambiguously. This study generates evidence on quality of care achieved by different skill mix arrangements in high quality centres, and explores factors that may contribute to successful configuration of skill mix. An advantage of this study design is that it reflects real-world performance, rather than a trial's carefully crafted, temporary conditions. Future research could investigate in more depth the impact of individual components of high quality care, and randomised controlled trials may play a useful role in this task. However, this lies beyond the scope of this thesis.

3.1 Background literature

This research topic is noteworthy for various reasons. The emergence of a new generation of anticoagulant medicines increases the need for rigorous evidence in selecting an anticoagulation strategy. In some circumstances, novel drugs such as dabigatran and edoxaban may enhance clinical effectiveness and convenience compared to Warfarin [81,134], but further data are required on the clinical effectiveness and safety of newer agents. There is also a need for further data on how to accommodate patients' preferences in situations of therapeutic equipoise, and data on the experience of patients taking warfarin is important for this.

The relationship between warfarin and health care spending bears emphasis. Investment in improved Warfarin management may generate net savings through the prevention of costly adverse events [135]. A similar relationship may exist for investment in the management of congestive heart failure. By contrast, investment in improved management of chronic conditions such as diabetes, asthma, and coronary artery disease, may be cost-effective but is perhaps unlikely to generate net savings [136]. Therefore, providers may view the redesign of Warfarin services as particularly attractive under "global payment mechanisms" that seek to reward value rather than volume. The attainment of value in warfarin therapy may be

facilitated by changes in skill mix.

3.1.1 Dosing and Patient Experience: key determinants of anticoagulation outcomes

High quality warfarin management is characterised by a number of key pillars. These include periodic tracking of blood clotting levels (measured by the international normalised ratio (INR)), a system to recall patients who have missed a scheduled blood test, and performance measurement to quantify the scope for improvement of clinical outcomes and the effect of care redesign [133].

Another critical aspect of Warfarin management is dosage adjustment. A post-hoc analysis of data from RE-LY, a prominent randomised controlled trial, found that concordance with a simple dosing algorithm predicted around 87% of variability in TTR between sites, and 55% of TTR variability between countries. Although the degree to which clinicians specified the dosage in concordance with the algorithm was measured, the researchers could not identify whether clinicians deliberately used the algorithm to inform decision-making. The addition of patient-level clinical variables, centre-level and country-level variables to the predictive algorithm resulted in a modest increase in inter-site prediction from 87 to 89% [137].

In the RE-LY trial, for each 10% increase in adherence to the algorithm there was an associated 6% increase in site-level TTR, and an 8% drop in the site-level primary composite endpoint of stroke, major hemorrhage, or death. In other, less-rigorously designed studies, such a relationship is vulnerable to criticism as the observed relationship may be spurious due to unobserved confounding. However, in the RE-LY study, centres with higher TTR had better outcomes for patients taking warfarin, but not for patients taking dabigatran [137]. Patients were randomly assigned to the intervention in each site, thus the characteristics of patients should be comparable. Therefore, the RE-LY study may have isolated the effect of the dosage algorithm on TTR, and isolated the subsequent effect of TTR on the composite endpoint. This suggests that the observed relationship between TTR and harder outcomes may be valid [138].

Other studies have used less rigorous designs to investigate the correlation between algorithm concordant dosing and TTR, and between TTR and harder

outcomes such as hemorrhage and death. For example, one study used a before-and-after analysis to compare algorithm guided dosing against the clinical judgment of experienced clinicians. For patients with a target INR range of 2.0 to 3.0 the TTR increased significantly from 67.2% to 73.2% following introduction of the algorithm, and increased from 49.8% to 63.8% for patients with a target range of 2.5 to 3.5. These findings are statistically and clinically significant. Yet studies of this nature are susceptible to confounding from concurrent changes in unmeasured dimensions of quality, such as communication standards, or changes in the characterisation of patients over time [139].

On balance, the evidence to date suggests that Warfarin dosing is a primary determinant of clinical outcomes in some circumstances. But the generalisability of findings from the RE-LY trial is open to question, as the conduct of patients and clinicians in routine care may be significantly different.

Another key dimension of care is the patient experience, defined as "the sum of all interactions, shaped by an organisation's culture, that influence patient perceptions across the continuum of care" [140]. Various aspects of patient experience may influence clinical outcomes of Warfarin therapy, including comprehension levels regarding dosing instructions and the implications of disease, and the perception of clinicians' communication and motivational skills. For example, the ability of clinicians to elicit actionable information from patients and to encourage medicines adherence, may be influenced by the degree to which patients comprehend their instructions.

There is evidence of significant miscommunication between clinicians and the patients taking warfarin. In one study of 220 patients, 50% could accurately state their weekly dosing regimen, and 66% of patients could correctly identify the regimen using a visual aid. Visual concordance was not associated with language and health literacy, whereas verbal concordance was positively associated with English as a first language and health literacy levels [141]. In the USA around 12% of the adult population has adequate health literacy, while over a third has difficulty conducting routine tasks such as following the instructions on prescription labels [142]. As Warfarin dosing may be complex and subject to frequent changes, Warfarin patients may be at heightened risk of miscommunication [60, 143].

Evidence suggests that elements of patients' experience of care, in addition to

the adherence of clinicians to dosing algorithms, strongly influence outcomes. In a study of Veterans Health Administration facilities, 48% of the between-site variability in TTR was explained by three factors: patient loss to follow up, promptness of follow-up following deranged INR values, and use of nonstandard INR targets [138]. There is strong face validity for the extent of loss to follow up being influenced by satisfaction and other elements of patients' experience, and patient experience measures may shed light on the degree of follow-up after deranged INR values. One study found that most ischemic strokes occurred after patients had discontinued Warfarin therapy [144]. This underscores the importance of mechanisms to improve patients' experience of care, such as enhancement of adherence and persistence with therapy, and education regarding beliefs about medicines and avoidance of drug-food interaction.

A recent study found that health-related quality of life was comparable in warfarin and dabigatran patients, despite the greater complexity of treatment with warfarin [145]. By contrast, another recent study of 364 patients found that dabigatran users reported greater satisfaction levels, despite a higher reported rate of adverse events [146].

The preferences of patients can vary widely in relation to anticoagulation strategies. In one study, 96 patients at risk of developing atrial fibrillation were interviewed. The patients were asked to state the number of additional bleeds they would tolerate in a group of 100 patients over two years, in order to prevent three strokes in the same group. The responses of patients ranged from zero to 100 bleeds. One cluster of patients would tolerate fewer than ten bleeds, while another cluster of patients would accept more than 35 bleeds. The authors concluded that physicians should consider tailoring treatment to the preferences of individual patients. However, this may be challenging, particularly if patients' preferences are inconsistent and fickle. The study had weaknesses such as the absence of a test-retest mechanism [147].

There is need for further evidence on the pathways between patients' satisfaction, knowledge, medicines adherence, and Warfarin control (e.g. TTR). For example, one study found that better medicines adherence was positively associated with TTR, but there was no association between TTR and knowledge about Warfarin care or the perceived effect of Warfarin on quality of life [148]. A recent

survey of 30 subjects found that pensioners and the unemployed were most adherent to their medicines regime [149]. Another study found that better knowledge of warfarin therapy was associated with superior medicines adherence [150]. In a Veterans Affairs Medical Centre, responses to the Anticoagulation Knowledge Assessment questionnaire were compared against INR control for 167 patients, but no significant correlation emerged [151].

A study in Hong Kong found a positive association between patient knowledge and TTR [152], while a study of over 15,000 Israeli patients found that patient education was inversely associated with bleeding events [153]. However the latter two studies were not designed to assess causality and may have limited generalisability to the USA and Western European contexts. The limited understanding of this relationship may be the result of underuse of existing instruments to evaluate patient experience, poor validity of the measurement tools, or may imply that causal links between these elements are weak or absent.

In summary, there have been significant advances in the management of warfarin, but quality remains uneven. There is a need for improved understanding of how the skill mix arrangements of warfarin management impact on key dimensions of care. There is also a need to further our understanding of the ability of patient experience measures to predict clinically important outcomes, and of the relationship between elements of patient experience and clinical outcomes. This study generates evidence to contribute to these goals.

Chapter 4

Methods of the Anticoagulation study

4.1 Participants

4.1.1 Provider Sites

This study examined quality of care in four anticoagulation management services in Massachusetts, USA. In the first site, pharmacists are the primary caregivers in a "collaborative drug therapy management" model. Patients do not attend the clinic in person. Instead, patients are notified by telephone about laboratory test results and dosage changes, and can ring their pharmacist regarding medication issues that arise. The second site is nurse-led and also operates in a remote manner, although patients attend the clinic for a single visit upon enrolment. The clinic notifies patients about laboratory test results by posted letter and rings patients if a dosage change is required. These two sites are located in major academic teaching hospitals in an urban area.

The remaining two provider sites are located outside of major urban centres, and are analyzed collectively as "community providers". In one site, patients attend the provider for face-to-face consultations with nurses. In the fourth site patients attend the on-site laboratory for blood testing, and are notified of results via telephone if the dose changes and via posted letter if the dose remains unchanged.

Three of these sites cooperate in a quality improvement collaborative, which

involves the sharing of clinic-level TTR results and transfer of innovations for enhancing care quality. The fourth site (a community provider) is actively engaged in quality assurance but does not participate in the collaborative.

4.1.2 Patient eligibility criteria

I gathered electronic medical record data for patients who were at least 18 years of age, and who had at least two successive INR readings in the clinic between February 1st 2012 and June 2013. I calculated the TTR for patients with a target INR range of 2.0 - 3.0 or 2.5 - 3.5, and excluded INR readings during the first 30 days of patients' treatment.

Patients aged at least 18 years of age were eligible to answer the survey, and carers such as family members were eligible to answer on behalf of patients who were physically or intellectually unable to respond.

4.2 Data Collection

Survey instruments

The survey contains three components to examine different aspects of the patient experience (see Appendix B for the full survey). The Duke Anticoagulation Satisfaction Scale (DASS) comprises 25 questions addressing negative consequences of anticoagulation treatment such as lifestyle limitations, and positive consequence such as confidence and reassurance. This instrument can compare patient experience across different anticoagulation therapies [154]. Following an initial pilot survey, I abbreviated the DASS to 19 questions to reduce respondent burden and to increase the response rate.

The Consumer Assessment of Healthcare Providers and Systems (CAHPS) comprises a series of surveys to rate patients' experience of health care in the USA. Its focus is predominantly on hospital care. A supplementary item set pertains to health literacy, measuring patients' views on how well clinicians communicate information. Based on CAPHS guidance for studies where the entire survey is infeasible, I administered a subset of five questions to cover topics such

HL9.	In the last 12 months, how often did this provider give you all the information you wanted about your health?
HL10.	In the last 12 months, how often did this provider encourage you to talk about all your health questions or concerns?
HL14.	In the last 12 months, how often did this provider ask you to describe how you were going to follow these instructions?
HL18.	In the last 12 months, how often were the results of your blood test, x-ray, or other test easy to understand?
HL21.	In the last 12 months, how often were these instructions about how to take your medicines easy to understand?

Table 4.1: CAHPS Health Literacy: Subset of questions prior to modification

as communication about medicines, blood tests, and clinicians' testing of patients' understanding. These questions are shown in Table 4.1 [155].

Third, I included the EQ-5D instrument, a generic measure of health-related quality of life (HRQoL) [156]. This is formally adopted by authorities in some nations, such as England, as an outcome metric for research to inform decisions on reimbursement of new medications [157]. I calculated a utility index value for the EQ-5D from a value set derived from a population in the United States, using the "eq5d" command in Stata [158]. In Ireland, there is not a nationally representative set of norms for a utility-based HRQoL measure. Arguably, the use of EQ-5D utility norms derived in England may be defensible for research in the Irish context in these circumstances, however the EQ-5D has limited generalisability due to cultural sensitivity. The EQ-5D also possesses inferior sensitivity compared to disease-specific instruments for certain conditions. However, this instrument is widely used and it therefore enables some degree of comparison of results across a wide range of studies [159].

Electronic medical record data

I extracted clinical data (INR readings, and the primary indication for warfarin) and demographic data (age and gender) from electronic medical records. I classified the primary indication for warfarin as either atrial fibrillation, venous throm-

boembolism, or other conditions, drawing on the approach of Rose et al. [48]. I excluded INR readings from the first 30 days of warfarin treatment (the inception phase) (see the Discussion for the underlying rationale (Section 5.2)). In sensitivity analyses I excluded readings from the first 60 and 90 days of warfarin treatment to test the sensitivity of the results to assumptions regarding the duration of the inception phase.

As an estimate of socioeconomic status, I linked the dataset to United States Census data to find the percentage of population living below the Federal poverty level in each patient's residential zip code [160]. I divided all zip codes in the USA into four quartiles, where quartile one had the lowest poverty rate and quartile 4 the highest.

Survey data collection

The four sites routinely collect the email addresses of patients, but these data are incomplete. Patients and carers were notified of the study by an email that directed patients to the survey on the Research Electronic Data Capture (RedCAP) website [161]. The online Patient Information Statement is presented in Appendix C.

Online survey respondents might not be representative of the entire patient population. To test the generalisability of results to patients who did not provide their email address to a clinic, I administered the questionnaire to a sample of these patients by telephone. This assessed potential systematic differences between online respondents and other patients. Given the timeframe of the study and the available resources, a sample of 70 patients was selected to explore this issue.

For the telephone survey, I created a database of patient names and telephone numbers, and I removed patients who had provided an email address to the anticoagulation clinic (as these patients were contacted for the online survey component). The sample of 70 patients was selected randomly, by generating a random number for each patient in the Excel dataset, and selecting the patients with the 70 highest values. These patients were contacted by telephone, and the conversation adhered to the template script for telephone contact with patients shown in Appendix C.

In cases where the telephone call was unanswered, the research team made a second telephone call on the following day. If the second telephone call went

unanswered, a third call was made on the subsequent day. If there was no answer to the third telephone call, no further calls were undertaken. If a telephone call was answered by someone other than the patient, and the patient was unavailable to speak with the researcher, the researcher left no message for the patient as any message from a healthcare provider may lead to distress for a patient or their family.

Ethical considerations

A number of ethical issues arise in the conduct of research surveys. The Declaration of Helsinki sets out ethical principles for medical research involving human subjects, and these principles have been updated numerous times [162]. In the United States, the Health Insurance Portability and Accountability Act (HIPAA) sets out requirements regarding the security and confidentiality of heath related information. Institutional ethics committees in the USA are compelled to comply with these requirements [163]. Ethical approval was obtained from the Partners Healthcare Institutional Review Board, Boston, Massachusetts, USA.

A key tenet of research on human subjects is confidentiality. Patients must be assured of confidentiality, apart from exceptional circumstances in which respondents waive confidentiality. Any legal requirements regarding data protection should be adhered to, such as HIPAA regulations. I restricted access to confidential data to research team members trained on appropriate use of study data, who had committed to maintain confidentiality. Data were used only for research study related purposes with appropriate ethical approval. When reporting study results, the anonymity of respondents must be maintained [164]. In this study, patients submitted their name and date of birth online before completing the questionnaire, and these data were downloaded and linked with electronic medical records in a secure and confidential manner. Patient identifiers were deleted from the dataset once linkage occurred.

Another ethical tenet is the minimisation of psychological distress or physical risks to respondents. The respondent burden should be kept as low as possible, and each question in the survey should map to a specific research objective. Questions should be asked in a way that is easy for respondents to answer and that minimises

distress. Participants should know that their care will not be affected in any way by a decision not to participate in a study [164], and these requirements are clearly addressed in the Patient Information Statement in Appendix C.

In general, researchers should avoid undue intrusion, and should use pre-existing data where possible rather than gather new data unnecessarily. Participation in a research study should be encouraged without engaging in personal harassment, and participants should not feel pressurised into participating. It may be appropriate to limit the number of times that a researcher visits a household or contacts an individual to attempt to recruit a participant. Subjects should be provided with contact information for a research team member whom they can contact [164], as in the Patient Information Statement in Appendix C.

Informed consent is another tenet of scientific research on human subjects. Participants should be fully informed about the study goals and what is involved, including potential risks and benefits associated with participation. Researchers should respect the rights of individuals to refuse to be interviewed, to refuse to complete any section(s) of the interview, and to terminate participation at any point. Researchers should be respectful and honest with survey respondents, for example about the duration of the interview, inducements being offered, and the purpose of the study. The Patient Information Leaflet should clearly indicate that participation is voluntary, and that the participant can reverse the decision to participate at any time [164]. In this research study, the Participant Information Statement conformed to these requirements, as shown in Appendix C.

4.3 Analysis

I measured the clinical quality of care using TTR, based on the Rosendaal method of linear interpolation [165]. Multivariate linear regression analysis assessed the effect of primary clinical indication, sociodemographic variables, and survey responses on TTR at the individual patient level. It is appropriate to adjust for clinical indication, as the observed TTR is expected to vary by indication in a systematic manner, but the target TTR (100%) remains constant for each indication. Consequently, this variable fulfils the criteria needed to be an effective risk adjuster [42]. As noted in the foregoing, patients whose target INR levels were

non-standard (i.e. were not the 2.0 - 3.0, or 2.5 - 3.5 range), were excluded from the regression analysis.

Categorical predictors such as gender were expressed as dummy variables. I used unpaired T-tests for an inter-site comparison of survey responses and TTR. I used the Analysis of Variance technique to measure the association between categorical and continuous variables, the Chi-Square test for association between categorical variables, and Pearson's Correlation Coefficient for correlation of continuous variables. I counted the frequency of missing values for survey items, and I assessed the variability for individual items using means, standard deviations, and frequency distributions.

Statistical analysis was conducted using Stata SE 12.1.

Chapter 5

Results and Discussion

5.1 Results

5.1.1 Response Rate and Patient Characteristics

For the TTR calculations there was a sample size of 8,446 patients, and this amounted to 7,678 patient years of observation between February 2012 and July 2013. This discrepancy occurs as some patients were treated in a centre for less than one year. Of these, 4,317 patient years were associated with a primary indication of Atrial Fibrillation, and 1,622 and 1,738 had primary indications of venous thromboembolism and other diagnoses respectively. Patient characteristics by site for the TTR analysis are depicted in Table 5.1.

The anticoagulation centres possessed email addresses for 3,574 patients. If it is assumed that each patient received the email sent to them in relation to the online survey, this corresponds to a response rate of 23% (822 patients) for the online component. However, it is not known how many patients received the notification email, therefore the true response rate may be significantly higher than 23%.

The researcher attempted to contact 70 patients via telephone, and spoke to 40 of these patients, of whom 32 agreed to participate in the study. In 30 cases there was no answer to the telephone call or the patient was unavailable to speak to the researcher. The percentage of respondents who completed each section of the survey is depicted in Table 5.5. Of the 854 respondents, 523 responded to each survey item. For the CAHPS, DASS, and EQ-5D subsections, the completion rates

	Pharmacist	Nurse	Community	Aggregate
Sample size	3045	4547	854	8446
Demographics				
Age (years)	67	69	74	69
Female (%)	45	40	45	42
Socioeconomic Status				
Poverty Quartile 1 (%)	55	45	51	49
Poverty Quartile 2 (%)	17	20	29	20
Poverty Quartile 3 (%)	18	26	16	22
Poverty Quartile 4 (%)	10	9	5	9
Diagnosis				
Atrial Fibrillation (%)	45	55	71	53
Venous Thromboembolism (%)	27	25	15	25
Other Diagnoses (%)	28	20	15	22

Table 5.1: Inter-site comparison of all patients

were 92%, 83% and 90% respectively.

Summary statistics for the 854 survey respondents are shown in Table 5.2. A majority were from the two urban academic centres, with 438 respondents from the pharmacist-led site, 347 from the nurse-led site, and 69 from the two community medical centres. The mean age of survey respondents was younger than the aggregate patient population (65 versus 69 years of age). There were modest differences in the percentage of females (42% versus 38%) and in the primary indication for warfarin between the two samples. Furthermore, survey respondents were more likely to live in areas with relatively low poverty levels (63% versus 49% lived in a zip code whose poverty levels were in the lowest quartile).

	Pharmacist	Nurse	Community	Aggregate
Sample size	438	347	69	854
Demographics				
Age (years)	64	66	69	65
Female (%)	43	30	42	38
Socioeconomic Status				
Poverty Quartile 1 (%)	60	63	78	63
Poverty Quartile 2 (%)	19	20	9	18
Poverty Quartile 3 (%)	14	13	9	13
Poverty Quartile 4 (%)	3	4	1	3
Diagnosis				
Atrial Fibrillation (%)	37	54	58	45
Venous Thromboembolism (%)	29	19	26	25
Other Diagnoses (%)	34	26	16	30

Table 5.2: Summary Statistics of Survey Respondents

	Excluded inception period (days)	Pharmacist	Nurse	Community
All Indications	30	66.9	69.1	69.3
	60	67.4	69.6	69.5
	90	67.7	70.2	69.9
Atrial Fibrillation	30	69.3	70.7	69.5
	60	69.9	71.2	69.6
	90	70.2	71.6	69.9

Table 5.3: Mean time in the therapeutic range by site

5.1.2 TTR and Survey characteristics

The TTR varies depending on the mechanism of calculation. For example, the exclusion of a longer inception period at the beginning of warfarin treatment results in a higher TTR. TTR is also higher for the subset of patients with a primary indication of atrial fibrillation than for patients with other clinical indications.

The mean TTR across sites is shown in Table 5.3. After the regression analysis adjusted for confounding, TTR was comparable across each site, as shown in Table 5.4. Age, gender, poverty (using residential zip code as a proxy), and primary clinical indication were significantly associated with TTR. TTR was positively associated with age, male gender, and lower poverty levels. However, the R-squared value was 26.1%, indicating that these variables collectively explain only 26.1% of variation in TTR between patients. A significant portion of variability may be idiosyncratic, perhaps related to genetic factors, or may be explained by behaviours such as medicines adherence that are partly and indirectly addressed in this set of covariates.

In each site, a majority of respondents were resident in the national quartile of zip codes with the lowest rate of poverty, ranging from 60% (Pharmacist site) to 78% (Community Providers sites) (see Table 5.2). The mean age of respondents ranged from 64 years (Pharmacy site) to 69 years (Community Providers sites), and a majority of respondents were male (62%). In Table 5.2, "poverty quartile 1" represents zip codes across the USA with the lowest poverty levels. Where percentages do not add to 100% this reflects rounding error, or, in some cases,

	(1) TTR
Age	0.00122***
	(0.000)
Female	-0.0241***
	(0.000)
Poverty Quartile 1 (Zip Codes)	0.0261***
	(0.000)
Poverty Quartile 2 (Zip Codes)	0.0266**
	(0.001)
Poverty Quartile 3 (Zip Codes)	0.0133
	(0.097)
Atrial Fibrillation	0.0168**
	(0.003)
Venous Thromboembolism	-0.0139*
	(0.025)
Pharmacist	0.0107
	(0.161)
Nurse	0.00571
	(0.436)
Constant	0.534***
	(0.000)
Observations	8446

p-values in parentheses

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table 5.4: Linear regression for all eligible patients

	CAHPS	DASS	EQ-5D
Answered all questions	92	83	90
Omitted one question	4	12	6
Omitted two or more questions	5	5	4

Table 5.5: Patterns of Missing Values (% of respondents)

missing data.

In Table 5.6 there are three sections. The first section relates to the Consumer Assessment of Healthcare Providers and Systems (CAHPS) instrument, the second relates to the Duke Anticoagulation Satisfaction Scale (DASS), and the third relates to the Euroqol quality of life instrument (EQ-5D). In the CAHPS section of Table 5.6, "CAHPS overall mean" refers to the mean of the responses to the five CAHPS questions, for patients who answered all five questions. "CAHPS - tell back" refers to question 3 in the survey in Appendix B ("...how often did your Warfarin medical team ask you to tell them how you were going to follow these instructions?").

In the DASS section of Table 5.6, "DASS - aggregate" refers to the mean of the responses to the 19 DASS questions, for patients who answered all of these questions. "Benefits - aggregate" refers to the mean of the responses to questions 22-24, 26, 28, and 30 in Appendix B. "Good overall" refers to question 26. "Limitations - aggregate" refers to the mean of the responses to questions 12-15, and 25, while "Affect - daily life" refers to question 15. "Hassles - aggregate" refers to the mean of the responses to questions 16-21, 27 and 29, "How complicated" refers to question 18, and "How hard" refers to question 21.

In the EQ-5D section of Table 5.6, "How good is your health today?" refers to question 11 of the survey in Appendix B. "EQ-5D aggregate score" refers to the composite health-related quality of life score, based on responses to the five EQ-5D items (questions 6-10), while "Pain levels" refers to question 9 in the survey.

The Student's T-tests showed that for most survey items, there were no significant differences in responses between provider sites. However, some exceptions emerged. Patients reported that clinicians in community facilities had significantly

	Pharmacist	Nurse	Community	Total
CAHPS communication standards				
CAHPS overall mean	3.3	3.2	3.4	3.2
CAHPS - tell back	2.5	2.3	2.9	2.4
DASS Satisfaction with therapy				
DASS - aggregate	41.0	41.8	44.1	41.6
Benefits - aggregate	15.1	16.3	16.7	15.7
Good overall?	2.8	3.0	3.1	2.9
Limitations - aggregate	8.6	8.2	9.2	8.5
Affect daily life?	2.2	2.2	2.5	2.3
Hassles - aggregate	18.3	18.3	20.3	18.5
How complicated?	1.6	1.6	1.8	1.6
How hard?	2.1	2.2	2.4	2.1
EQ-5D Quality of life				
How good is your health today?	77.1	77.0	78.4	77.2
EQ-5D aggregate score	83.5	86.1	83.9	84.6
Pain levels	1.47	1.39	1.47	1.44

Table 5.6: Inter-site comparison of survey responses[1]

better communication standards, but that the convenience of care was poorer. Over 84% of patients responded that the instructions on how to take warfarin were "always" easy to understand.

Although the mean responses for most DASS and CAHPS survey items were quite high, which indicates quite high satisfaction levels and perceptions of patient-centredness, the responses of individual patients were distributed quite widely for some items. For example, a respective 33% and 29% of patients said that clinicians "never" and "always" asked how they would follow instructions relating to medicines usage.

The Pearson correlation coefficient showed that the EQ-5D quality of life measure was the only survey metric that significantly predicted TTR. The results are depicted in Table 5.7. There was a significant positive association between TTR and the composite EQ-5D utility values ($R = 0.1281$, $P = 0.0011$), as well as a significant association between TTR and the responses to three of the five EQ-5D items (relating to pain, usual activities, and presence of worry and sadness), whereby greater symptom burden was associated with poorer TTR. There was no significant association between TTR and the self-care and mobility items of the EQ-5D. ANOVA found no significant association between TTR and the DASS or CAHPS items.

Reverse causality may play a part in the relationship between the EQ-5D instrument and TTR. For example, higher TTR values may result in patients reporting lower levels of worry and sadness, if patients are more satisfied with the management of their condition. This could explain, at least in part, the correlation between TTR and survey item 10 ("Feeling worried, sad or unhappy"). It seems less likely that higher TTR would result in lower reported levels of pain or discomfort (survey item 9), however there is a significant psychogenic component to the human experience of pain. For example interventions to reduce pain may exert a pronounced placebo effect, therefore reverse causality is plausible in this relationship. From a biomedical standpoint it appears unlikely that higher TTR would result directly in a higher rating of "usual activities" among patients (survey item 8), however, reverse causality cannot be precluded as patients may alter their behaviour due to their TTR levels.

Table 5.8 depicts the linear regression results when the sample is restricted to

		EQ-5D						
		Mobility	Self-care	Usual activities	Pain	Worried	Overall	Aggregate
TTR	Correlation	-0.0613	-0.0481	-0.1186	-0.0768	-0.1228	0.0298	0.1281
	P-value	*0.1159*	*0.2098*	*0.0019**	*0.0442**	*0.0013**	*0.4368*	*0.0011**

Table 5.7: Pearson Correlation Coefficient: TTR and EQ-5D

patients who answered every question (N = 523). In this smaller sample, poverty levels, gender, and the primary indication for anticoagulation are no longer significant predictors of TTR, but age retains its significance.

	(1) TTR
Age	0.00188**
	(0.002)
Female	-0.0172
	(0.235)
Poverty Quartile 1 (Zip Codes)	0.0101
	(0.755)
Poverty Quartile 2 (Zip Codes)	0.0141
	(0.684)
Poverty Quartile 3 (Zip Codes)	0.0214
	(0.558)
Atrial Fibrillation	0.0309
	(0.072)
Venous Thromboembolism	0.0197
	(0.284)
Pharmacist	-0.00382
	(0.871)
Nurse	0.0139
	(0.566)
EQ-5D quality of life	0.0901*
	(0.010)
Telephone	0.00467
	(0.886)
CAHPS	-0.000207
	(0.929)
DASS Benefits	0.000148
	(0.877)
DASS Hassles	-0.000856
	(0.506)
DASS Limitations	-0.000744
	(0.743)
Constant	0.494***
	(0.000)
Observations	523

p-values in parentheses

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table 5.8: Linear regression for survey respondents

5.2 Discussion

This study has addressed the impact of skill mix on warfarin management services, in the context of four centres in the USA. In the USA, there is some impetus for reconfiguration of skill mix, as health care providers are under increasing pressure to deliver care that is effective, efficient, and considerate of patients' preferences. Demographic changes are increasing the number of elderly people requiring management of chronic illness or risk factors, and recent changes in the institutional and reimbursement environment are incentivising prudent use of resources. There is a perception that changing the mix of clinical personnel is a key tool to align care with patients' needs and to bolster efficiency [131, 166–168]. But further evidence is needed on the effects of alternative models of care delivery, to help providers to fulfil these goals.

The effectiveness of warfarin in routine care is often less than optimal, due to challenges such as a narrow therapeutic index and idiosyncratic pharmacokinetic profile [169]. Effective management requires a number of features, such as evidence-based dosing and engagement with patients to assure adherence. A structured, multifactorial approach to high quality care is specified by the Joint Commission's National Patient Safety Goals [133]. However, this framework leaves scope for providers to pursue a variety of skill mix arrangements.

This study has compared the performance of centres that adopt different blends of skill mix (pharmacist or nurse as primary caregiver, with involvement of physicians as required). This is complemented by differences in a number of other operational features, particularly the adoption of remote management versus face-to-face consultations, the principal mode of remote communication with patients, and setting (urban academic hospital versus non-urban, community based centres). Although it is difficult to disentangle the effects of these intertwined interventions, this study offers insight into the levels of performance attainable by different configurations of skill mix.

5.2.1 Clinical performance

Of the four sites in this study, each achieved a high standard of care compared to recent studies in the literature. The clinical quality of care was measured using the TTR, and there were no significant differences between sites after adjusting for variables such as age and the primary indication for warfarin.

The TTR varied according to clinical indication, with a higher TTR for patients for whom the indication for warfarin treatment was atrial fibrillation. The TTR also depended on the duration of the inception period omitted from the TTR calculation, and the exclusion of a longer inception period was consistently associated with higher TTR. This is consistent with other studies, and reflects the challenges in stabilising INR readings within the target range during the early phase of warfarin therapy. For an inception period of 30 days and with the inclusion of patients with all clinical indications, the TTR ranged from 66.9% (pharmacy site) to 69.3% (community sites). By contrast, when the sample was restricted to patients with an indication of atrial fibrillation and the inception period was 30 days, the mean TTRs were 69.3% and 69.5% in the pharmacy and community sites respectively.

The level of clinical quality is a function of multiple aspects of care delivery. As noted, it is difficult to disentangle the effects of individual components of care on clinical performance in a non-experimental context. However, the results of this study suggest that provider organisations can utilise a variety of skill mix arrangements to achieve high quality warfarin care. There appears to be flexibility regarding the provision of warfarin care by pharmacists, nurses, or physicians, provided that a number of criteria are fulfilled. These criteria include rigorous training, supervision and managerial systems including performance measurement, and a culture of continuous improvement. There may also be flexibility regarding the decision to operate remotely or via face-to-face consultations, and this decision appears to be associated with trade-offs with regard to patient-reported convenience of care and the degree of satisfaction with clinicians' communication.

The TTR in this study compared favourably to a number of recent trials, such as the RE-LY trial in which 18,113 patients underwent randomisation at over 900 sites to warfarin or dabigatran. In RE-LY, the median TTR was 65.5%, and the other interquartile thresholds were 57.1% and 72.6% [53].

The results of this thesis study are towards the upper end of the mean TTR levels in observational, real-world studies, but the high TTR results are not unique. In a number of other non-trial contexts, clinical quality has been comparable to trials such as RE-LY. In Finland, the mean TTR in the RE-LY trial was 74%. By comparison, in a retrospective study of a Finnish warfarin registry involving 2,746 patients the mean TTR was 65.2%, and was 74.5% among the subset of patients without any gaps exceeding 56 days between consecutive INR tests. The registry patients were comparable to Finnish participants in RE-LY in terms of age and comorbidities (apart from hypertension) [170].

In other registry studies of warfarin therapy, the TTR (or proportion of INR tests within the target range) ranged from 57.8% to 76.2%, but many of these studies lacked information on clinical indication and therefore assigned a target INR range of 2 to 3 to all patients [170]. The Finnish registry study calculated TTR in a more valid fashion, based on different INR target ranges for different clinical indications, in a similar manner to this thesis study.

The novel contribution of this thesis study is the comparison of high-performing anticoagulation management centres with disparate blends of skill mix. However, there are different methodologies for the calculation of TTR which may yield different conclusions. In this paper I omitted any INR readings recorded during the first 30 days of treatment in a centre, to boost comparability with the published literature and to focus the study on a phase of treatment where genetic differences in the metabolism of warfarin are likely to exert a lesser impact on TTR [46,51,169].

An alternative approach is to divide patients into inception and experienced groups, where the inception phase covers the first phase of warfarin treatment, and to calculate TTR separately for each group. One study reported a mean TTR of 48% for inception patients and 61% for the experienced phase, where the inception phase was classified as the first six months of warfarin treatment. In the "experienced" phase, the site mean TTR ranged from 41% to 72%, and deviations from the expected site mean TTR ranged from -19% to +12% [47]. However, an inter-site comparison of TTR results during the inception period may lead to spurious findings, as fluctuations in INR are particularly idiosyncratic during this period (due to variation in patients' genetic profile) [46, 51, 169]. Therefore, an inception period comparison was not conducted. Similarly, the comparison of

TTR during the inception and experienced periods may lead to spurious findings.

Table 5.6 shows that pain levels are higher for patients attending the nurse-led clinic, according to the EQ-5D instrument. This may reflect differences in casemix, for example patients in the nurse-led clinic may be more acutely ill than those in other sites. In general, it is important to adjust for casemix differences when comparing clinical outcomes. In this study, although the EQ-5D was a significant predictor of TTR, inclusion of the EQ-5D as a covariate did not significantly impact the main findings, as there was no significant difference in TTR between pharmacist-led and nurse-led sites in Tables 5.4 and 5.8.

More generally, a number of studies have compared the quality of prescribing between physicians and other health care professionals across a range of clinical areas. These findings are broadly consistent with the findings of this thesis. For example, a systematic review of 35 studies found that nurse prescribing appeared comparable to prescribing by physicians in terms of the characteristics and numbers of patients, the types and dosages of medicines, and subjective and objective outcomes of care. Nonetheless the body of evidence on the relationship between skill mix and prescribing quality is limited and 30 of the 35 studies had a high risk of bias [171].

5.2.2 Survey metrics

Section 5.1 showed that responses were comparable between sites for most items in the CAHPS, DASS, and EQ-5D survey instruments. However, significant differences emerged with regard to patients' perceptions of communication standards and convenience of care, measured by questions 3 and 15 in the survey, from the CAHPS and DASS instruments respectively (see Appendix B).[2] In addition, there was a significant degree of variability (based on the standard deviation) in responses to some survey items, which suggests scope exists to enhance patient experience and communication skills, even in high-performing centres where the mean response to surveys is high.

[2]Question 3 (from the CAHPS instrument): "In the last 12 months, how often did your Warfarin medical team ask you to tell them how you were going to follow these instructions?" Question 15 (from the DASS instrument): "Overall, how much does Warfarin affect your daily life?"

The survey results are consistent with other studies, for example, a recent English study found that patients expressed high levels of satisfaction with nurse and pharmacist independent prescribers. A majority of patients reported no difference between the experience of care with physicians and non-medical prescribers, in dimensions such as access to services, support for adherence, control of condition, and perceived quality and safety [172].

In this thesis study, the metrics of patient experience were not predictive of TTR. Previous studies suggested that there is scope to improve the validity of available measures of patients' experience of care, including the experience of warfarin therapy. By contrast, the EQ-5D quality of life measure and patients' age were positively associated with better (higher) TTR after controlling for variables such as gender and primary clinical indication.

Some results are sensitive to the precise blend of variables included in a regression model. In the regression model including all patients whose TTR was calculated, the poverty levels in a patient's zip code of residence, patient gender, and clinical indication for warfarin therapy, all were predictive of TTR, whereas none were predictive of TTR in a model including only patients who completed the survey. This may be a selection issue, or a statistical power issue, but it illustrates the difficulty in using regression techniques to compare clinical sites in a non-experimental context.

These findings are compatible with the study of Witt et al., which found that the predictors of stable INR management were male gender, age of over 70 years, and the absence of heart failure. The authors postulated that a reason for higher TTR in older patients is superior medicines adherence [173]. Of note, evidence from Sweden indicates that although TTR tends to be better in older patients, the rate of major bleeding tends to increase significantly with age [44].

5.2.3 Strategies for improvement

The level of TTR control in this study was high compared to other studies. Nonetheless, nurses and pharmacists in other settings cannot necessarily achieve comparable performance levels. Rigorous training and managerial supervision is required, with a need for considerable education and supervised prescribing. In

Australia, for example, training in prescribing for pharmacists is taught over a three to six month period on a part-time basis, equivalent to 26 days in total. The training incorporates a 12 day period of practice and mentoring under a medical practitioner [174]. In New Zealand, pharmacists undergo 150 hours of prescribing practice under the supervision of a medical practitioner, as well as a two semester training programme, to achieve accreditation to prescribe independently [175]. In the sites participating in this thesis study, education occurs on an ongoing basis.

Changes in skill mix may be complemented by tools such as patients surveys to gauge the effectiveness of change. Surveys can identify specific activities that are amenable to quality improvement, such as the communication of blood test results. Surveys can also identify behaviours that impede effective communication, such as speaking in an excessively rapid manner, and can identify underuse of potentially beneficial behaviours by clinicians, such as the "talk-back" process to assess the degree to which patients remember instructions.

Each item in the CAHPS Health Literacy has been linked to an improvement practice by the Agency for Healthcare Research and Quality (AHRQ) [155]. To improve performance on the question "In the last 12 months, how often were these instructions about how to take your medicines easy to understand?", providers can divide information for patients into two or three concepts and test patients' recall, as well as increase the rate of medication review and/or medication reconciliations. Similarly, to improve responses to the question "In the last 12 months, how often were the results of your blood test, x-ray, or other test easy to understand?", providers should aim to provide written information at a reading level of fifth- to sixth-grade.

Nonetheless, although existing survey instruments may illuminate suboptimal aspects of care, further work is required to measure patients' experience of warfarin treatment in an accurate manner, and to understand the causal pathways between patient experience and clinical outcomes. This will increase the degree to which measures of patient experience are actionable.

As noted, a major determinant of outcome for warfarin patients is medication dosage. Irrespective of the clinical profession that provides warfarin care, a useful avenue to improve care may be to monitor the adherence of clinicians to warfarin dosing algorithms, and the reasons for over-riding an algorithm. This can consti-

tute routine tracking of care processes and outcomes, and interrogation of these data to distinguish deviations from the algorithm that are positive (i.e. that improve outcomes, and therefore are an opportunity to refine current algorithms) and those that are detrimental to care. This interrogation may improve the clinical characterisation of warfarin therapy [176].

Ultimately, changes to skill mix and the provider mix can impact performance in various dimensions such as clinical quality and patient-centredness. This thesis paper has shown that it is possible to achieve comparable and quite high levels of performance in centres with a variety of skill mix arrangements. In the context of equivalent performance in terms of clinical care and patient experience, it bears emphasis that it is appropriate to pursue a skill mix option that imposes lower costs (i.e. lower costs without compromising quality). This frees up resources for investment in other areas of the healthcare system, *ceteris paribus*. This thesis paper did not compare costs of care by site, as this was a condition of access to the research data. However, this study can serve as a preliminary step for a comprehensive cost-effectiveness comparison of different categories of clinicians.

5.2.4 Limitations

This study has some limitations. First, survey respondents may be unrepresentative of the broader patient population in participating clinics. Of the 8,446 patients in the TTR regression analysis, only 3,574 patients provided an email address to the clinics, and only 23% (822) of these patients responded to the survey online. There may be systematic differences between at least five distinct patient subpopulations: patients who answered the survey online, patients who answered by telephone, patients who spoke to a researcher by telephone and refused to answer the survey, patients who provided an email address but did not answer the survey, and patients who did not provide an email address and did not receive a phone call. These differences may limit generalisability of survey results to other clinics, and to other patient subpopulations in the same clinics.

As noted in the foregoing, online survey respondents tended to be younger and healthier (as measured by the EQ-5D instrument) than respondents who answered by telephone. The 32 telephone respondents expressed higher levels of satisfaction

and rated communication standards more highly, relative to online respondents. The online survey respondents were also younger than the general patient population in these clinics.

According to the literature on patient satisfaction with health services, older patients tend to report greater levels of satisfaction than younger patients [177–179]. This may account for the higher reported satisfaction levels among telephone respondents in this study, compared to online respondents. However, there may be additional bias, as telephone respondents could be more likely to respond in a manner viewed as favourable by the researcher. Telephone respondents may rate services favourably if they believe that the researcher desires to hear this. By contrast, online respondents may believe they have a greater degree of anonymity, and may be less susceptible to this source of bias. In addition, researchers speaking on the telephone may inadvertently give cues to respondents about how to answer [180, 181].

Despite these limitations, the response rates are comparable to other survey studies that have used a comparable (predominantly online) design, and the results can offer actionable information for quality improvement. For the TTR calculations, data were available for all eligible patients during the study period which boosts the validity of results.

Second, there were limitations regarding the forms of data collected for this study, due to the inherent resource constraints of this thesis project. The survey was cross-sectional and did not track longitudinal changes. A significant fraction of data on hospitalisations and emergency department attendances for this patient population is collected in an unstructured format and could not be quantified in this study.

By contrast, data for TTR was available in structured format for most patients. The validity of TTR as a surrogate outcome is supported by numerous studies, such as an examination of 2,223 British nonvalvular atrial fibrillation patients in which each 10% increase in the time spent out of range was associated with a significantly increased odds ratio of 1.29 for mortality, 1.10 for ischemic stroke, and 1.12 for other thromboembolic events. Whilst the correlation is imperfect between TTR and harder outcomes such as stroke and mortality, the correlation is sufficiently strong for TTR to be widely used as a surrogate outcome benchmark

of quality [50].

Third, comparatively few patients were sampled from the two community providers. For the survey, 69 of 854 respondents were from the two community sites, while for the TTR regression 854 of the 8,446 patients were from community sites. However, the sample sizes of the survey and TTR analyses compare favourably to other studies of warfarin patients. For example the DASS was initially tested on an aggregate sample of 262 patients receiving oral anticoagulation, compared to 854 in this thesis study. The study was powered to detect differences between sites for the primary outcome of interest (TTR) and the survey instruments.

Fourth, the study sites are unrepresentative of warfarin management services that have not initiated improvement programmes. According to one study, the decision of pharmacists regarding whether to become prescribers was dependent on factors such as the form of innovation (i.e. features of the prescribing programme), the readiness of the system for change, communication strategies between clinicians, and power and influence. Of the 38 pharmacists who participated in interviews in the foregoing study, each stated that the characteristics of their relationship with a physician influenced their prescribing behaviour [182].

Consequently, these TTR levels and survey results may not be achieved in the short term by other provider organisations employing similar cohorts of professionals. However, the intention of this thesis is to explore the relative performance of various professional categories of clinicians in a selected group of high-performing warfarin management centres. Accordingly, this study generates lessons which may be applicable to other provider organisations seeking to improve quality of care.

Part III

The cost-effectiveness of influenza vaccination in Ireland: Examining the consequences of alternative models of provision [3]

[3]Professor Charles Normand, Professor Susan Smith, and Professor Martin Henman contributed to the design and revision of this paper

Chapter 6

Background to Influenza Vaccination

6.1 Influenza Vaccination Policy

All health care systems must contend with two fundamental problems. The first is flawed execution, arising when the evidence base clearly favours a specific course of action, yet implementation is absent or unreliable. This can be termed the implementation challenge. The second overarching problem is a dearth of evidence on which to base clinical and policy decisions, which occurs in many circumstances [37]. Each of these problems, failure to implement established evidence or a lack of evidence, has major implications for clinical quality and efficiency.

The focus of this paper is the provision of influenza vaccination in Ireland. Vaccination imparts demonstrable benefits to many recipients, in particular to individuals at elevated risk of serious complications such as the elderly or those with chronic respiratory disease or congestive heart failure. But in many nations, including Ireland, there is failure to meet target vaccination rates for these subpopulations, and a need to develop alternative models of care delivery to increase vaccine uptake [110, 111, 121]. There is an implementation challenge to achieve an increased vaccination rate at a reasonable cost. Changes to skill mix may be a tool to accomplish this.

In an effort to increase vaccination rates for specified subpopulations in Ireland,

community pharmacists in Ireland were recently authorised to administer the influenza vaccine. This thesis paper addresses the question, can this alternative model of vaccine administration, operating via an enhanced role for community pharmacists, succeed in increasing the uptake of this intervention?

Yet there are also gaps in our understanding of the cost-effectiveness of influenza vaccination using different skill mix arrangements. To calculate this, the clinical effectiveness and cost-effectiveness of influenza vaccination must be calculated, while taking into account the different vaccine uptake rates and unit costs associated with different blends of skill mix. Some studies estimate that vaccine efficacy is 70-90% when vaccine components are well matched against circulating influenza strains.

But the evidence base is undermined by methodological deficiencies. A more rigorous analysis suggests that effectiveness has been overstated [183]. Moreover, a systematic review found that government funded studies were less likely than industry-funded studies to have favourable conclusions regarding vaccination's effectiveness. In more rigorously conducted studies (defined in terms of criteria to quantify the propensity to biased results), the stated results were more likely to concord with the stated conclusions [184]. Some analysts have postulated that a pro-vaccine industry bias exists in the literature [185]. This impacts on the clinical and cost-effectiveness of vaccination by different categories of health care professional.

Influenza imparts a significant clinical and economic burden. Around 10-20% of the global population is infected with an influenza virus each year [186], however many cases are asymptomatic, and many symptomatic patients do not attend a physician. There may be three to five million cases of severe influenza illness each year, leading to 250,000 to 500,000 deaths globally [187]. In the USA during 1976 to 2007 the number of influenza-associated mortalities ranged from 3,349 to 48,614 each year, and there was around 200,000 hospitalisations per year [188].

In response to this burden, The Strategic Advisory Group of Experts of the World Health Organisation advises that every country should promote vaccination in risk groups such as young children, elderly people, and patients with conditions such as chronic obstructive pulmonary disease. The vaccination of pregnant women should be prioritised in order to protect the future young infant and the mother

[189].

Some studies suggest that vaccination falls within generally accepted ranges of cost-effectiveness across various subpopulations and settings, and may even result in net cost savings [117,186,190]. But in the Irish context, there is a lack of evidence on the economic cost of influenza and the cost-effectiveness of vaccination from the perspective of the health system, patients, and society. Changes to skill mix arrangements should represent an efficient use of resources, and it is important to assess this in the Irish context.

6.1.1 The administration of vaccines by pharmacists

Internationally, there is a growing trend towards administration of vaccines by pharmacists. In the United States, nine states permitted pharmacists to vaccinate by 1995, and by 1999 this had increased to 30 states [191]. By 2004, this number reached 43 states [192]. Pharmacist vaccination occurs also in Canada, Portugal, New Zealand, the United Kingdom, Ireland and Australia [193,194].

A review found that while pharmacists in Scotland, Australia, New Zealand and Portugal are permitted to administer injections, they are ineligible for the receipt of public funding for this service. In England and Wales, administration fees for pharmacists ranged from £7.00 to £10.00, while fees in Canada ranged from $7.50 CAD to $20.00 CAD across regions. The reviewers identified 34 separate programmes for publicly funded reimbursement of pharmacist administered injections, and the average fee was €9.38 per injection ($13.12 CAD, converted into euros according to exchange rates in July 2015) [194].

A review published in 2006 found that vaccination by community pharmacists is widespread, but that there is scant empirical research on this topic. The authors argued that vaccination is one of the major drivers of enhanced pharmacy services in the United States [115].

The literature suggests it can take time to embed practice changes in pharmacy. In 2000, legislation permitted pharmacists in Oregon, USA, to administer influenza vaccinations. From 2000-01 to 2002-03, the number of pharmacies participating in the scheme increased from 56 to 132, and the number of vaccinations increased from 13,116 to 30,218 [192].

There is evidence that pharmacists can increase vaccination rates in high-risk patients with established cardiovascular disease [195], while pharmacist vaccination during off-clinic hours (evening, weekends, holidays) may increase vaccination rates, particularly among individuals aged under 65 years [196].

In the United States, Steyer et al. used a matched pairs analysis to investigate the association between vaccination rates among individuals aged 65 years and older, and pharmacist administration of vaccines. In states in which pharmacists are permitted to administer influenza vaccine, there was a significantly higher ($P < 0.01$) influenza vaccination rate in this subpopulation. The authors concluded that legislation permitting pharmacists to vaccinate increased influenza vaccination rates for individuals aged 65 years and older [191].

Implications for Ireland

The administration of influenza vaccination by pharmacists may impact cost-effectiveness in Ireland, due to some peculiar features of pharmacist care. Pharmacists tend to interact with patients more frequently than other clinicians, as many patients collect a prescription from a pharmacy on a monthly basis [197]. Consequently, pharmacists may be well placed to increase vaccination rates. This is not a direct consequence of the skills of pharmacists, but it is an indirect result of the pharmacist's role in dispensing prescriptions in the community. In addition, differences in reimbursement structures between pharmacists and physicians may modulate cost-effectiveness. The primary objective of this paper is to assess the impact of pharmacists on vaccination rates, and a secondary goal is to assess the cost-effectiveness of pharmacist-led vaccination in Ireland, as detailed in the following chapter.

Independent of skill mix, the cost-effectiveness of vaccination is mediated by local epidemiological trends, referral and hospitalisation patterns, and input prices such as vaccines and staffing. Changes in vaccination rates may exert non-linear effects on infection prevention and on cost-effectiveness, due to indirect (herd immunity) consequences of vaccination, and modelling of pharmacist vaccination must consider these effects.

To address these factors, a multi-year study is necessary to model annual vari-

ability. This paper evaluates data from Ireland over a seven year period, from 2005 to 2011. This period encompasses outbreaks of both seasonal and pandemic influenza, and generates an expected cost-effectiveness of pharmacist vaccination that accounts for non-linear effects and annual variability. The analysis uses primary data on health care utilisation, costs and epidemiological trends, and includes a critical appraisal of the published literature on vaccine effectiveness and cost-effectiveness.

This research question is important due to the significant clinical and economic burden of influenza in industrialised and developing countries [109, 110, 186]. In addition, vaccination programmes to prevent influenza are costly [121]. The administration of vaccines by pharmacists may impact the vaccination rate and the unit cost of vaccination, but research is required to elucidate the effects in the Irish context. It is important to increase our understanding of the impact of mechanisms to increase vaccination of at-risk individuals, and of the relative cost-effectiveness of alternative skill mix models. This can guide the allocation of scarce resources. Moreover, an assessment of the cost-effectiveness of changes to skill mix is timely, as a quite recent, rigorous analysis casts doubt on the perception of influenza vaccine as having high clinical effectiveness. It is important to fathom the economic implications of these revised estimates of clinical effectiveness on administration of vaccine by pharmacists.

6.2 The clinical effectiveness of influenza vaccination

In the United States of America (USA), according to one estimate, influenza vaccination prevented from 1.1 (2006 - 2007 season) to 5 million cases of influenza per year (2010 - 2011 season) between 2006 and 2011. The number of hospitalisations avoided ranged from 7,700 to 40,400. The highest prevented fraction, in 2010 - 2011, occurred due to an expansion of vaccination following the influenza pandemic [198]. Yet there is significant uncertainty in relation to estimates of the incidence of influenza, its clinical complications, clinical effectiveness, and cost-effectiveness [184, 186, 199–201]. In this section I shall discuss six areas of

uncertainty relating to the effectiveness of influenza vaccine.

The first issue is an insufficient number of randomised controlled trials on which to determine the effectiveness and efficacy of influenza vaccination. For instance, despite a longstanding recommendation to vaccinate all people over 65 years, this practice is not underpinned by robust evidence. These recommendations are based on extrapolations from trials that reported high levels of effectiveness in healthy, young adults. Randomised, placebo-controlled trials are typically considered unethical in elderly populations, due in part to the high burden of influenza related morbidity and mortality in this subpopulation. Many studies examining the effect of vaccination in elderly patients have been observational studies.

There are significant gaps in the evidence base for various subpopulations. Clinical efficacy has not been demonstrated in children younger than two years and in institutionalised elderly people. In young children, the humoral response induced by the inactivated vaccine may be inadequate and may decline quickly, leading to reduced effectiveness [202]. In Ireland, pharmacists administer influenza vaccine to individuals aged 18 years and older.

Although 90% of mortality linked to seasonal influenza occurs in patients aged over 65 years, this is the age group for whom data to support efficacy or effectiveness is the most scant [183]. Of the ten randomised controlled trials (RCTs) of trivalent inactivated vaccine, all were confined to the 18-65 year age groups, while all of the ten RCTs of live attenuated influenza vaccine were confined to patients aged between six months and seven years [183]. A Cochrane systematic review found that evidence from RCTs in elderly patients has been scant and poorly reported. In a mixed population of elderly, the effectiveness and efficacy of vaccination were 41% and 58% respectively [203].

After the application of stringent eligibility criteria, Osterholm et al. found large gaps in the evidence base for certain age groups regarding the efficacy of TIV and LAIV. There were no RCTs demonstrating efficacy of TIV among people aged 65 years or older, or from two to seventeen years. For LAIV, there were no RCTs demonstrating efficacy for people aged 8 to 59 years [183].

In healthy adults, some studies have reported the effectiveness of seasonal influenza vaccines at around 70-90% when the vaccine is well matched to circulating strains [204, 205]. But in their more stringent analysis, Osterholm et al. found this

level of effectiveness only among children under seven years following the LAIV vaccine. The effectiveness for healthy adults was around 59% [183].

The second issue is that observational studies of influenza vaccination are vulnerable to extensive confounding, as vaccination is more likely among healthier older people than their severely ill peers [206]. Some studies have erroneously estimated the relative risk reduction for all-cause mortality following influenza vaccination at around 40-50%. This is implausible as influenza probably causes less than 10% of mortality even during winter months [207].

Logistic regression techniques appear to overstate the effect of influenza vaccination, despite adjustment for confounders. A Canadian study using regression analysis reported an adjusted odds ratio of 0.67 for all-cause mortality in vaccinated versus unvaccinated elderly people during the influenza season. By contrast, instrumental variable analysis, a method which seeks to control for unobserved confounders by uncovering natural variation that mimics the process of randomisation, yielded a non-statistically significant odds ratio of 0.94. The latter, more conservative estimate may be a more plausible reflection of vaccination's effects [207]. In general, if a valid instrument is found that naturally randomises a subset of patients to an intervention, this may improve the internal validity of observational analysis [208].

A third issue is that systematic reviews find disparities between vaccination's "effectivenes" and "efficacy" [202]. One review found that efficacy, the reduction in laboratory-confirmed influenza cases, was 73% (44%) in adults if the vaccine matched (did not match) the circulating influenza strains. Effectiveness, defined as the reduction in influenza-like illness cases, was more modest at 30% even when vaccines matched circulating strains [203, 209]. These terms are not defined uniformly in the literature. For the empirical component of this study we use the term effectiveness in quantifying the reduction in influenza related illness in Ireland.

A fourth issue is the varying sensitivity of laboratory methods to detect influenza infection. This can bias the perceived effectiveness of vaccination. Most studies use a serologically-confirmed endpoint, but this method under-counts influenza cases among patients vaccinated with live attenuated influenza vaccine (LAIV). This leads to exaggeration of vaccine effectiveness [183, 210]. Osterholm

et al. restricted their meta-analysis to studies using a more robust test for influenza infection (reverse-transcriptase polymerase chain reaction, or viral culture confirmation), and estimated vaccine effectiveness to be 59% for healthy adults aged 18-65 years (2012). This is at least 11% less than the more commonly cited estimate of 70-90% effectiveness [211].

A fifth issue is that different statistical models of influenza transmission may lead to different estimates of effectiveness. A key choice is whether to adopt dynamic or static modelling. Dynamic modelling quantifies indirect, herd immunity benefits of influenza vaccination, conceptualised in the economic literature as a "positive externality". In essence, the benefits of vaccination are not restricted to its recipients: if the recipient had not undergone vaccination, they may have transmitted the infection to other individuals. A person is less likely to contract influenza when those around them have been vaccinated. For instance, "cocooning" is a technique whereby high-risk individuals for whom vaccination is contraindicated (such as infants younger than six months) are protected by vaccinating their family members and carers [36]. Static models do not quantify these indirect effects. In this thesis paper, I implement both dynamic and static models of transmission, to calculate the cost-effectiveness of pharmacist-administered influenza vaccination, and I compare the results.

Infected children are considered likely to infect a relatively high number of people. Consequently, indirect effects are most pronounced when vaccinating children, and individuals in this subpopulation are sometimes characterised as "super spreaders". One study found that vaccination prevented a mean of 0.39 infections per dose, and 1.74 mortalities per 1,000 doses, during 14 influenza seasons in England and Wales. Extending the programme to high transmitters in the 5 to 16 year old age group would enhance efficiency, resulting in aggregate prevention of 0.70 infections per dose and 1.95 mortalities per 1,000 doses. By contrast, targeting 50 to 64 year olds (i.e. the next subpopulation most at risk) would prevent an aggregate of only 0.43 infections per dose and 1.77 mortalities per 1,000 doses [212]. Another study found that the indirect, "herd immunity" effect was greater than the direct effect of influenza vaccination [213]. This adds to the evidence base characterising children as important recipients of influenza vaccination.

Despite these possible benefits, it is potentially difficult to increase the vacci-

nation rate among children aged over six years. This age group does not suffer significantly from influenza, and parents may be reluctant to allow their children to undergo vaccination to benefit other people [117, 214]. Pharmacists in Ireland must obtain the signature of a parent or guardian before vaccinating a child under the age of 16 years [113].

There may be other limitations to the "super spreader" vaccination strategy. Arguably, the benefits of increased vaccination of "super spreader" individuals may be counteracted by behavioural responses in non-super spreader subpopulations, who in response may become less likely to undergo vaccination. In addition, the rate of vaccine failures among super spreaders may be higher than is typically acknowledged, because of their relatively frequent exposure to infected individuals [215].

Dynamic models are typically expressed as a set of differential equations. This method views time as a continuous variable, rather than as divided into distinct time periods. Although a continuous model may enhance accuracy, it also increases the computational burden. Consequently, differential equations are often approximated into discrete rather than continuous models [216–220].

In addition, dynamic models require data on infection rates, rather than on the use of services, which inhibits their wider use [212]. In an empirical analysis (Chapter 7) I adopt the discrete time period approach, and I assume that the rate of GP consultations for influenza like illness is equivalent to the rate of influenza infection. This is an approximation of the true influenza rate, as some patients with influenza like illness may not have influenza, while some patients with influenza may not seek clinical care. These two countervailing sources of inaccuracy may offset each other. In the absence of data on the true rate of influenza illness, this approximation is an appropriate approach.

The sixth issue is quantification of the loss of quality adjusted life years (QALYs) due to influenza related morbidity and mortality. One review found that derivation and application of QALYs in the published literature was generally poor. Studies of higher methodological quality tended to derive age-adjusted utility weights from a multi-attribute utility instrument [221]. Most models do not account for the QALY impact of adverse effects of vaccination, however evidence suggests that serious adverse effects are rare [213]. These include oculo-respiratory syndrome and

Guillain-Barre syndrome, the latter estimated at 1.6 cases per 1 million additional vaccinations based on three cohort studies [209]. Adverse effects of a more minor nature include local tenderness and pain, skin rash, and myalgia.

In the absence of data to directly measure influenza incidence, it may be necessary to assume a relationship between utilisation of health services and influenza incidence. By contrast, in the study of Aballea et al., data were collected on the rate of laboratory confirmed influenza, but not on healthcare utilisation. This study was restricted to the 50 to 64 year old population. It was assumed that the relative rate reduction for laboratory-confirmed infection equalled the relative reduction in hospitalisation and all-cause mortality [190]. This approach has been criticised. First, its outcome was non-specific to influenza. Second, the age group was criticised as inappropriate, as the vaccine effectiveness estimates were derived from a meta-analysis of vaccination in mostly institutionalised elderly people whose median age was around 80 years. This thesis paper uses a variety of estimates of vaccine effectiveness to test the sensitivity of the results to this assumption.

Vaccine effectiveness may differ for different outcomes [221]. Rigorous evidence is scant on the impact of vaccination on hospitalisation and mortality arising from laboratory-confirmed influenza in healthy adults. Consequently, it is defensible to apply the estimates of vaccine effectiveness against laboratory-confirmed influenza to the more serious outcomes of hospitalisation and mortality due to laboratory-confirmed influenza [221]. This approach was adopted in a number of studies [222–224]. However, applying this estimate to non-specific outcomes, such as the reduction of all-cause mortality, appears less defensible [221]. Another study suggested that a multi-serotype model would enhance the predictive accuracy of seasonal influenza models [225].

Most studies have not considered that average life expectancy may have been lower for people who die from influenza illness, even if they had not contracted influenza [221]. Therefore, cost-effectiveness may be exaggerated.

Of note, different studies have used a wide range of estimates of vaccine effectiveness for each outcome. This ranges from prevention of 16% of medically attended influenza like illness cases, to the prevention of 74% of hospitalisations or mortalities arising from influenza, drawing on the Cochrane reviews of influenza vaccination in healthy adults [209]. The Cochrane Review reported effectiveness

levels against laboratory-confirmed influenza, but not against hospitalisation or mortality arising from influenza.

In the studies that extrapolated vaccine effectiveness of 69 - 74% against influenza illness to reductions in mortality, the mortality rate from influenza ranged from 4.9 per 100,000 for healthy patients [224] to 16.6 per 100,000 in high-risk patients [223]. One study used a quite high mortality rate of 14.6 per 100,000 but a lower effectiveness of 43% [226]. This variability in the literature underscores the importance of varying the parameters in a range of sensitivity analyses, as I shall do in this thesis paper.

There is significant variation in health related quality of life (HRQoL) across different age groups and socioeconomic strata, as well as differences in life expectancy. One study assessed individuals' willingness to pay for influenza health-related quality of life, and found that respondents were more likely to choose to prevent uncomplicated influenza illness in children than in working-age adults [227]. An ideal study would account for variation in HRQoL and life expectancy when estimating the loss in QALYs arising from influenza [228], but this is dependent on rich data. In this study I adopt an estimate of the mean loss in QALYs per influenza case.

6.3 Evidence on the economic effects of influenza vaccination

The effectiveness of influenza vaccination is weaker than vaccination to protect against conditions such as measles, mumps and rubella. Nonetheless, influenza vaccination is commonly estimated to be cost-effective [36]. A rich stream of literature assesses the economic consequences of influenza vaccination, but there remain gaps in the evidence base. One limitation is the potentially erroneous estimate of effectiveness in many studies, while other limitations relate to limited data on costs, and the assumptions of the cost analysis. There has been scant analysis of the relative cost-effectiveness of different skill mix arrangements in influenza vaccination. This section reviews evidence on the cost-effectiveness of influenza vaccination, and shall inform the subsequent analysis of the expanded

role for pharmacists.

6.3.1 Cost of illness

The economic burden of influenza is consistently reported to be substantial across high-income countries. In the USA, the annual cost of seasonal influenza illness may be $US71 to 167 billion from a societal perspective [229]. In some countries, indirect (productivity) costs such as absenteeism can be 5 - 10 times greater than direct medical costs, amounting to US$ 10-15 billion per year across the USA [121, 230].

A recent review by Peasah et al. examined the costs and cost-effectiveness of influenza vaccination globally. The review uncovered 140 studies considering the cost of seasonal influenza illness, or cost-effectiveness or cost-benefit of influenza vaccination. In 101 studies a cost-effectiveness or cost-benefit analysis was undertaken, while 39 studies analyzed the cost-of-illness [186]. In this review, 118 studies were conducted in high income settings, and the remainder in upper-middle income settings.

The total direct and indirect cost of influenza per capita ranged from $27 to $52 in European countries, from $45 to $63 in the USA, and was $1 in Thailand and $3 in Hong Kong. The European countries included in this study were Norway, France, Spain and Germany. As a percentage of Gross Domestic Product the total cost ranged from 0.01% in Hong Kong, to 0.04% to 0.13% in European countries, and to 0.14% in the USA. The direct medical costs of influenza illness were less than $10 per capita in all countries, with the exception of Spain, Japan and the USA ($21, $44, and $39 respectively) [186].

6.3.2 Value for money of influenza vaccination

In the review of Peasah et al., of the 51 cost-effectiveness studies that contained sufficient data, influenza vaccination was reported to be cost saving in 22 studies (12 in children, 2 in pregnant women, and 8 in older adults). The review examined a number of cost per outcome ratios: cost-effectiveness ratios, cost-benefit ratios, cost per QALY, and cost per DALY. In thirteen of these studies, the ratio per outcome was under $10,000 (equivalent to a cost-benefit ratio of around one), while

for another 13 studies the ratio was between $10,000 and $50,000 (equivalent to a cost-benefit ratio of below six). In three studies the estimated ratio exceeded $50,000. It is difficult to generalise these findings due to differences in methodology [186]. There is pressing need for standardised approaches to cost-effectiveness analysis of influenza vaccination, in particular for the risk groups recommended by the World Health Organisation.

Cost-effectiveness estimates are often highly sensitive to the underlying assumptions. For instance, a Belgian study found influenza vaccination to be cost-effective for pregnant women (€6,589 per QALY) and health care workers (€24,096 per QALY), but the results depended heavily on assumptions such as the impact on the neonate's health and the number of preventable secondary infections, respectively. For individuals with underlying illness, vaccination appeared highly cost-effective for individuals aged over 50 years and was borderline cost-effective for younger people, and these results were influenced by factors such as relative life expectancy [231].

The economic implications of vaccination may differ between subpopulations. For instance, two thirds of the studies in children reported net cost savings from vaccination (12 of 18), compared to a third of studies in older adults (8 of 27), and a third of studies in pregnant women (2 of 6) [186].

Vaccination of individuals under the age of 18 years

The vaccination of children against influenza has been recommended in the UK and is under consideration in other countries [232]. Vaccinating people under the age of 18 years may be an appropriate policy option, because of their perceived role as "super spreaders" of influenza virus. As noted, two-thirds of studies in children reported net cost savings from vaccination (12 of 18) in the review by Peasah et al (2013). The age profile of recipients of vaccination from pharmacists compared to other healthcare professionals, can be an important determinant of cost-effectiveness.

In a review of 20 articles assessing the economics of influenza vaccination in this population, the conclusions were mostly favourable for vaccination. However, the literature suffered from various weaknesses. Many studies applied a societal

perspective that included productivity losses, which deviates from the reference case for economic evaluation in numerous countries. Some analyses were based on single-year epidemiological studies, and these may have poor generalisability due to annual variation in virus transmissibility, virulence, prior immunity and vaccine match. With the exception of a single study, no analyses adopted a dynamic transmission model that fully incorporated indirect, herd immunity effects [233].

The seasonal variability of influenza may produce counter-intuitive results, as low transmission seasons are easier to control via vaccination but result in fewer benefits. In a study of vaccination in Australian schoolchildren, the net economic effect amounted to savings of A$56 million when productivity gains were included, but a loss of A$19 million when excluded. From the health system perspective, the ICER was $3,500 per QALY saved. As most of the estimated cost savings arose from productivity gains for parents or caregivers, the study perspective exerted an important effect on ICER values [232].

The methodological approach is a key determinant of measured cost-effectiveness. Dynamic models are particularly helpful for capturing the population-wide implications of vaccination targeted at children. As most studies of vaccination in people less than 18 years of age adopted a static modeling approach, the beneficial effects of vaccinating this subpopulation may have been frequently under-estimated [233].

Vaccination of healthy, working adults

For healthy working adults there is an incentive to minimise the number of days missed from work. A review of influenza vaccination for healthy working adults in the USA uncovered ten economic evaluations, of which nine were judged to use credible methodology. Of these, eight studies uncovered favourable economic effects, implying the economic benefits of vaccination outweighed the costs, or that value for money fell within acceptable limits [234]. However, despite the high productivity losses associated with influenza illness, vaccinating workers may result in only 0.13 fewer work days lost per person [235].

Influenza vaccination in England

Although there are important differences between the health systems in England and Ireland, the patterns of influenza morbidity and treatment in England may be relatively comparable to Ireland. The annual vaccination programme in England targets individuals of 65 years or above and those in clinical risk groups. Around 20% of the population is vaccinated each year (74% of 65+, 13% of 15 to 65 years, and 3% of under 15s), leading to significant direct and indirect protection.

In the absence of vaccination, the incidence of influenza-attributable ILI may range from a median of 17% in 15-24 year olds, to 3% in 65+ year olds, over a single season [236]. Vaccination may prevent between 1,000 and 2,700 cases of influenza per 100,000 people each year. When the vaccine is well-matched to circulating strains, the national programme may lower the incidence of laboratory-confirmed influenza from 8.2% to 5.9%. Of this reduction, 56% to 73% would arise from indirect protection. The vaccine is likely to be cost-effective unless the outbreak severity is mild and the vaccine is poorly matched to the circulating strain. This study assumed that immunity arose two weeks after vaccination, and that 10% of people who contract ILI would consult a primary care physician [236], the latter based on the results of a survey from the 2010 - 2011 season [199].

When the vaccine was poorly matched to circulating strains, the assumed efficacy was lowered by 40% in accordance with the results of a systematic review [209]. The number of mortalities for patients aged over 65 years was only 179 based on a study of the GPRD database [200], whereas the numbers from another prominent study suggest that influenza A results in 9,200 deaths annually in this age group [201], highlighting important variability in the assumptions underpinning economic analyses.

6.3.3 Economic effects of complementary interventions

A number of studies have examined the economic effects of interventions that are complementary to influenza vaccination. Social distancing can involves strategies such as school closure, workplace reduction (non-attendance), and other interventions to reduce community contact between individuals (e.g. cancellation of public gatherings). According to one analysis, the most cost-effective interventions to

constrain an influenza pandemic would combine sustained social distancing with prescription of antiviral agents [237].

In another study it was shown that for severe pandemics of category 3 or above, the lowest total cost of any strategy was a combination of antiviral treatment and prophylaxis, sustained community contact reduction, and extended school closure. At a cost of $1,584 per person at category 5, this strategy reduced the attack rate to 5%. In low severity pandemics, costs of influenza arise predominantly from productivity losses induced by illness and social distancing interventions. For higher severity pandemics, costs arise mostly due to healthcare costs and productivity losses due to mortality. Social distancing is considered inappropriate for low severity pandemics because of the associated cost and societal disruption [238].

A limitation that pervades much of the literature on economic evaluation is the short-term perspective on costs. For example, an intervention may lower mortality in the short-term, but the additional surviving patients may incur substantial health care costs in future years. These future costs, which may arise due to increased longevity following an intervention, are rarely modelled in economic evaluation [239, 240]. There have been preliminary efforts, in particular in the Netherlands, to improve modelling of future costs to mitigate this limitation [241].

In the case of influenza, health care costs may be lower for patients who die from influenza-related illness as compared to survivors, *ceteris paribus*, as these patients avoid future costs of health and long term care. A feature of the recent influenza pandemic was its high severity in younger patients relative to elderly patients, in contrast to seasonal influenza. The pattern of future cost implications may fluctuate annually according to variability in the distribution and severity of disease by age. In this thesis, an ideal analysis would incorporate future costs of unrelated and related clinical conditions into an economic model, but this is precluded by data constraints.

Another study assessed the interplay between the timing of interventions, vaccine availability, and the dynamics of a pandemic. The study assumed a gap of six months between the onset of an influenza pandemic and the first availability of a vaccine matched to the circulating strain. For each pandemic scenario, vaccination-only strategies were not cost-effective as vaccination costs were sub-

stantial and saved few lives [242].

For moderate and severe pandemics, a cost-effective strategy was vaccination in conjunction with sustained social distancing, antiviral treatment, and antiviral prophylaxis. This combination could save lives and lower the aggregate cost of a pandemic. In the absence of vaccination, a combination of social distancing and antiviral medications was significantly less effective, as influenza incidence would rebound when social distancing interventions were tapered. Implementing social distancing until the initiation of a vaccination campaign would significantly reduce attack rates and total costs [242]. This thesis paper did not consider the impact of interventions that are complementary to changes in skill mix. These complementary interventions are not considered to have played a significant role in containing influenza outbreaks during the study period [110].

Chapter 7

Aims and methods of the Influenza study

7.1 Aims

The aim of this paper is to model the clinical effectiveness and cost-effectiveness of pharmacist provision of influenza vaccination in Ireland, as a case study of a change in skill mix arrangements. The objectives are to:

1. Review the literature on the evidence of the clinical effectiveness and cost-effectiveness of influenza vaccination, and evidence on the role of pharmacists in providing influenza vaccination
2. Quantify the direct and indirect costs of influenza illness in Ireland
3. Quantify the costs of administration of the influenza vaccine by pharmacists and by physicians in Ireland
4. Estimate the impact on vaccine uptake of pharmacist provision of the influenza vaccine in Ireland
5. Quantify the cost-effectiveness of influenza vaccination by pharmacists in Ireland

Type of data	Source
Vaccination rate	Primary Care Reimbursement Service
Hospitalizations	Hospital Inpatient Enquiry Scheme, Economic and Social Research Institute
Price of hospitalizations	National Casemix Programme, Health Service Executive
Influenza like illness consultations	Irish College of General Practitioners
Pharmaceuticals	Primary Care Reimbursement Service

Table 7.1: Overview of Primary Data Sources

7.2 Methodology

7.2.1 Datasets

Vaccination data

I obtained data on influenza vaccinations in GP practices from 2005 - 2011 and in community pharmacies during 2010 and 2011 from the Primary Care Reimbursement Service (PCRS). Data are subdivided into age categories. There are no other variables pertinent to individuals' risk of influenza complications, such as the presence of chronic illness. Pharmacists are legally required to notify the PCRS of each vaccination, therefore this dataset should capture all pharmacy vaccinations, however this did not necessarily occur in a reliable manner during 2010 and 2011. In addition, pharmacy vaccination data were obtained from a chain of Irish pharmacies for the 2010 - 2011 influenza season, to check the comprehensiveness of the PCRS data source. For GP vaccinations, PCRS data are limited to patients who possess a medical card or GP visit card, therefore it overlooks patients who pay out of pocket for consultations.

Hospital utilisation data

I obtained data on hospital discharges data for all acute hospitals in Ireland over the years 2005 - 2011, which was routinely collected by the Hospital Inpatient

Enquiry Scheme of the Economic and Social Research Institute. This includes all cardiac and respiratory discharges (codes I00-99 J00-99 of the International Classification of Disease system).

I obtained the following information for each discharge:

- Patient age group (5 year bands)
- Gender
- Medical card
- Public/ private status
- Length of hospital stay
- Clinical diagnosis codes
- Australian-Refined Diagnosis Related Group
- Days in Intensive Care Unit
- Discharge Destination (Home, Nursing Home/Convalescent Home/Hospice, Transfer to another Hospital, Died, Other)

Influenza like illness primary care consultations data

I obtained influenza-like-illness (ILI) GP consultation rates per 100,000 people for each year from 2000 - 2011 from the Irish College of General Practitioners (ICGP). These data were obtained at the aggregate population level and also for the following age bands: 0-4, 5-14, 15-64, and 65+ years [243]. These data are gathered by sentinel GP practices whose population base represents around 4% of the Irish population.

Pharmaceutical utilisation data

I gathered data on monthly prescribing of oseltamivir (Tamiflu) for the years 2005 to 2011 from the PCRS. Data were categorised according to the route of administration, dosage, and packet size. The use of Tamiflu is restricted to treatment and

prophylaxis of influenza. Another antiviral indicated for influenza is Zanamavir, but according to PCRS data this was not dispensed in Ireland during 2005-2011. These data are limited to primary care. The costs of hospital prescribing are incorporated into the DRG costs of hospitalisation, therefore I do not explicitly calculate these costs.

7.2.2 Quantitative Analysis

The quantitative analysis consists of two steps. The first step quantifies the economic cost of influenza in Ireland. The second estimates the incremental cost-effectiveness of influenza vaccination in Ireland, and the impact of pharmacist administration on vaccination rates.

Step 1: Quantifying the economic cost of influenza illness in Ireland

The analysis quantifies four categories of influenza-associated costs: hospital inpatient costs, attendances to GPs (i.e. primary care physicians) relating to influenza like illness symptoms, the costs of antiviral and symptom-relieving pharmaceuticals, and the indirect costs of days missed from work due to influenza like illness. Each category of cost was quantified according to the methods specified by the national guidelines on economic evaluation in Ireland [244].

Hospital costs For hospital costs, I counted patients hospitalised for whom at least one of the diagnostic codes (using the ICD-10 classification) related to influenza (ICD codes J10-J11) between 2005 and 2011. I attached a unit cost to each admission based on its assigned diagnosis related group (DRG). I subdivided hospitalisations according to whether influenza was a primary or secondary diagnosis.

General practitioner costs I used a nationally representative dataset of ILI consultations to calculate the aggregate number of consultations in Ireland. These data are collected by sentinel GP practices in collaboration with the ICGP and Health Protection Surveillance Centre. I also obtained the population of people in Ireland in each age category from national census data for the years 2002, 2006

and 2011 [245], and used linear interpolation to calculate these populations for 2005, and 2007 - 2010. I applied the ILI consultation rates per 100,000 population for each week to the national population in each age group, to extrapolate the number of consultations in sentinel practices to the national level. These figures include private patients who pay out-of-pocket and public patients for whom GPs receive a capitated government payment. I assumed a unit cost per consultation of €50 based on published data [25].

Pharmaceutical costs In terms of pharmaceuticals, the key cost driver is antiviral medication (Tamiflu). I calculated this for the primary care sector based on data from the PCRS in 2011 prices.

Various assumptions have been used to quantify the costs of symptom-relieving pharmaceuticals. Xue et al assumed that a mean of one pack of symptom-relieving medicines was purchased per patient, and varied this in the sensitivity analysis, while excluding Value Added Tax from cost estimates [246]. By contrast, Aballea et al. did not incorporate the cost of over-the-counter self-medication when modelling the impact of antiviral medication in preventing complications and absence from work [190]. I assumed that patients purchased a mean of one packet of symptom-relieving medication per episode of ILI.

The indirect cost of productivity losses I assumed that productivity losses were limited to patients aged 18 to 64, based on the age structure of the Irish workforce. International evidence suggests that lost productivity for this age group amounts to approximately 1.3 days for each episode of ILI [190, 247, 248]. This finding was consistent across France, Germany, Italy and the USA, but the losses were lower in the middle-income setting of Brazil. I used the average daily industrial wage in Ireland for 2011 (€137.53) as a surrogate measure of the economic cost of each day of lost productivity [249].

Step 2: The cost-effectiveness of influenza vaccination

The price of vaccine administration was used as a surrogate for cost. The results were expressed in 2011 values. For private patients I estimated the out-of-pocket

price, while for patients enrolled on government programmes I adopted the price paid by the public health service.

To quantify the incremental cost-effectiveness of influenza vaccination, I considered the cost of vaccine administration, the cost of influenza illness, the effect of vaccination on influenza's incidence, and the impact of the novel pharmacist role on vaccination rates and direct costs. I constructed static models and dynamic models, to illustrate the net impact of incorporating herd immunity effects. In the base case, I used a vaccination rate of zero as the counterfactual, to estimate the value for money of the influenza programme in Ireland each year.

I modelled the transmission of influenza virus using a susceptible - infectious - recovered model with an additional compartment for individuals with immunity conferred by vaccination. Individuals for whom vaccination does not confer immunity remained in the susceptible compartment. Based on data on strains of circulating influenza virus from the National Virus Reference Laboratory each year from 2005 to 2011, I assumed that vaccines were well-matched to influenza each year.

I based the estimates of vaccination's clinical effectiveness on the stringent methodology of Osterholm et al. [183], and used this to estimate the potential reduction in morbidity, mortality and health care costs resulting from increased vaccination rates [250]. I assumed that vaccine effectiveness was consistent from year to year.

I calculated cost-effectiveness from a societal perspective. Although the clinical and demographic characteristics of vaccine recipients may differ between pharmacists and other providers, available data were not sufficiently detailed to incorporate into the model. I compared vaccination rates for 2010 and 2011 against the projected rate based on the trend in 2005 - 2009, to gauge the effect of the novel pharmacist role on uptake levels. All statistical analysis was conducted using STATA SE 12.0 (StataCorp).

The value for money of influenza vaccine was expressed in three ways. First, the results were expressed as cost-effectiveness ratios, the ratio of incremental costs incurred to the change in QALYs. The QALY metric is an effort to adjust the number of years of life to reflect health-related quality of life. For example, two years at an estimated "50% health" would be equivalent to one year at "100%

health". As noted in Chapter 4, the QALY has a number of limitations, such as inferior sensitivity relative to disease-specific measures for a range of clinical conditions. Nonetheless, this is a widely used approach that enables comparison across different disease areas to inform resource allocation decisions.

Second, the net monetary benefit is used to express the incremental cost (or benefit) of the intervention in entirely monetary terms. This involves calculation of the net financial impact (in monetary terms) and the net health impact (expressed in QALYs). The net health impact is then converted to a monetary amount based on the threshold that specifies an acceptable range of cost-effectiveness. For example, if the threshold is €20,000 per QALY, and the incremental effect of the intervention is an increase of ten QALYs, this equates to €200,000 in monetary terms. If the incremental financial cost of the intervention is €100,000, this results in a net monetary benefit of €100,000.

Third, the net health benefit was used to express the impact of the intervention in terms of health outcomes. The monetary impact is translated into a quantum of QALYs, using the same threshold as in the net monetary benefit. In the previous example, the cost of €100,000 would be translated into five QALYs, as this represents the predicted loss of QALYs elsewhere in the health system if €100,000 was spent on the intervention of interest and was displaced from other interventions. In this case the net health benefit would be five QALYs [251].

Quality Adjusted Life Years Lavelle et al. calculated the loss of quality adjusted life years (QALYs) for episodes of influenza related illness during a pandemic outbreak within the period 2005 - 2011, using a time trade off technique and a sample of over 1,000 survey respondents. The mean QALY loss for uncomplicated pH1N1 illness for all ages was 0.0207 [252]. I assumed a loss of 0.0207 QALYs for each case of ILI in this study.

To calculate the loss of QALYs due to influenza-related mortality, I used the findings of Pitman et al. to estimate the mortality rate for patients with ILI who present to a GP, and for patients hospitalised with an ICD diagnosis of influenza [201], in the primary analysis. This provided the mortality rates for three separate age groups: zero to 14 years, 15 to 64 years, and 65 years and older. I assumed that every decedent's age corresponded to the mean age of all patients in that

age group hospitalised with an influenza diagnosis in that influenza season. I estimated the loss in life years of each decedent based on their age and their life expectancy (sourced from Irish life tables), and I integrated this with EQ-5D quality of life norms from the United Kingdom to quantify the loss in QALYs. The EQ-5D population norm values decrease every ten years between the ages of 25 to 75 years [228], therefore a higher QALY value was attached to years of life lost at an earlier age. I discounted future QALYs at the standard rate for economic evaluations in Ireland [244].

Sensitivity Analysis I tested the robustness of the findings by systematically varying the values of key parameters across plausible ranges. I constructed nine scenarios using static infectious disease modelling as follows.

- Scenario 1: Cost effectiveness comparator: 100% vaccination by the first week of the season
- Scenario 2: Cost effectiveness comparator: 75% vaccination by the first week of the season
- Scenario 3: Cost effectiveness comparator: 75% vaccination by the end of the year
- Scenario 4: Cost effectiveness comparator: 75% vaccination by the first week of the season and lower vaccine effectiveness
- Scenario 5: Cost effectiveness: 75% vaccination by the first week of the season and higher vaccine effectiveness
- Scenario 6: Cost effectiveness: 75% vaccination by the first week of the season, 15 euro per vaccination
- Scenario 7: Cost effectiveness: 75% vaccination by the first week of the season, 50 euro per vaccination
- Scenario 8: Increased number of work days lost due to influenza like illness among adults of working age

- Scenario 9: Reduced influenza associated mortality rate based on studies from the United Kingdom. In the GPRD study the mortality rate was 0.19% for influenza patients during the 30 days after diagnosis. For control patients the mortality rate was 0.06%. Consequently the mortality rate attributable to influenza appears to have been 0.13% per ILI case. The study also presented the mortality rates stratified according to age group.For influenza patients aged 0-14 years of age the mortality rate was 0.0048%, for 15-64 years it was 0.048%, and for patients aged 65 and older it was 10.92%.

The rationale for these nine scenarios is as follows. Scenario 1 assumes 100% vaccination levels, in order to model the impact of reaching the upper bound of vaccination coverage. Scenario 2 assumes 75% vaccination levels, to reflect the World Health Organisation's target vaccination level of 75% of the elderly population. Scenario 3 assesses the importance of the timing of vaccination. The administration of influenza vaccine sooner in the season should prevent more cases of influenza, *ceteris paribus*, therefore this scenario assumes an identical aggregate number of vaccinations as Scenario 2, but the vaccinations are spread evenly across the influenza season rather than occurring in Week 1.

According to the literature, key determinants of cost-effectiveness are vaccine effectiveness, mortality rates, and the price of vaccination. In addition, a majority of influenza-related costs may arise due to indirect costs (productivity losses), and significant uncertainty surrounds the estimation of this parameter [186]. Consequently, scenarios 4-9 vary the values of these four parameters across plausible ranges.

The modification of vaccine effectiveness is based on the international evidence base. Effectiveness of 0.70 is adopted in Scenario 5 (i.e. prevention of 7 out of 10 cases), while a value of 0.29 is adopted in Scenario 4 as a lower bound (based on the analysis of Aballea et al. [190]). Modelling of the price of vaccination adopts the pharmacist payment rate (€15) as a lower bound, while the payment rate by private patients to GPs serves as an upper bound (€50), in Scenarios 6 and 7 respectively. Pandemic influenza may exert a disproportionate impact on individuals of working age, although scant data are available regarding the effect on indirect costs. To explore the effect of an increased burden of influenza

on individuals of working age, the number of working days lost per ILI case was increased from 1.3 to 3.0 in Scenario 8. In Scenario 9, modification of the mortality rate parameter is based on the large-scale GPRD study, as discussed in Section 8.2.3.

I modelled a number of scenarios using dynamic infectious disease modelling, to illustrate the impact of different methodological assumptions regarding influenza transmission. For dynamic modelling the base case scenario involves zero vaccination as the comparator (compared to the "intervention" of the observed vaccination rates from 2005 - 2011). The sensitivity analyses covered the following scenarios: 100% vaccination in week 1 of the season, 75% vaccination by week 1 of the season, higher and lower vaccine effectiveness, a price of €15 and €50 per vaccination, and a reduced mortality rate.

The incidence of influenza in each season is idiosyncratic, widely variable and unpredictable [183]. I modelled the cost-effectiveness of vaccination in past seasons for which data are available, and did not explicitly predict cost-effectiveness in future years. However, as this analysis modelled costs across seven years and compared both pandemic and seasonal influenza outbreaks, these findings can shed light on the likely future cost-effectiveness of influenza vaccination, and can have relevance for future policy-making.

Chapter 8

Results and Discussion

8.1 Results

8.1.1 Part 1: Vaccine uptake

Pharmacy vaccination

The introduction of influenza vaccination by pharmacists during the 2010 - 2011 season coincided with a marked increase in the vaccination rate among people aged 65 years or older from 51.4% to 59.9%. Did vaccination by pharmacists substantively impact vaccination levels? According to the PCRS database, pharmacists administered 1,774 influenza vaccinations during 2011, and pharmacists administered zero vaccinations in each preceding year. During the 2012-2013 influenza season (until 18 February 2013) pharmacists administered 18,358 influenza vaccinations (4.2% of total influenza vaccinations), according to the PCRS dataset. In the 2013-14 influenza season this number increased to 40,908 (6.9% of total influenza vaccinations) [253]. There is a risk that these data for pharmacists omit certain private patients who were not vaccinated under a PCRS scheme, therefore these figures may be biased towards the elderly, chronically ill, and individuals of lower socioeconomic status.

Only a single chain of pharmacies administered influenza vaccinations during the 2010 - 2011 influenza season. Of this chain, 47 pharmacies participated in influenza vaccination. Data supplied by this chain quantifies the total number

of influenza vaccinations administered in pharmacies across Ireland during this season. Between 2 October 2010 and 31 January 2011, these pharmacies administered a total of 4,673 seasonal influenza vaccinations. Consequently, the PCRS database appears only to capture 38% of vaccinations in pharmacies during this period. However, as pharmacy vaccinations account for a small proportion of total vaccinations, this does not significantly impact the cost-effectiveness calculations.

These data indicate that while pharmacists may have contributed to the increased vaccination rate among people aged 65 years and older during the 2010 - 2011 influenza season (see Figure 8.1), the initiation of pharmacist vaccination was not a major factor driving this increase.

During the 2010 - 2011 influenza season, 2,623 of the recipients in pharmacies were female and 2,040 were male. A large majority of recipients (85.6%) were aged under 65 years, around 12.8% were aged 65 years or above, and age was unknown for 1.6% of recipients. Dublin-based pharmacies accounted for 51.4% of vaccinations, while 42.3% of vaccine recipients stated that they resided in Dublin. Pharmacists assessed around 49% of recipients as being at elevated risk of influenza-related complications, and there were two or more risk factors recorded for 4.7% of clients. For 42.1% of recipients, clinical risk status was deemed to be elevated as they were aged over 50 years. The second most common risk factor was chronic respiratory disease, which affected 3.3% of recipients.

Aggregate vaccination levels

During the 2010 - 2011 influenza season, it is estimated that 59.9% of people aged 65 years or above underwent vaccination against influenza. The following season this figure dropped to 56.6%, and 61.7% were vaccinated in the age group 75 years and older. Data from consecutive seasons between 2004 - 2005 and 2011- 2012 are presented in Figure 8.1. During this period the proportion of people who underwent vaccination ranged from 51.4% to 62%. The nadir was the 2009 - 2010 season, followed by an increase of 8.5 percentage points in the following season.

Figure 8.2 presents the total number of influenza vaccinations recorded by the PCRS system for each season between 2005 - 2006 and 2010 - 2011, and Figure D.1 (Appendix D) depicts the number of vaccinations each year from 2005 to 2011.

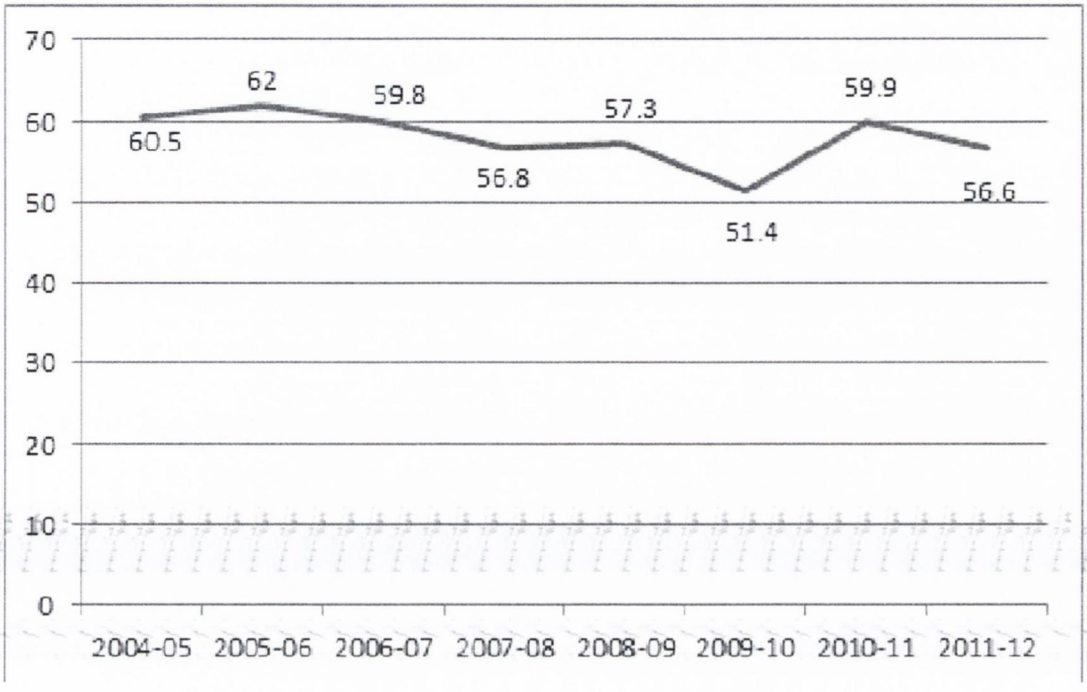

Figure 8.1: Vaccination rate for individuals 65 years and older

Figures 8.2 and D.1 were constructed based on a primary dataset received from the PCRS. Figure 8.1 was constructed based on published data from the HPSC [243]. In each season the vaccination rate has been below the World Health Organisation recommended target of 75% uptake for individuals aged 65 years and older [243].

8.1.2 Part 2: Economic and health burden of influenza illness

The estimation of the incremental impact of pharmacist administered vaccination requires a calculation of the economic and clinical burden of influenza in Ireland, to serve as a foundation for the calculation of the net change. Table 8.1 depicts the breakdown of influenza-related costs for each season between 2005 and 2011. The largest component is indirect costs, which amounted to €30 million in aggregate. Hospital costs are the second largest component at €26 million, while pharmaceutical costs are estimated at €13 million. The total cost of ILI consulta-

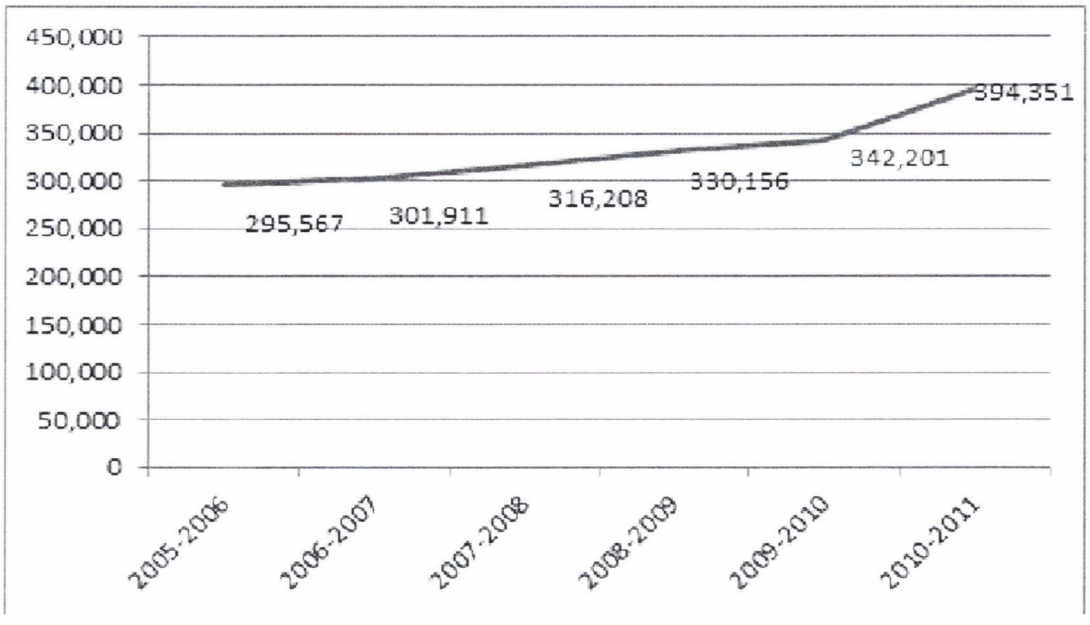

Figure 8.2: Vaccinations per season

tions is estimated at €12.6 million, which is a virtually even split between public (government) costs and private (patient) costs.

The cost associated with influenza fluctuated widely between seasons. The two most costly seasons were 2009 - 2010 and 2010 - 2011 at €22.8 million each, compared to €4.8 million during the 2006 - 2007 influenza season. As noted in the previous chapter, the unit costs of 2011 are applied in each season. Influenza associated costs tend to be significantly lower during the summer months.

Table 8.2 shows that the majority of antiviral pharmaceutical costs, as recorded by the PCRS, are prescribed under the Drug Payment Scheme and the General Medical Services scheme. Less than 1% of spending on antiviral prescriptions was under the Long Term Illness scheme (see Section 8.2 for additional information on these schemes).

According to data from sentinel GP practices, a large majority of ILI consultations in primary care involved patients aged 15 - 64 years. This is shown in Table 8.3. Individuals aged 5 to 14 years comprised the second largest category, followed by individuals aged zero to four years. Consultations for individuals aged 65 years

and older accounted for fewer than 5% of consultations.

Table 8.4 shows the relationship between the estimated number of days of absenteeism from work for each ILI presentation to a GP, and the associated indirect costs (productivity losses). Although the health system does not incur these indirect costs, there is a significant societal burden. The quantum of indirect costs was highest in the 2009 - 2010 and 2010 - 2011 influenza seasons.

Tables 8.5 and 8.6 present the direct costs of ILI consultations from the perspective of government and patients respectively. In each case the costs are concentrated in the 15 to 64 year old age group. It is assumed that all consultation costs for individuals aged 65 years or older are incurred by the third party, public payer. These results are based on data from Table 8.3, which illustrates the relatively large number of consultations among the 15 to 64 year old age group.

Table 8.7 presents the costs of influenza-related hospitalisations by age group. More than 80% of hospitalisation costs related to individuals aged zero to 14 years, while individuals aged 65 years and above accounted for 14% of hospital costs. Table D.1 in Appendix D shows that hospital expenditure was comparable for males (€13.3 million) and females (€13.0 million).

For each hospitalised patient, influenza may be coded as a primary or secondary diagnosis. Of the €26 million in aggregate hospitalisation costs, admissions where influenza was the primary diagnosis accounted for €11.99 million, compared to €14.38 million for influenza coded as a secondary diagnosis (see Table 8.8).

Table 8.9 depicts the estimated number of influenza-related mortalities for each season. As noted in the foregoing chapter, these figures derive from a modelling exercise in which the mortality rate per ILI case for each age group, based on a prominent study from the United Kingdom, was applied to the Irish ILI rates.

Table 8.1: Spending on influenza per season

Influenza Season	Indirect	ILI - Public	ILI - Private	Pharma	Hospital	Total
2005 - 2006	3,345,604	706,693	639,370	370,415	1,269,176	6,331,257
2006 - 2007	2,897,215	560,002	500,321	198,119	637,974	4,793,632
2006 Summer	216,631	42,639	37,055	19,415	396,243	711,983
2007 - 2008	2,944,272	564,374	515,880	292,415	524,638	4,841,578
2007 Summer	176,801	34,157	28,998	26,271	226,669	492,896
2008 - 2009	4,260,363	863,087	756,014	855,888	691,943	7,427,295
2008 Summer	244,362	50,681	44,954	34,765	254,042	628,804
2009 - 2010	6,797,926	1,757,499	1,653,935	4,642,306	8,005,326	22,856,992
2009 Summer	2,974,187	626,909	564,554	2,089,515	2,810,175	9,065,340
2010 - 2011	6,017,616	1,324,262	1,217,185	3,411,633	10,866,924	22,837,621
2010 Summer	311,082	63,894	52,829	1,682,675	570,286	2,680,767
2011 Summer	250,412	48,026	41,334	96,030	120,644	556,446
Total	30,436,471	6,642,222	6,052,430	13,719,447	26,374,040	83,224,610

Source: Tabout.dta

Table 8.2: Antiviral pharmaceuticals: Spending per season and per scheme

	Pharmaceutical spending (Euros)			
Season	**DPS**	**GMS**	**LTI**	**Total**
2005 - 2006	288,590	80,423	1,402	370,415
2006 - 2007	114,069	84,051	0	198,119
2006 Summer	14,326	5,089	0	19,415
2007 - 2008	176,612	115,054	750	292,415
2007 Summer	14,465	11,806	0	26,271
2008 - 2009	550,667	301,998	3,223	855,888
2008 Summer	25,855	8,909	0	34,765
2009 - 2010	1,917,872	2,670,252	54,182	4,642,305
2009 Summer	880,185	1,185,238	24,092	2,089,515
2010 - 2011	1,413,517	1,983,236	14,880	3,411,633
2010 Summer	1,548,202	133,964	509	1,682,675
2011 Summer	40,846	55,184	0	96,030
Total	6,985,205	6,635,204	99,038	13,719,447

Source: Tabout.dta

Table 8.3: ILI Consultations by Age and Season

	Influenza like illness cases				
Influenza Season	**0 to 4 years**	**15 to 64 years**	**5 to 14 years**	**65 years and older**	**Total**
2005 - 2006	1,315	19,907	4,352	1,346	26,920
2006 - 2007	1,094	17,239	1,678	1,193	21,204
2006 Summer	83	1,289	109	111	1,592
2007 - 2008	1,285	17,519	1,830	969	21,603
2007 Summer	81	1,052	26	103	1,262
2008 - 2009	1,635	25,350	3,253	2,141	32,379
2008 Summer	138	1,454	204	114	1,910
2009 - 2010	9,368	40,449	16,339	2,071	68,227
2009 Summer	1,295	17,697	3,588	1,247	23,827
2010 - 2011	4,302	35,806	8,579	2,141	50,828
2010 Summer	144	1,851	117	221	2,333
2011 Summer	125	1,490	37	133	1,785
Total	20,865	181,103	40,112	11,790	253,870

Source: Tabout.dta

Table 8.4: Indirect Costs of Influenza

Influenza Season	ILI days	ILI cost
2005 - 2006	24,326	3,345,604
2006 - 2007	21,066	2,897,215
2006 Summer	1,575	216,631
2007 - 2008	21,408	2,944,272
2007 Summer	1,286	176,801
2008 - 2009	30,978	4,260,363
2008 Summer	1,777	244,362
2009 - 2010	49,429	6,797,926
2009 Summer	21,626	2,974,187
2010 - 2011	43,755	6,017,616
2010 Summer	2,262	311,082
2011 Summer	1,821	250,412
Total	221,308	30,436,471

Source: Tabout.dta

Table 8.5: ILI Consultation Costs (public sector, third party payer)

	Public sector direct spending on ILI				
Influenza Season	**0 to 4 years**	**15 to 64 years**	**5 to 14 years**	**65 years and older**	**Total**
2005 - 2006	32,875.1	497,680.5	108,814.4	67,322.4	706,692.5
2006 - 2007	27,365.1	430,998.5	41,957.6	59,681.1	560,002.3
2006 Summer	2,086.3	32,239.5	2,729.1	5,583.7	42,638.6
2007 - 2008	32,125.1	437,985.9	45,768.6	48,493.9	564,373.6
2007 Summer	2,031.0	26,311.9	655.5	5,158.7	34,157.1
2008 - 2009	40,898.9	633,767.4	81,348.0	107,072.8	863,087.1
2008 Summer	3,463.1	36,374.7	5,116.7	5,726.6	50,681.0
2009 - 2010	234,205.7	1,011,232.4	408,497.4	103,563.5	1,757,499.1
2009 Summer	32,392.6	442,445.3	89,715.8	62,354.9	626,908.7
2010 - 2011	107,557.3	895,151.4	214,476.4	107,077.3	1,324,262.3
2010 Summer	3,610.6	46,285.7	2,933.0	11,064.3	63,893.6
2011 Summer	3,135.7	37,263.4	934.9	6,692.4	48,026.4
Total	521,746.4	4,527,736.7	1,002,947.5	589,791.6	6,642,222.2

Source: Tabout.dta

Table 8.6: ILI Consultation Costs (out-of-pocket)

	Out of pocket direct spending on ILI consultations				
Influenza Season	**0 to 4 years**	**15 to 64 years**	**5 to 14 years**	**65 years and older**	**Total**
2005 - 2006	32,875.1	497,680.5	108,814.4	0.0	639,370.1
2006 - 2007	27,365.1	430,998.5	41,957.6	0.0	500,321.2
2006 Summer	2,086.3	32,239.5	2,729.1	0.0	37,054.9
2007 - 2008	32,125.1	437,985.9	45,768.6	0.0	515,879.6
2007 Summer	2,031.0	26,311.9	655.5	0.0	28,998.4
2008 - 2009	40,898.9	633,767.4	81,348.0	0.0	756,014.3
2008 Summer	3,463.1	36,374.7	5,116.7	0.0	44,954.4
2009 - 2010	234,205.7	1,011,232.4	408,497.4	0.0	1,653,935.5
2009 Summer	32,392.6	442,445.3	89,715.8	0.0	564,553.8
2010 - 2011	107,557.3	895,151.4	214,476.4	0.0	1,217,185.1
2010 Summer	3,610.6	46,285.7	2,933.0	0.0	52,829.3
2011 Summer	3,135.7	37,263.4	934.9	0.0	41,334.0
Total	521,746.4	4,527,736.7	1,002,947.5	0.0	6,052,430.6

Source: Tabout.dta

Table 8.7: Influenza Hospital Costs

	Hospital Spending: Influenza				
Influenza Season	**0 to 4 years**	**15 to 64 years**	**5 to 14 years**	**65 years and older**	**Total**
2005 - 2006	101,209	28,224	589,500	550,243	1,269,176
2006 - 2007	72,576	10,082	279,419	275,897	637,974
2006 Summer	4,048	19,893	188,706	183,596	396,243
2007 - 2008	219,065	31,116	207,887	66,570	524,638
2007 Summer	76,501	0	97,956	52,211	226,669
2008 - 2009	150,400	15,137	271,429	254,976	691,942
2008 Summer	98,954	4,566	115,420	35,103	254,042
2009 - 2010	1,838,831	575,701	4,745,892	844,902	8,005,326
2009 Summer	645,754	77,723	1,923,972	162,726	2,810,175
2010 - 2011	1,750,541	326,816	7,477,337	1,312,230	10,866,924
2010 Summer	328,757	5,916	112,131	123,482	570,286
2011 Summer	16,176	0	85,869	18,599	120,644
Total	5,302,812	1,095,173	16,095,519	3,880,536	26,374,039

Source: Tabout.dta

8.1.3 Part 3: Cost-effectiveness

The base case analysis estimates the cost-effectiveness of the influenza vaccine programme in Ireland. This is done by comparing the levels of influenza vaccination each season against a counterfactual in which nobody is vaccinated, thereby generating the incremental cost-effectiveness of transitioning from zero vaccinations to the recorded vaccination levels. Tables 8.10 and 8.11 present cost-effectiveness estimates based on two different modelling approaches, static and dynamic infectious disease modelling, as specified in Chapter 7. The column headed "NHB" depicts the net health benefit, "NMB" signifies net monetary benefit, and "CE ratio" signifies the cost-effectiveness ratio, as described in the foregoing chapter.

The static model is shown in Table 8.10. The mean cost-effectiveness is €34,866 per quality adjusted life year (QALY). There is significant variability between seasons, ranging from €13,346 to €43,488 per QALY. For the summer periods the cost-effectiveness is significantly less, ranging from €29,044 to €272,064 per QALY.

Table 8.8: Influenza Hospital Costs: Primary versus secondary diagnosis

	Hospital Spending: Influenza		
Influenza Season	**Primary**	**Secondary**	**Total**
2005 - 2006	726,992	542,184	1,269,176
2006 - 2007	341,617	296,358	637,974
2006 Summer	174,680	221,563	396,243
2007 - 2008	162,599	362,038	524,638
2007 Summer	127,999	98,670	226,669
2008 - 2009	282,028	409,915	691,942
2008 Summer	44,743	209,299	254,042
2009 - 2010	3,672,943	4,332,383	8,005,326
2009 Summer	1,691,070	1,119,105	2,810,175
2010 - 2011	4,614,249	6,252,675	10,866,924
2010 Summer	111,411	458,876	570,286
2011 Summer	40,737	79,907	120,644
Total	11,991,067	14,382,973	26,374,039

Source: Tabout.dta

Table 8.9: Mortality Estimates: 2005 - 2011

	Base Case - Mortalities			
Influenza Season	**0 - 14**	**15 - 64**	**65 plus**	**Total**
2005 - 2006	0	76	374	450
2006 - 2007	0	66	331	397
2006 Summer	0	4	31	35
2007 - 2008	0	67	270	337
2007 Summer	0	4	28	32
2008 - 2009	0	97	597	694
2008 Summer	0	5	31	36
2009 - 2010	0	154	573	727
2009 Summer	0	68	346	414
2010 - 2011	0	122	540	662
2010 Summer	0	7	61	68
2011 Summer	0	5	37	42
Total	0	675	3,219	3,894

Source: Tabout.dta

Table 8.10: Cost Effectiveness: Base Case, Static Modelling

Influenza Season	NHB	NMB	CE ratio
2005 - 2006	-218	-4,365,417	38,683
2006 - 2007	-263	-5,256,081	43,488
2006 Summer	-66	-1,318,068	84,383
2007 - 2008	-132	-2,637,113	33,314
2007 Summer	-239	-4,770,859	272,064
2008 - 2009	84	1,676,837	17,479
2008 Summer	-279	-5,584,380	262,751
2009 - 2010	226	4,517,688	13,346
2009 Summer	-94	-1,870,475	29,044
2010 - 2011	139	2,771,826	18,770
2010 Summer	-303	-6,063,050	157,782
2011 Summer	-368	-7,366,987	267,095
Aggregate	-1,513	-30,266,096	34,866

Source: .dta

The dynamic modelling approach generates superior estimates of cost-effectiveness compared to static modelling, as shown in Table 8.11. The mean cost-effectiveness is €2,784 per QALY. Cost-effectiveness per season spans from €1,885 to €4,871 per QALY, while cost-effectiveness for the summer periods ranges from €1,826 to €58,686 per QALY. There is an inverse relationship between the incidence of influenza and the cost-effectiveness of vaccination in a given season, *ceteris paribus*, as vaccination prevents a greater number of influenza cases in seasons with a high influenza incidence. Accordingly, influenza vaccination was more cost-effective in 2005-2006 than in 2006-2007, although the rates of influenza-related mortality and morbidity were higher in 2005-2006. Tables 8.12 and 8.13 depict the annual number of influenza-related mortalities and costs by season in the counterfactual. This counterfactual assumes that no person was vaccinated against influenza in any season.

Vaccination costs

GPs tend to charge between €45 and €65 for vaccination of private patients [25]. For the cost-effectiveness modelling it was assumed that private patients pay €50

Table 8.11: Cost Effectiveness: Base Case, Dynamic Modelling

Influenza Season	NHB	NMB	CE ratio
2005 - 2006	5,076	101,512,216	2,800
2006 - 2007	3,694	73,888,240	3,315
2006 Summer	481	9,623,814	4,802
2007 - 2008	1,559	31,183,422	4,871
2007 Summer	-163	-3,268,979	58,686
2008 - 2009	6,035	120,693,688	1,885
2008 Summer	1,201	24,010,596	5,597
2009 - 2010	3,412	68,238,600	3,357
2009 Summer	30,835	616,696,000	1,826
2010 - 2011	8,238	164,761,360	3,272
2010 Summer	5,542	110,844,184	4,375
2011 Summer	2,421	48,423,044	4,020
Aggregate	68,330	1,366,606,208	2,784

Source: .dta

out of pocket for vaccination by a GP. I estimated that each GP consultation costs the public payer (HSE) €50 per patient enrolled on a government programme, including the price of a vaccine, and zero per private patient. Patients enrolled on the State funded General Medical Services (GMS) scheme do not pay out-of-pocket charges [25]. The analysis did not consider the indirect costs incurred when patients undergo vaccination (e.g. taking time off work to visit a clinician), due to a lack of reliable data.

It was assumed that private patients pay €20 for vaccination in a pharmacy. Pharmacists incur a number of costs for participating in influenza vaccination. The wholesale price of the "influvac" brand of vaccine during the study period was €5.65. After including a standard mark up and dispensing fee this reaches €13.05. For pharmacies, a typical administration fee for private patients was €6.95, though this varies between pharmacies and patient subpopulations. These figures add up to the estimated €20 price per private patient in a pharmacy setting.

Pharmacies must possess four Anapen 0.3mg injection of epinephrine (adrenaline) in order to reverse the occurrence of anaphylactic shock during an acute allergic reaction to influenza vaccination, but pharmacies need not incur costs for this if it is already in stock. In addition, pharmacists must pay a fee to undergo training in

vaccine administration, to become licensed to vaccinate patients. It was assumed that these additional costs are paid from the payments that pharmacists receive for influenza vaccination, therefore these costs were not explicitly included in the analysis as this would constitute double-counting.

Clinical Effectiveness Based on the methodology of Osterholm et al. [183], vaccine effectiveness for adults is estimated as 59% when the vaccine is well-matched to circulating strains of virus. Influenza vaccination is more clinically effective for young and healthy individuals, and less effective for older and chronically ill individuals. The mean level of vaccine effectiveness in the Irish population was estimated as 59% in the base case analysis. In one sensitivity analysis, the impact of higher levels of vaccine effectiveness (70%) was tested, while another sensitivity analysis tested the impact of lower vaccine effectiveness (22% mean effectiveness).

8.1.4 Sensitivity Analysis

As noted in the previous chapter, I tested the robustness of the findings by systematically varying the values of key parameters across plausible ranges. I constructed nine different scenarios using static infectious disease modelling, and a number of additional scenarios using dynamic infectious disease modelling.

In the first scenario, influenza-associated costs and mortalities are calculated on the assumption that 100% of the population is vaccinated by the first week of the season. These results are shown in Tables 8.15 and 8.14 respectively. Cost-effectiveness is calculated for the incremental effects of shifting from the observed vaccination rates (in the base case) to 100% vaccination (see Table 8.16). Scenario 2 adopts the same approach but assumes that 75% of the population is vaccinated by the first week of the season (see Appendix D and Tables D.2, D.3 and D.4), while Scenario 3 assumes that 75% of the population is vaccinated by the end of the season (see Tables D.5, D.6 and D.7). In each of these scenarios the number of mortalities and the quantum of influenza associated costs are reduced relative to the base case.

Table D.2 depicts the number of mortalities when 75% of the Irish population in each age group are vaccinated in the first week of the influenza season, and there is no further vaccination throughout the season. The assumed mortality rate per ILI case in this scenario is equivalent to the base case. The aggregate number of mortalities across each season is reduced to 2,354.

Scenarios 4 and 5 examine the impact of changing the assumed level of vaccine effectiveness. In Scenario 4, the comparator for the cost-effectiveness estimate constitutes 75% vaccination by the first week of the season and lower vaccine effectiveness (22% effectiveness). Vaccine effectiveness of 22% is a lower bound of the estimates in the literature. This intervention is compared against the observed vaccination rate (in the base case) coupled with the 22% level of effectiveness. The reduction in effectiveness leads to an increase in influenza related costs and mortalities, and a reduction in cost-effectiveness. In Scenario 5, vaccine effectiveness is increased to 70%, resulting in a reduction in costs and mortalities, and an increase in cost-effectiveness. These two scenarios are depicted in Tables D.8 to D.13).

In Scenarios 6 and 7, the cost per vaccination is varied to €15 and €50 respec-

tively. The cost-effectiveness estimates are depicted in Tables D.14 and D.15. In each case the incremental change is from the base case vaccination levels to 75% vaccination coverage by the first week of the season.

In scenario 8, there is an increase in the number of work days lost due to each case of influenza like illness among adults of working age. The cost of illness is depicted in Table D.16, and the cost-effectiveness in Table D.17.

In the final scenario, there is a reduction in the estimated mortality rate per ILI case. The vaccination rate is identical to Table D.2, but the mortality rate per ILI case is reduced to reflect a more conservative epidemiological study from the United Kingdom. This results in fewer mortalities (N = 806) (see Table D.18) and a reduction in cost-effectiveness (see Table D.19).

The results for the dynamic modelling scenarios are shown in Tables D.20 to D.32 of Appendix D. In scenarios where there is an increase in vaccination levels or in vaccine effectiveness, this results in an increase in cost-effectiveness relative to static models, and a reduction in mortalities and influenza-associated costs. By contrast, where the vaccination level or the vaccine effectiveness are reduced, the number of mortalities and the quantum of influenza associated costs are larger (reflecting the larger magnitude of vaccination's effects).

In tables D.16 and D.17, it is assumed that the mean number of days of work absenteeism increases from 1.3 to 2.0 for each case of ILI in working age adults.

Table 8.12: Mortalities: Zero Vaccination

	Mortalities - Sensitivity Analysis			
Influenza Season	**0 - 14**	**15 - 64**	**65 plus**	**Total**
2005 - 2006	0	79	388	467
2006 - 2007	0	68	344	412
2006 Summer	0	5	32	37
2007 - 2008	0	70	281	351
2007 Summer	0	4	29	33
2008 - 2009	0	101	622	723
2008 Summer	0	5	33	38
2009 - 2010	0	160	593	753
2009 Summer	0	71	364	435
2010 - 2011	0	128	565	693
2010 Summer	0	7	64	71
2011 Summer	0	6	39	45
Total	0	704	3,354	4,058

Source: .dta

Table 8.13: Influenza Costs: Zero Vaccination

	Sensitivity Analysis - Costs (Euro)					
Influenza Season	**Indirect**	**ILI - Public**	**ILI - Private**	**Pharma**	**Hospital**	**Total**
2005 - 2006	3,476,610	734,365	664,406	384,920	1,318,874	6,579,174
2006 - 2007	3,011,037	582,003	519,977	205,903	663,038	4,981,957
2006 Summer	226,131	44,508	38,680	20,266	413,620	743,206
2007 - 2008	3,064,982	587,512	537,030	304,404	546,147	5,040,074
2007 Summer	184,910	35,724	30,328	27,476	237,065	515,502
2008 - 2009	4,440,279	899,535	787,941	892,032	721,164	7,740,951
2008 Summer	256,057	53,107	47,106	36,428	266,200	658,898
2009 - 2010	7,039,271	1,819,895	1,712,654	4,807,120	8,289,536	23,668,475
2009 Summer	3,131,140	659,992	594,346	2,199,782	2,958,473	9,543,733
2010 - 2011	6,304,087	1,387,304	1,275,130	3,574,046	11,384,248	23,924,814
2010 Summer	327,031	67,169	55,538	1,768,946	599,525	2,818,210
2011 Summer	264,447	50,718	43,651	101,412	127,406	587,633
Total	31,725,980	6,921,832	6,306,787	14,322,734	27,525,294	86,802,627

Source: .dta

Table 8.14: Mortality: All Vaccinated in Week 1

	Mortalities - Sensitivity Analysis			
Influenza Season	**0 - 14**	**15 - 64**	**65 plus**	**Total**
2005 - 2006	0	36	177	213
2006 - 2007	0	31	156	187
2006 Summer	0	2	14	16
2007 - 2008	0	30	123	153
2007 Summer	0	1	13	14
2008 - 2009	0	43	265	308
2008 Summer	0	2	13	15
2009 - 2010	0	83	307	390
2009 Summer	0	29	150	179
2010 - 2011	0	54	239	293
2010 Summer	0	2	25	27
2011 Summer	0	2	16	18
Total	0	315	1,498	1,813

Source: .dta

Table 8.15: Influenza Cost: All Vaccinated in Week 1

	Sensitivity Analysis - Costs (Euro)					
Influenza Season	**Indirect**	**ILI - Public**	**ILI - Private**	**Pharma**	**Hospital**	**Total**
2005 - 2006	1,586,234	335,060	303,141	175,623	601,748	3,001,806
2006 - 2007	1,368,226	264,464	236,279	93,563	301,287	2,263,820
2006 Summer	98,957	19,477	16,927	8,869	181,004	325,234
2007 - 2008	1,341,368	257,120	235,027	133,220	239,017	2,205,753
2007 Summer	81,201	15,688	13,318	12,066	104,105	226,378
2008 - 2009	1,895,004	383,900	336,274	380,698	307,775	3,303,652
2008 Summer	106,856	22,162	19,658	15,202	111,089	274,967
2009 - 2010	3,649,124	943,425	887,832	2,491,987	4,297,255	12,269,622
2009 Summer	1,291,942	272,320	245,234	907,654	1,220,698	3,937,847
2010 - 2011	2,670,252	587,627	540,113	1,513,875	4,822,080	10,133,947
2010 Summer	128,472	26,387	21,818	694,921	235,520	1,107,118
2011 Summer	109,095	20,923	18,008	41,837	52,560	242,422
Total	14,326,731	3,148,554	2,873,629	6,469,514	12,474,137	39,292,565

Source: .dta

Table 8.16: Cost-Effectiveness: Comparator, All Vaccinated in Week 1

Influenza Season	NHB	NMB	CE ratio
2005 - 2006	-3,691	-73,826,056	43,032
2006 - 2007	-4,111	-82,221,712	47,094
2006 Summer	-374	-7,476,937	-5,239
2007 - 2008	-4,724	-94,485,400	52,966
2007 Summer	-497	-9,947,306	-21,793
2008 - 2009	-2,384	-47,684,036	30,219
2008 Summer	-595	-11,901,304	-20,943
2009 - 2010	-2,194	-43,870,204	31,460
2009 Summer	-4,037	-80,739,280	-1,037
2010 - 2011	-1,925	-38,496,108	31,263
2010 Summer	-961	-19,227,584	-10,532
2011 Summer	-718	-14,368,422	-25,386
Aggregate	-11,846	-236,922,720	30,308

Source: .dta

Table 8.17: Mortalities: Dynamic Modelling, Zero Vaccination

	Mortalities - Sensitivity Analysis			
Influenza Season	**0 - 14**	**15 - 64**	**65 plus**	**Total**
2005 - 2006	0	137	673	810
2006 - 2007	0	110	551	661
2006 Summer	0	10	64	74
2007 - 2008	0	89	360	449
2007 Summer	0	4	34	38
2008 - 2009	0	158	970	1,128
2008 Summer	0	21	124	145
2009 - 2010	1	197	730	928
2009 Summer	1	401	2,045	2,447
2010 - 2011	0	215	951	1,166
2010 Summer	0	47	413	460
2011 Summer	0	34	223	257
Total	2	1,423	7,138	8,563

Source: .dta

Table 8.18: Costs of Influenza: Dynamic Modelling, Zero Vaccination

	Sensitivity Analysis - Costs (Euro)					
Influenza Season	**Indirect**	**ILI - Public**	**ILI - Private**	**Pharma**	**Hospital**	**Total**
2005 - 2006	6,020,764	1,271,767	1,150,613	666,601	2,284,014	11,393,759
2006 - 2007	4,818,266	931,322	832,068	329,486	1,060,995	7,972,137
2006 Summer	452,070	88,979	77,327	40,515	826,886	1,485,776
2007 - 2008	3,923,348	752,048	687,428	389,654	699,098	6,451,576
2007 Summer	214,999	41,537	35,264	31,947	275,641	599,388
2008 - 2009	6,918,772	1,401,642	1,227,757	1,389,950	1,123,705	12,061,826
2008 Summer	955,067	198,083	175,700	135,874	992,902	2,457,626
2009 - 2010	8,656,060	2,237,891	2,106,019	5,911,225	10,193,488	29,104,683
2009 Summer	17,555,932	3,700,495	3,332,429	12,333,920	16,587,807	53,510,583
2010 - 2011	10,601,567	2,333,026	2,144,382	6,010,463	19,144,860	40,234,298
2010 Summer	2,090,328	429,335	354,988	11,306,797	3,832,061	18,013,509
2011 Summer	1,502,347	288,134	247,983	576,131	723,804	3,338,399
Total	63,709,518	13,674,259	12,371,959	39,122,563	57,745,261	186,623,560

Source: .dta

Table 8.19: Mortality: Dynamic Modelling, All Vaccinated in Week 1

	Mortalities - Sensitivity Analysis			
Influenza Season	**0 - 14**	**15 - 64**	**65 plus**	**Total**
2005 - 2006	0	3	16	19
2006 - 2007	0	2	13	15
2006 Summer	0	0	0	0
2007 - 2008	0	7	31	38
2007 Summer	0	0	2	2
2008 - 2009	0	3	18	21
2008 Summer	0	0	0	0
2009 - 2010	0	46	172	218
2009 Summer	0	0	0	0
2010 - 2011	0	2	13	15
2010 Summer	0	0	0	0
2011 Summer	0	0	0	0
Total	0	63	265	328

Source: .dta

Table 8.20: Influenza Cost: Dynamic Modelling, All Vaccinated in Week 1

	Sensitivity Analysis - Costs (Euro)					
Influenza Season	**Indirect**	**ILI - Public**	**ILI - Private**	**Pharma**	**Hospital**	**Total**
2005 - 2006	147,395	31,134	28,168	16,319	55,915	278,931
2006 - 2007	115,770	22,377	19,992	7,917	25,493	191,549
2006 Summer	5,086	1,001	870	456	9,303	16,715
2007 - 2008	347,116	66,537	60,820	34,474	61,852	570,800
2007 Summer	15,172	2,931	2,489	2,254	19,452	42,299
2008 - 2009	134,006	27,148	23,780	26,921	21,764	233,618
2008 Summer	0	0	0	0	0	0
2009 - 2010	2,045,494	528,831	497,669	1,396,868	2,408,801	6,877,663
2009 Summer	0	0	0	0	0	0
2010 - 2011	147,312	32,418	29,797	83,517	266,024	559,069
2010 Summer	0	0	0	0	0	0
2011 Summer	0	0	0	0	0	0
Total	2,957,351	712,377	663,584	1,568,727	2,868,604	8,770,644

Source: .dta

Table 8.21: Cost-Effectiveness: Dynamic Modelling, Comparator All Vaccinated in Week 1

Influenza Season	NHB	NMB	CE ratio
2005 - 2006	-697	-13,947,270	24,101
2006 - 2007	-1,369	-27,372,692	26,241
2006 Summer	-601	-12,023,004	-2,268
2007 - 2008	-2,766	-55,310,800	33,023
2007 Summer	-662	-13,243,040	-12,407
2008 - 2009	1,844	36,878,868	17,644
2008 Summer	-821	-16,425,406	-11,219
2009 - 2010	967	19,332,058	21,474
2009 Summer	-6,807	-136,140,576	78
2010 - 2011	2,830	56,603,792	18,789
2010 Summer	-1,387	-27,745,358	-4,948
2011 Summer	-964	-19,285,142	-13,874
Aggregate	12,052	241,046,448	18,290

Source: .dta

8.2 Discussion

Changes to skill mix influence performance in a variety of ways, including access to services, clinical effectiveness and value for money. This paper has used available data from Ireland to assess the impact of a change in skill mix in influenza vaccination services, by examining changes in influenza vaccine uptake rates from 2005 to 2011. It was assessed whether the introduction of vaccination by pharmacists was associated with a change in vaccination rates, and whether any such change would be cost-effective.

Changes in skill mix should ideally be informed by a variety of forms of evidence, to ensure these changes facilitate access to services that are clinically and cost-effective. The methods adopted in this paper are tailored to these questions, with a focus on leveraging quantitative data to assess the impact of an expanded role for pharmacists in Ireland.

In the first instance, data on resource use and unit prices from a variety of sources were gathered to construct a model of the direct and indirect costs of influenza illness. Second, this was linked to evidence on the clinical effectiveness of influenza vaccination, the epidemiological patterns of influenza transmission in Ireland, and the cost of influenza vaccination in Ireland, to model the incremental cost-effectiveness of pharmacist administration of influenza vaccination. This enables an estimation of the net effect of the expanded role for pharmacists.

In addition, this paper modelled the incremental effect of pharmacist administration of influenza vaccination on morbidity and mortality. The quantum of QALYs lost due to illness and mortality was quantified as a component of the modelling of cost-effectiveness. A range of sensitivity analyses illustrate the potential effects of pharmacist administered vaccination across plausible scenarios. Collectively these analyses enhance the evidence base on the consequences of the change in skill mix.

This paper sought to fulfil a number of objectives, as specified in Chapter 7. Each of these objectives is outlined below, alongside the sections where these objectives are completed.

I Review the literature on the evidence of the clinical effectiveness and cost-effectiveness of influenza vaccination, and evidence on the role of pharmacists

in providing influenza vaccination

- Section 6.2 reviews international evidence on the clinical effectiveness of influenza vaccination
- Section 6.3 reviews international evidence on the cost-effectiveness of influenza vaccination
- Section 6.1.1 reviews international evidence on the impact of pharmacists on influenza vaccination rates

II Quantify the direct and indirect costs of influenza illness in Ireland

- Section 8.1.2 presents the costs of influenza in Ireland
- Section 8.2.2 discusses the costs of influenza in Ireland in light of international evidence

III Quantify the costs of administration of the influenza vaccine by pharmacists and by physicians in Ireland

- Section 8.1.3 quantifies these costs

IV Estimate the impact of pharmacists on influenza vaccination rates in Ireland

- Section 8.1.1 presents empirical results on the impact of pharmacists on vaccine uptake in Ireland
- Section 8.2.1 draws conclusions regarding this matter

V Quantify the cost-effectiveness of influenza vaccination by pharmacists in Ireland

- Sections 8.1.3 and 8.1.4 present empirical results on the cost-effectiveness of influenza vaccination by pharmacists in Ireland
- Section 8.2.3 draws conclusions regarding this matter

8.2.1 Vaccination Rates and Costs

A key question is whether pharmacist provision of vaccination has increased the vaccination rate. For individuals aged 65 years and above who are enrolled in a PCRS scheme, the vaccination rate increased from 51.4% to 59.9% between the 2009 - 2010 and 2010 - 2011 seasons, as noted in Figure 8.1. These data do not provide evidence that pharmacists substantively improved the vaccination rate among individuals aged 65 years and older during the 2010 - 2011 influenza season. This increase may have reflected increased public awareness of vaccination campaigns related to the emergence of the influenza pandemic, as well as greater efforts of clinicians to vaccinate at-risk groups. In the subsequent year the vaccination rate dropped to 56.6% for this subpopulation.

A number of issues bear emphasis. The PCRS data are likely to underestimate the number of vaccinations, as many individuals vaccinated in physicians' offices are not enrolled in government schemes such as the General Medical Services scheme, and therefore would not have been captured in this dataset. Pharmacists are formally obliged to notify the PCRS of each patient undergoing vaccination, but data acquisition may have been incomplete during 2010 and 2011. Pharmacists, as compared to GPs, may have vaccinated a disproportionately high number of individuals who are not enrolled in PCRS schemes, due to the incentive structures faced by patients. Individuals who are not enrolled in the GMS and LTI schemes typically encounter lower out-of-pocket charges if influenza vaccination occurs in a pharmacy setting than in a GP setting.

The absolute number of influenza vaccinations increased each year (and each season) between 2005 and 2011, according to the PCRS database. The cumulative increase in vaccinations was over 30 percentage points (see Figures 8.2 and D.1). By contrast, in the subset of individuals aged 65 years and older enrolled in the General Medical Services scheme, the proportion undergoing vaccination during this period decreased, as depicted in Figure 8.1. In part this reflects changes in the demographics of the Irish population (i.e. an increase in the numbers of individuals aged at least 65 years during this period). This could also result from changes in the criteria for inclusion in the PCRS schemes during this period.

An important mechanism for influenza vaccination is opportunistic vaccination

when a patient presents to the clinician for another purpose. There is not rigorous evidence on the extent to which opportunistic vaccination occurs in Ireland. In the USA, one survey suggested that vaccination of all patients who attended a healthcare provider at least once and who expressed (to the researcher) a willingness to undergo vaccination if recommended by the provider, would halve the level of ethnic and racial disparities in influenza vaccination rates. This suggests that in some circumstances there are missed opportunities for clinicians to administer influenza vaccination [254]. The extent to which this applies to pharmacists in Ireland is unclear.

8.2.2 Cost of Illness

This section discusses some general features of the cost of influenza illness in Ireland. The pattern of influenza costs across different age groups has implications for the cost-effectiveness of pharmacist administered vaccination, as pharmacists appear to target different age groups than GPs.

As shown in Table 8.3, ILI consultations for individuals aged 65 years and older accounted for fewer than 5% of total ILI consultations. This is lower than the findings of a number of international studies [186]. This result may reflect an increased likelihood of older individuals being admitted directly to hospital rather than attending a GP, may be a consequence of coding error, or may reflect accurately the epidemiology of influenza in Ireland in which there is a large burden on individuals aged 65 years and older.

In a similar fashion, individuals aged 65 years and older accounted for a relatively small proportion of influenza-related hospital costs (14%) (see Table 8.7). This may reflect coding practice in Ireland hospitals, for example clinicians and coders may be more likely to code an influenza-related admission as a secondary complication of influenza (rather than as influenza) for patients in this age cohort. It is also plausible that this figure, which is relatively low in comparison to other jurisdictions, may reflect the pattern of influenza incidence in Ireland.

The incidence of influenza in Ireland by age group has implications for the cost-effectiveness of influenza vaccination. As noted, pharmacists appear to vaccinate a younger cohort of patients than GPs. International evidence indicates that younger

adults experience a lower incidence of influenza related complications. However, vaccine effectiveness is higher for patients in this cohort, and these individuals can be important vectors of influenza transmission, therefore vaccination can exert important protective effects via herd immunity. The unusually high proportion of costs in this age cohort in Ireland, in addition to herd immunity issues, are factors that increase the likelihood of pharmacy vaccination being cost-effective.

A number of other issues bear emphasis. Antiviral medicines are prescribed for many influenza patients at high risk of complications. According to the PCRS database, these medicines were prescribed predominantly through the Drug Payment Scheme (DPS) and the General Medical Services (GMS) scheme. Virtually any resident of Ireland with a personal public service number is eligible to enrol in the DPS scheme, whereas eligibility for the GMS scheme is based on age and socioeconomic status. The DPS scheme covers the price of pharmaceuticals for enrolled individuals or families beyond a specified threshold (€120 in 2011 and €144 in 2014). The Long Term Illness scheme provides medicines free of charge for patients with specified chronic conditions such as epilepsy, cystic fibrosis, or diabetes mellitus. However, the PCRS data do not include the prescription of antivirals for individuals who are not enrolled in these three schemes. The quantum of spending attributable to non-enrolled individuals is anticipated to be small, as most elderly and chronically ill patients are enrolled in the GMS or LTI scheme, while a majority of the remaining families with regular prescription usage are likely to be enrolled in the DPS [25].

A majority of hospitalisation costs related to admissions where influenza was coded as a secondary diagnosis (€14.4 million) rather than primary diagnosis (€12.0 million) (see Table 8.8). This illustrates the role of influenza complications, such as pneumonia, in triggering hospitalisation. Influenza associated costs are generally significantly lower during the summer months, reflecting the lower incidence of influenza during this period.

These findings indicate that the economic impact of influenza in Ireland is not trivial. Influenza is estimated to have imposed total (direct and indirect) costs of €83.2 million between the 2005 - 2006 influenza season and the Summer of 2011. The most costly seasons imposed costs of over €22 million each. The indirect cost of productivity losses comprised 36% of total costs. The aggregate impact

of influenza may be understated as many hospitalisations triggered by influenza may not have been recorded as influenza cases, but this is counterbalanced by the possibility that numerous cases may have been incorrectly classified as influenza. Mechanisms to increase vaccination rates, such as changes in skill mix, can potentially serve as tools to mitigate this cost burden.

A number of supplementary tables relating to this influenza study are in Appendix D. Tables D.33 to D.55 present figures on hospital spending for a range of conditions. These tables illustrate patterns of hospital spending in Ireland, and provide a benchmark against which to compare the magnitude of spending on influenza. Of note, each condition is potentially triggered by influenza infection in some circumstances.

Influenza may lead to secondary bacterial pneumonia and this can precipitate cardiac and respiratory admissions [255]. Xue et al. estimated the number of hospital admissions attributable to influenza but not coded as influenza, using a Poisson regression analysis to analyze the association between weekly rates of "influenza-like illness" (ILI) in the community and admission rates for certain diagnostic codes [246].

In Ireland, it is possible to conduct this analysis for the following ICD codes: J20-J25 (pneumonia), J00-J06 (upper respiratory tract infections), I12-I18 (ischaemic heart disease), and I600-I698 (cerebrovascular disease). Each of these hypotheses has a biological basis to mitigate the risk of false positives, for example influenza may result in pulmonary complications of primary influenza infection or secondary bacterial infection, of which bacterial infection is the more frequent cause [235].

Based on the foregoing methodology, Xue et al. found sizeable influenza-associated costs that were not coded as influenza, and included these costs in their primary results [246]. However this analysis is vulnerable to confounding and over-estimation of influenza-associated costs. For example, environmental humidity and temperature appear predictive of influenza outbreaks [256], and may also play a role in outbreaks of pneumonia even when influenza infection is not a mediating factor [257, 258]. There is also evidence that patients' blood pressure tend to increase during winter months [259], which might plausibly increase hospitalisation rates for ischaemic heart disease and cerebrovascular disease, con-

current to yet independently of increases in ILI. Therefore regression techniques that do not control for these potential confounding variables might lead to inaccurate quantification of influenza-related hospitalisations. To attempt to validate these results for inclusion in the primary analysis, would necessitate testing these patients for influenza infection. This is not possible in the constraints of this study.

According to evidence from the Netherlands, influenza-related hospitalisations may be coded as diabetes mellitus, chronic heart disease, and cardio-vascular accidents, but the associated costs are non-significant [260]. Evidence also indicates that the influenza-triggered costs of myocardial infarction are modest. A systematic review identified 37 observational studies and two randomised controlled trials that investigated this link. For patients with established vascular disease, one trial found a significant association between influenza and myocardial infarction, while the second found inconclusive results. A pooled analysis of these two trials found a non-significant protective effect of influenza vaccination (relative risk 0.51, 95% confidence interval 0.15 - 1.76). For patients without established vascular disease, evidence of a link between influenza and myocardial infarction was weaker [261].

Definitive, large-scale randomised controlled trials are required to clarify the relationship between influenza and cardiovascular disease [262]. Collectively, the evidence base suggests that these non-influenza costs triggered by influenza are modest compared to the costs of influenza captured routinely in hospitals [261,262].

Of note, some GP consultations may be repeat visits by an individual patient. In one study of influenza-associated health care utilisation, an estimated 90% of influenza-related GP visits, 85% of emergency department visits, and every influenza-associated hospitalisation was assumed to be a distinct new case of influenza. This study deemed other visits as repeat visits [120]. This impacts the number of ILI presentations preventable through vaccination. However, this is counterbalanced by the likelihood that many patients with symptoms of ILI do not attend a physician.

8.2.3 Cost-effectiveness

One important consideration in adjusting skill mix arrangements is whether this constitutes satisfactory value for money. Changes to skill mix may serve as a tool

to enhance resource allocation. But careful evaluation of the effects is warranted. It is plausible that pharmacist vaccination may be a cost-effective intervention. Out-of-pocket charges are lower in the pharmacy setting than the GP setting for many patients, therefore there is an economic case for an expanded pharmacist role in some circumstances. This paper assessed the general cost-effectiveness of influenza vaccination under a range of assumptions, to ascertain the potential net impact of pharmacist vaccination.

This paper illustrates the impact of methodology on measured cost-effectiveness. In dynamic models that account for herd immunity effects, cost-effectiveness rates predominantly fall within standard norms of cost-effectiveness (e.g. £20,000 - £30,000 per QALY in the United Kingdom, and €20,000 per QALY in the Republic of Ireland during the study period). Static models, by contrast, generate inferior cost-effectiveness estimates that do not meet standard thresholds in Ireland and are marginally cost-effective according to the threshold specified for the United Kingdom.

This disparity between static and dynamic models conforms to the existing literature. According to one study, for example, influenza vaccination would have to cost at least €17.19 to be inefficient if a dynamic modelling approach was deployed, compared to €4.00 for a static modelling approach. In a dynamic model, influenza vaccination yielded a return on investment of €1.22 per €1.00 invested, compared to a return of €0.28 per €1.00 invested in a static disease transmission model [213]. Comparable results exist for the transmission of varicela [263], *Meningococcal* [264], and hepatitis A [265].

As pharmacists tend to vaccinate a younger cohort of patients who may play a pronounced role in disease transmission, it is important to capture transmission effects in a dynamic model. The role of this subpopulation in influenza transmission is counterbalanced by the lower rate of complications in this age group. On balance however the evidence suggests that an increase in vaccination rates by pharmacists can be a cost-effective intervention.

A number of assumptions exert an important influence on the measured cost-effectiveness. The assumed mortality rate per ILI case is a strong predictor of the number of mortalities, whereas the level of influenza vaccine coverage is a relatively weak predictor. Table D.18 shows that the estimated number of mortalities is

reduced to 806 when the mortality rate is specified as the rate of the GPRD study in the United Kingdom, while Table D.2 shows the estimated number of mortalities as 2,354 when the mortality rate from the Pitman study is applied (as in the base case scenario). The vaccination rate is identical in both scenarios, with 75% of the population vaccinated by week 1. The limited impact of increasing the vaccination rate is linked to the limited vaccine effectiveness for elderly people, a subpopulation at greater risk of dying from influenza and its complications.

Of note, the age profile of influenza patients in the GPRD study differed from a number of previous studies. The GPRD study was more heavily weighted towards patients aged between 15 and 64 years, and it is not clear if this played a role in the lower mortality rate for individuals aged 65 years and older. This may limit generalisability to other settings and other time periods. As I used the GPRD results for a sensitivity analysis, rather than the primary analysis, this serves to illuminate a potential lower bound of influenza-related mortality and the ensuing impact on cost-effectiveness.

The findings are coherent with international evidence in that the cost-effectiveness of influenza vaccination is greater during years with a higher incidence of influenza, such as the pandemic influenza outbreak of 2009. However, *ex-ante*, it is not possible to predict the severity of an influenza outbreak. Therefore, despite the heterogeneity between years, the appropriate measure of cost-effectiveness is the mean, expected value. Over time the health service is expected to pay and receive the mean.

A key determinant of cost-effectiveness is the estimated impact on QALYs. The key determinants of quality of life (QOL) impact are morbidity and mortality resulting from influenza infection, particularly lost life years resulting from mortality. The satisfaction derived from being vaccinated against infection may affect QOL, but this is offset by the potential reduction in QOL arising from vaccination's adverse effects. For this reason and a lack of rigorous data, QOL effects of satisfaction and a sense of security from vaccination were not included.

The findings are broadly consistent with international evidence, which suggests that vaccination is commonly cost-effective, and that changes to skill mix can play a viable role in expansion of vaccination programmes. However, the literature suggests that vaccination may result in net savings in some circumstances, which

was not reflected in this study. For example, one study suggested that hospitalisations costing €1.59 billion may be averted by vaccinating all eligible people in five European countries (France, Italy, Germany, Spain and the United Kingdom), for an implementation cost of €1.52 Billion [121]. This disparity may be due to the stringent assessment of vaccine effectiveness in this thesis. The literature on vaccine effectiveness suffers from a range of methodological defects, and it is difficult to compare findings between studies due to heterogeneous methodological approaches [117, 186].

Changes to skill mix may be a mechanism not only to increase vaccination rates, but to administer vaccination at an earlier point in the influenza season. This thesis demonstrates the importance of the timing of influenza vaccination. Cost-effectiveness estimates are superior when 75% of the population is vaccinated at the beginning of an influenza season rather than by the end of a season, as shown in the sensitivity analyses earlier in this chapter. The administration of vaccination by pharmacists may be a tool to administer vaccines more rapidly.

More generally, this illuminates the inherent trade-offs in dealing with an influenza pandemic. Ideally an influenza vaccine would be matched to circulating strains in order to achieve optimal effectiveness. However, the production of a matched vaccine would require at least six months, and could therefore only be used following the peak of pandemic with a novel strain of influenza virus. Consequently, there is a case for using a poorly matched vaccine (of lower effectiveness) in a pre-emptive manner during the early stages of a pandemic. A recent study found that if a pre-pandemic vaccine is at least 30% efficacious and achieves a high level of coverage, the pre-emptive strategy prevents more cases and is more cost-effective than a reactive strategy deploying a vaccine of greater clinical effectiveness [266]. This illustrates the importance of a provider infrastructure capable of targeting at-risk subpopulations in a relatively short timeframe.

In the foregoing analyses the summer periods are treated separately in the cost-effectiveness tables and should not be viewed as reflective of the cost-effectiveness of an influenza vaccination campaign. Vaccination campaigns typically focus on mitigating the relatively high incidence of influenza during the influenza season. The cost-effectiveness of vaccination is lower when the incidence of influenza is low, *ceteris paribus*.

The formal threshold that determines the cost-effectiveness of an intervention is noteworthy. In Ireland this threshold varied from €20,000 to €30,000 per QALY during the study period. For both of these thresholds, influenza vaccination is predicted to be cost-ineffective when static modelling methods are adopted, and cost-effective based on dynamic modelling methods. By contrast, viewed in light of the ranges of cost-effectiveness that are generally accepted by policy makers in the United Kingdom (£20,000 to £30,000 per QALY), influenza vaccination by pharmacists in Ireland can be deemed cost-effective using either static or dynamic modelling approaches.

8.2.4 Limitations

This paper has some limitations. First, the accurate quantification of indirect costs is challenging. Data on absenteeism are often unavailable, attribution of absenteeism to influenza may be erroneous, and some patients who are absent due to influenza infection may have taken a similar volume of annual paid sick leave even if they had not contracted influenza. Due to the lack of data in the Irish context, I based the estimate on international evidence and modified it in a sensitivity analysis. A Belgian study surveyed 2,250 individuals who had recently experienced ILI (during the 2011-2012 influenza season). Half of these individuals had sought formal medical care. Each ILI episode led to a mean of four days of absence from work or education, and a loss of 0.005 QALYs [267].

Second, I subdivided the population into four age bands for the analysis. Narrower age bands have been used in other studies such as 0-4, 5-19, 20-49, 50-64, 65-74, 75-84, and 85+ years [120], and could plausibly yield more refined estimates. However, this was not possible in the study due to a lack of data.

Third, vaccination should be conducted alongside other control measures such as social distancing (i.e. avoiding others while ill), and hand and respiratory hygiene ("cover your cough") [36]. As noted in Section 6.3.3, social distancing includes interventions such as school closures to reduce the rate of contact between individuals in society. I did not model the role of antiviral medicines and other control measures in containing an influenza epidemic. Using antiviral medicines early in an epidemic may contain influenza's spread, but may also promote the

spread of resistant microbes. The H5N1 virus (avian influenza) may be resistant to all available antivirals.

Fourth, I did not include data on private sector hospitalisations. In Norway the costs of private clinics were estimated at 20% of public sector costs [246]. Most Irish private hospitals do not provide emergency services, therefore this sector may not be a large cost driver. However, GPs may triage influenza patients directly to acute medical admission, and the extent of this is unclear. The rate may differ between not-for profit private hospitals and commercial private hospitals. The potential implications of this were explored in a sensitivity analysis.

Fifth, data on vaccination rates and public sector spending on pharmaceuticals were expressed at a monthly level, but more granular, weekly data could bolster efficiency. Since the emergence of the H5N1 virus in 2003, investment in influenza surveillance and research has increased. This investment has enhanced the quality of surveillance data globally [268], but there remain notable gaps in these systems [109].

Sixth, there is uncertainty surrounding the exact number of people vaccinated in Ireland each year. Some of the economic cost of influenza illness can be considered unavoidable, as it occurred in vaccinated individuals (i.e. vaccination confers less than 100% protection to all subgroups). In the analysis I assumed that only costs incurred by unvaccinated individuals could be prevented by policy changes. However measurement error for the vaccination rate from 2005 - 2011 may influence the estimated cost effectiveness.

For illustrative purposes, consider this simplified example. If annual costs of influenza illness are €1.5 million for a population of 1 million people, and the measured vaccination rate is 50% with an effectiveness of 50%, then €1 million of the costs are incurred by unvaccinated individuals (€2 per unvaccinated person). Increasing the vaccination rate by 10 percentage points would reduce the cost of illness by €100,000 (i.e. (€1 million) X (20% relative increase in vaccination) X (50% effectiveness)). If the true vaccination rate is 60% (i.e. with zero measurement error), ceteris paribus, €857,142 of costs would be incurred by unvaccinated individuals (i.e. €2.14 per unvaccinated person). Increasing the vaccination rate by 10 percentage points would lower costs by €107,142, rather than €100,000. Measurement error that understates the vaccination rate will lower the estimated

cost-effectiveness, and the contrary also holds. One commentator has argued that official figures may understate the vaccination rate by 5% [129].

There is evidence that PCRS understates the number of vaccines administered in the pharmacy setting. In 2011, the number of vaccinated individuals in pharmacy settings was 1,774, and there were no vaccinations in preceding years, according to primary data obtained from PCRS. By contrast, primary data obtained from a chain of pharmacies indicates that 4,673 individuals underwent influenza vaccination in pharmacies during the 2010 - 2011 influenza season. This suggests that pharmacies disproportionately vaccinate patients who are ineligible for government schemes such as the General Medical Services scheme. There may be a shift whereby individuals previously vaccinated by physicians switch to the pharmacy setting, or these individuals may not have received influenza vaccination in the absence of the pharmacy initiative. It is not possible to draw firm conclusions due to the lack of a counterfactual, as the policy was introduced simultaneously in all areas of the Republic of Ireland, and there is no valid control area. Second, there is a lack of rigorous data on individuals who are vaccinated by physicians but who are not enrolled in a PCRS scheme.

Seventh, data were not available to enable measurement of quality of care. As noted in the foregoing, a number of pharmacists in Ireland mistakenly administered paediatric dosages to adult patients during the 2011 - 2012 influenza season. This dosage error may have diminished or obviated the effectiveness of vaccination [130], underscoring the importance of rigorous training and quality assurance when implementing changes to skill mix. The sensitivity analysis explored the impact of this dosing error in an indirect manner, by quantifying the impact of a reduction in vaccination effectiveness on cost-effectiveness.

Part IV
Ambulatory Surgery Center market entry: price and volume effects [1]

[1] Professor Charles Normand contributed to the design and revision of this paper. Discussions with a number of individuals contributed to the design of this study including Michael Chernew and Rick McKellar

Chapter 9

Background to the Ambulatory Surgery Centre market

9.1 Ambulatory Surgery Centres: The Policy Context

Surgical interventions exert a significant impact on population health and are a major driver of healthcare spending. Surgery may address an acute illness or injury, or may treat the manifestations of chronic illness. The traditional setting for surgery is the hospital, but in recent decades there have been marked changes in the organisational setting of much surgery. Many countries have witnessed dramatic increase in the volume of surgery provided on an ambulatory (outpatient) basis, for procedures such as cataract removal, knee arthroscopy, and laparoscopic cholecystectomy. A comparable shift has occurred for a number of non-surgical procedures including colonoscopy and endoscopy. The shift to ambulatory surgery facilitates a transition to alternative forms of provider organisations.

In the United States of America (USA), ambulatory surgery is provided mostly by private sector facilities, although public sector facilities such as the Veterans Health Affairs system also play a significant role. Ambulatory surgery is provided by three principal facility types: hospital outpatient departments (HOPDs), ambulatory surgical centres (ASCs), and office-based surgeries (OBS) [93]. Each of these settings also provides a number of non-surgical procedures such as en-

doscopy. ASCs and OBSs shift the setting of surgery away from the traditional hospital setting.

This paper analyses the role of ASCs in the USA. According to proponents, ASCs seek to enhance convenience of care, efficiency and value, and instil constructive competition against hospitals. By contrast, critics argue that ASCs cream-skim more profitable patients and induce unnecessary demand. But there is scant evidence of their effects on performance. This study addresses this gap in the evidence, by empirically assessing the impact of ASCs on the price and volume of surgery.

9.1.1 Evolving patterns of care

In 1981, outpatient surgery accounted for around 20% of total surgery in the USA, with the remainder comprising inpatient surgery. By 2006, this ratio had reversed, as outpatient surgery comprised 83% of surgery. This reflected around 41.6 million ambulatory procedures each year [93]. Since 1991, HOPDs have accounted for around 44% of surgeries in the USA.

The growth in outpatient surgery has facilitated an expansion of care in non-hospital settings. From 1991 to 2001, the proportion of all surgeries (inpatient and outpatient) provided in ASCs increased from 10% to 17% (compared to around 44% in HOPDs) [93]. For Medicare beneficiaries, the volume of procedures provided in ASCs grew by 6.1% per year in ASCs during 2005 - 2009, but the volume of ASC-eligible procedures remained virtually constant in HOPDs. This trend abated in 2010, when the volume of these services increased by 1.0% in both ASCs and HOPDs [269]. Collectively, these data reflect a trend in the migration of increasingly complex procedures from inpatient to outpatient settings.

ASCs are typically of modest scale. In 2007, ASCs contained around 2.7 operating rooms on average, a modest increase from 2.5 in 2005 [269]. A majority of ASCs are single-specialty facilities, and over a half specialise in ophthalmology, orthopedic surgery, or gastroenterology [270]. In 2010 there were 5,316 Medicare-certified ASCs, and this number grew by a mean of 4.6 percent per year from 2005 to 2009 (reflecting 279 new facilities and the closure or merger of 71 facilities per year), before falling to 1.9% in 2010 [269]. From 2002 to 2011 the number of ASCs

grew substantially, at a mean rate of 6.7% per year.

Despite their modest size, ASCs have achieved sizeable market share in many states. The market penetration of ASCs varies significantly across the USA. In 2010, four states had more than 30 ASCs per 100,000 Medicare beneficiaries (Maryland, Idaho, Washington, Georgia), while four states had fewer than 6 ASCs per 100,000 beneficiaries (Vermont, New York, Kentucky, West Virginia) [269]. Most ASCs operated on a for-profit basis and were based in urban areas.

9.1.2 Incentives

Two key influences on the rate of expansion of ASCs are financial incentives and regulatory practice. In the USA providers typically do not receive an additional payment for an overnight stay following surgery. Since the 1980s, surgeons have been remunerated identical amounts for both inpatient and outpatient surgery [93]. Other facilitating factors are changes in clinical practice and technology, greater convenience for patients, and lower coinsurance charges for private insurance enrollees and Medicare beneficiaries.

As noted, since 2010 the rate of ASC growth has slowed. This may be due to lower Medicare payment rates for ASCs compared to HOPDs. In 2012, the payment rate to ASCs was 42% lower than for HOPDs. For example, the price of cataract surgery with intraocular lens insertion, a common ambulatory procedure, was $962 in ASCs compared to $1,633 in HOPDs (2010 data) [269]. According to the Medicare Payment Advisory Commission (MedPAC), the rationale for a price differential is that HOPDs serve more medically complex patients than ASCs, and provide emergency and specialist services for patients who experience complications [269,271]. The available data are inadequate to clarify whether existing price differentials are appropriate.

MedPAC recommended that The Congress should require ASCs to submit cost data [270]. At present, Pennsylvania is the only state to enforce this [272]. Although data on ASC costs are scant, one study found that ASC costs per case are typically lower than in HOPDs [273], another found that surgery time in ASCs is almost 40% shorter than in HOPDs [271]. A recent study found that mean surgery time in ASCs is 25% (31.8 minutes) shorter than hospital settings [274]. This may

be due to differences in casemix or efficiency levels.

In 2010, ASCs served 3.3 million fee-for-service Medicare beneficiaries, and Medicare spending on ASCs was $3.4 billion. A majority of patients served by ASCs are commercially insured. But although Medicare patients comprised 34% of patients attending ASCs, they accounted for only 17% of ASCs' revenue in 2009 [275].

Another price differential exists between payments to ASCs and office-based surgeries. During the decade from 2001 to 2011, the office-based surgery sector rate of growth surpassed the ASC sector, as its market share grew from around 14% to 20% of all surgeries [93]. Medicare payments to ASCs and HOPDs include a facility fee for inputs such as non-physician personnel, pharmaceuticals, and supplies, whereas Medicare payments to OBS do not include a facility fee [276].

There is little empirical evidence on the impact of ASCs on quality or efficiency. Proponents argue that as physicians in ASCs can exert greater autonomy over their work patterns, ASCs can support the development of customised surgical environments and recruitment of specialised staff [269]. This may support innovation and lead to superior efficiency, outcomes and value.

On the other hand, ASCs may select less complex and more profitable patient subpopulations, such as patients enrolled with commercial payers or Medicare (whose prices are higher than Medicaid). A concern is that ASCs are exempt from the Stark Law which prohibits physician self-referral. As physician ASC owners have a profit motive to carry out interventions, this may incentivise unnecessary care in the form of supplier induced demand [277, 278]. For a clinical standpoint, there appears to be significant scope for overuse of a number of procedures frequently conducted in ASCs (e.g. [279–281]). There is need for further evidence on the consequences of ASC market entry.

If ASCs cream-skim profitable patient subgroups, this can impinge on the ability of hospitals to cross-subsidise less profitable forms of care and to provide care for uninsured or under-insured patients [282–284]. General hospitals have deployed a number of strategies in response to this perceived threat. Some general hospitals have attempted to deny admitting privileges to physician-owners of ASCs, and there have been attempts to lock ASCs out of insurance contracts for outpatient surgery [285]. Furthermore, hospitals may seek to counter the competitive threat

of ASCs by inducing physicians to enter into a hospital-physician alignment, to preclude physicians from practicing in an ASC [286].

9.2 Literature on the competitive effects of ASCs

9.2.1 Price effects

Numerous studies have detected a positive correlation between provider market concentration and price [287]. This supports the hypothesis that provider organisations with greater market power are in a stronger negotiating position *vis-a-vis* hospitals. Whilst most studies examined data from the USA, there is also evidence from settings such as the Netherlands [288]. The evidence indicates that market structure is not the only factor at play, but it is a significant determinant of market conduct and price.

One study suggested that the costs of ambulatory surgery are 25% to 68% lower than for the same interventions on an inpatient basis [289]. There are a number of potential benefits of ambulatory surgery:

- Reduced length of stay can enable greater numbers of patients to be treated, with a resultant fall in waiting lists
- Inpatient facilities can be freed for more complex and acute cases
- There can be a reduction in the number of cancelled surgeries due to bed shortages in inpatient facilities
- Fixed scheduling and more efficient use of operating theatres
- Less disruption of patients' daily routines, reduced absenteeism from work
- Reduced staff numbers
- In dedicated facilities, increased potential for clinicians to redesign care processes leading to reduced perioperative time, and a reduction in cost of care [289]

It is plausible that ASCs instill competitive pressure on HOPDs and enable insurers to negotiate better bargains, resulting in a lower rate of spending growth. Around 90% of ASCs have one or more physician owners, while around 25% of ASCs are jointly owned by physicians and hospitals [275, 290]. It appears counterintuitive that hospitals would encourage the growth of rival organisations, but there is some evidence to suggest that hospitals may develop ASCs in partnership with physicians in order to limit their losses, judging it preferable to lose a portion of, rather than all of, their ambulatory surgery income [291].

But there is scant literature on the price effects of ASC market entry. One study used fixed effects models to estimate the effects of ASCs on the costs, revenues and profits of general hospitals that provide the same services as ASCs. The study was restricted to three states: Arizona, California, and Texas, during the years 1997 to 2004, and the hospital/ year was the unit of analysis. ASC market presence was associated with reduced revenues and costs, and with a net increase in the profits of hospitals [270].

This three state study included as covariates the number of specialty hospital market entrants and the number of specialty hospitals in the market for two or more years, as well as each hospital's number of staffed beds and a binary variable for whether a hospital was part of a multi-hospital system. The fixed effects were specified at the level of the state for each year. However, the study was limited by examining only the aggregate hospital revenues, costs and profits, rather than at the level of the procedure. There was positive association between revenue, cost and the number of orthopedic or surgical specialty hospitals in a market for at least two years, whereas there was negative association between revenue and the number of cardiac specialty hospital entrants in a year.

Apart from the foregoing study, the literature review found no analysis of the price effects of ASC market entry. By contrast, a number of studies examined the effects of "specialty hospitals" on market price. These hospitals specialise in providing a narrow range of interventions which require an overnight stay, such as cardiac surgery. Specialty hospitals are another competitor to the general hospital model. One study found that specialty hospital market entry did not impact negatively on the financial performance of general hospitals. The general hospitals experienced reduced costs and wider profit margins after a specialty hospital

entered the market [282].

9.2.2 Volume effects

In general, physician self-referral is forbidden by the Stark Law in the USA. But ASCs are exempt from this law, and this heightens concerns over the potential for ASCs to induce unwarranted demand. This is an important issue for public and private payers. For instance, although Medicare prices are lower for ASCs than for HOPDs, induced demand could partly or entirely offset any savings from lower unit costs. Accordingly, the impact of ASC market entry on volume warrants attention.

Limited evidence suggests that ASC market entry may increase the overall production of services. One study examined the utilisation rates of four ambulatory procedures, and indicated that physician owners of ASCs perform a greater volume of these procedures than their non-owner counterparts. But the study was restricted to a single state and it measured physician ownership in an indirect manner [292]. It may be the case that physician ownership of an ASC led to greater specialisation rather than increased volume. Another study, again limited to a single state, found evidence that ASC market entry is associated with increased rates of colonoscopy and upper gastrointestinal tract endoscopy [293].

The state of Florida has a relatively high level of ASC penetration. In a study of urological surgery in Florida, physicians who became owners of ASCs increased their rate of surgery from 9 per 100,000 to 94 per 100,000 ($P < 0.01$). Most growth in these procedures occurred in ASCs rather than hospitals (53% versus 0.9% increase) [294]. In another study of Florida data, the intervention rate for urinary stone surgery use was two times higher for physician owners than non-owners. In calculating the utilisation rate, a methodological limitation was the adoption of an area's population as the denominator in the rate variable, rather than the number of individuals who attended the physician with a relevant diagnosis [295].

Ownership of ASCs may incentivise physicians to conduct procedures offering a greater profit margin, rather than procedures associated with a more modest profit margin. According to a study by Strope et al., during the first year of ownership the ASC owners increased the proportion of procedures with a comparatively high

profit margin from 50% to 61% [294]. Another study found that for every 10% increase in the profitability of a surgery, there was a 1.2 to 1.4% increase in the likelihood of performing a surgery in an ASC rather than HOPD. The investigators estimated the costs of care indirectly, by assuming that the relative cost of care in an ASC and HOPD is similar for most surgeries [276].

A recent study examined the impact of ASC market entry on the volume of Medicare services. The predictor variable was the number of ASC operating rooms per 100,000 population. For each unit increase, there was a 1.8% increase in the number of colonoscopies provided to Medicare patients, and the market share of ASCs increased by 4 to 6 percentage points [296]. There was no significant association with arthroscopy, upper gastrointestinal procedures, or cataract surgery. A limitation was the use of aggregate ASC operating rooms, rather than a subdivision of operating rooms by specialty. This may have reduced the study's validity and power. As noted, Medicare services constitute around 34% of ASC care, but around 17% of total payments to ASCs. Another study used utilisation data from the American Hospital Association, and found that ASCs are associated with reductions in the volume of HOPD surgery at the metropolitan statistical area level [297]. Again, this study could not disaggregate ASCs by specialty. In addition, the study lacked data on utilisation rates in ASCs, and did not look directly at the price differentials between ASCs and other settings and across payer types.

A recent study assessed the impact of ASC market entry on outpatient surgery rates between 2001 and 2010. The population-based rate of surgery in areas without an ASC was compared to areas with an ASC. Multiple propensity-score methods were used to adjust for differences between these areas, and to quantify the impact of ASC market entry into an area previously without any ASCs. The study was restricted to Medicare patients. The adjusted ambulatory surgery rates increased from 2,806 to 3,940 per 10,000 population during this time period. During the four years after ASC market entry, the rate increased by 10.9% (from 3,338 to 3,701 per 10,000 people) in an area previously without an ASC. By contrast, the rate grew by 2.4% and 0.6% in areas in which an ASC was present from 2001 or never present, respectively [298].

Another recent study examined the impact of ASC market entry on utilisa-

tion and quality of ambulatory urologic surgery. The study covered the 2001-2010 period and was confined to Medicare enrolees. There was significant change in quality as measured by mortality. ASC market entry was associated with a reduction in surgery rates in the more expensive hospital setting, and there was no detected increase in aggregate surgical rates across all settings [299].

Section 9.2.1 noted the existence of another organisational form, the specialty hospital. There is evidence that physician-ownership of specialty hospitals is associated with greater volume of coronary artery bypass grafting in a market [300]. However, this model of care is not directly relevant to ambulatory surgery and shall not be discussed further.

The foregoing studies have been unable to judge the clinical appropriateness of additional procedures. An increase in the level of production may fulfil previously unmet need, rather than constituting excessive supply. Moreover, the ASC model of delivery may increase the level of specialisation of physician-owners, which could lead to an increase in quality of care. Proponents of ASCs argue that clinical specialisation in a narrow range of procedures enables increased efficiency and superior value for money [301].

It is plausible that an increase in utilisation rates and other changes in care delivery patterns following ASC market entry could be clinically and economically beneficial or harmful. Given this uncertainty, it is important to gather further evidence on the effects of ASCs. Due to issues of data availability, this study does not address all of these questions. However, this study does increase our understanding of key issues surrounding the impact of ASCs on price and volume.

Chapter 10

Methods of the Ambulatory Surgery Centre study

10.1 Aim

The aim of this paper is to quantify the association between ambulatory surgical centre (ASC) market entry and the change in volume and price of services, for a set of procedures commonly performed in ASCs and a comparator group of procedures and consultations not typically performed in ASCs.

10.2 Methods

10.2.1 Analysis 1: The impact of ASC market entry on price

Econometric model

This paper addresses the research question using panel data. Panel data are repeated observations on the same units of analysis over time, and in this case the unit of analysis is a market (defined by geographic area). Interrogation of panel data is useful for dynamic phenomena whereby changes occur over time.

In this study, multiple ASCs may enter or exit a market in a given year. The net change in ASC numbers in each area can be compared against the net change in all other markets, and also against the net change in the same market during

different time periods, to estimate the incremental effect of ASC market entry. This contrasts with the standard evaluation methods for health care interventions where the comparison may be dichotomous. For example, in a trial, half of the study participants may obtain the intervention and the other half do not. In this thesis study of ASCs, the more complex and dynamic pattern of market entry and exit requires a different set of analytical tools.

The principal method of analysis in this study is the fixed effects model. This is regarded as the most rigorous method to reduce bias in panel data of this nature, as it removes unobserved confounding between the units of analysis [302]. In essence, fixed effects is an ordinary least squares regression analysis in which the intercept terms vary across the units of analysis, i.e. the fixed effects approach assigns a distinct constant to each unit of analysis (in this case each geographic market), to mitigate potential correlation between the error term and the unit of analysis. This is expressed in the standard regression framework by inserting a dummy (binary) variable for each geographic market, depicted as ω_m in the model in Equation (10.1).

$$P_{mt} = \beta_0 + \beta_1 \chi_{1mt} + ...\beta_k \chi_{kmt} + \gamma_t + \omega_m + \epsilon_{it} \tag{10.1}$$

In Equation (10.1), m signifies geographic area, and t signifies time (year). The dependent variable is the mean price in a geographic unit of analysis for a given year (P_{mtj}). As noted, the fixed effects is: ω_m. A dummy variable is included for year: γ_t, and the error term is signified by: ϵ_{itj}. The constant is specified as β_0, and the remaining covariates are included as χ variables. The model was run separately for each procedure (defined using Current Procedural Terminology (CPT) codes). To explore the sensitivity of results to the specification of the model, I also constructed a model without any covariates, and a model including short-term general hospitals as a covariate.

This analysis was carried out using the *xtreg* command in STATA SE 12.1, combined in turn with the *re* and *fe* options. The *xtreg* command fits regression models to panel data, while the *fe* option specifies a fixed-effects model using a within panel regression estimator. The *re* option fits a random effects model by using a generalised least squares estimator to produce a matrix-weighted mean of

the between and within panel results. For each model I estimated the intraclass correlation coefficient, representing the proportion of variance attributable to geographic variation, and this is expressed as *rho* in the regression output in the following chapter [303, 304].

Dependent variable: price Price, the dependent variable, is defined as the mean price for a surgical procedure in a MSA in a given year. Data on price and utilisation were obtained from the Truven Marketscan database, for around 30 million enrollees in the USA each year from 2007 to 2011. There are approximately 370 geographic areas of analysis, defined as metropolitan statistical areas, although some areas are metropolitan divisions (sub-divisions of large urban metropolitan statistical areas) or micropolitan statistical areas (whose populations are smaller). I refer to these geographic areas collectively as MSAs.

The analysis involves a set of the most common procedures performed in ambulatory surgery. These procedures are classified using the CPT system. I obtained i) a list of the 100 most common CPTs provided by Ambulatory Surgery Centres to Medicare enrollees in 2011, ii) a list of common CPTs provided by ASCs to Medicare beneficiaries and to other (non-Medicare) enrollees, from the analyses of previously published studies (e.g. [296]). From these, I selected for analysis the most commonly performed and most costly (volume multiplied by mean price) procedures (see Table E.26).

Comparator groups I conducted analyses for two comparator groups: a set of inpatient diagnosis related groups (DRGs), and a set of "evaluation and management" (E&M) codes. E&M consultations are frequently conducted in outpatient settings. Due to data constraints, the comparison of volume involved both E&M and DRG codes, but the price comparison involved only E&M consultations.

I hypothesised that price and volume changes in these variables would be unrelated to ASC market structure, but would be affected by other covariates in the econometric model. This can isolate the effect of ASC numbers (i.e. therefore reduce or obviate confounding or endogeneity).

This analysis can also generate hypotheses about cost-shifting in hospitals. For example if ASC market entry is associated with no measured change in CPT

price but with an increase in the volume of hospital DRGs, the ASC may be drawing profitable patients away from hospitals, and hospitals may compensate by increasing the volume of other profitable forms of intervention. On the other hand, hospitals may lose the ability to cross-subsidise less profitable interventions, and there may be a drop in the production of these interventions.

Comparison of price between settings An ideal analysis would distinguish between services provided in the following provider categories:

I ASC independently owned

II ASC hospital owned (or joint hospital owned)

III Hospital outpatient departments (HOPD)

IV Office based surgeries

In this study it was assumed that a surgery occurred in an office-based surgery setting if the payment did not include a facility fee. To infer whether a procedure takes place in an ASC there are three relevant variables in the Marketscan database: BILLTYP, STDPLAC, and STDPROV. The BILLTYP variable represents facility bill type codes, constituting the setting (e.g. hospital inpatient, ASC, intermediate care facility) and type of bill (e.g. "replace prior encounter", "new abbreviated encounter", "nonpayment/zero claim"). The variable STDPLAC refers to "place of service" (e.g. pharmacy, school, nursing facility, hospital). The variable STDPROV refers to "provider type" (e.g. ASC, acute care hospital, podiatry, urology, pain management). The values of each variable that correspond to the ASC setting are presented below:

i BILLTYP: codes = 83* signify ASC

ii STDPLAC: code = 24 signifies ASC

iii STDPROV: code = 5 signifies ASC

It was assumed that a service was provided in an ASC if at least two of these variables corresponded to an ASC classification. If only one variable corresponded

Category of variables (Level of analysis: MSA, Year)	Variables	Data source
Key explanatory variable	ASCs per 100,000 population	CMS Provider of Service file
Provider market	Medicare registered hospitals	CMS Provider of Service file
Sociodemographics	Age, race, poverty rates	Area Health Resource File
General wage inflation	Wage indices	CMS website (Centers for Medicare and Medicaid Services)

Table 10.1: Predictor Variables

to an ASC, the setting was considered to be unknown and was not included in the HOPD or ASC descriptive comparison of price, but was included in the regression analysis of all settings. It was not possible to distinguish between independently owned ASCs and hospital owned ASCs in this study, as the POS dataset does not contain a variable to reflect ownership status. The implications of this lack of data are discussed in the Limitations section in the following chapter.

Main predictor variable The main predictor variable is the change in the number of ASCs per capita. I extracted the number of ASCs from the Centres for Medicare and Medicaid Services (CMS) Provider of Service (POS) Files. The POS provides the number of ASCs at zip code level per year. I assigned each ASC to its MSA using a crosswalk from the United States Housing Department.

I expressed this variable as a ratio of ASC numbers per 100,000 population in a MSA. For each year, I used the same denominator (2007 population), therefore changes in the main predictor only reflect changes in ASC numbers, rather than changes in population.

There may be some double-counting of ASCs in the POS file. In some instances, two ASCs had the same name, zip code, and street address, but had different CMS Certification Numbers. I adopted two rules to address this. First, if the ASCs had the same pattern of market entry and exit, I dropped one ASC. Second, if one entered and another exited the market in the same year, I assumed this was an administrative change and I counted this as one ASC continually present during this year.

Other predictor variables I obtained other predictor variables at zip code level (see Figure 10.1), and used a crosswalk file to express these variables at the country and then MSA level. These variables were sourced from the CMS, and from the Area Health Resource File (AHRF), rather than from the Truven database.

10.2.2 Analysis 2: The impact of ASC market entry on volume

To estimate the effect of ASC market structure on volume, a fixed effects model was used at the MSA level. The dependent variable was constructed from the Truven database, as a ratio of the volume of procedures (numerator) to the number of enrollees in each MSA (denominator). The analysis only included individuals enrolled for an entire year. Covariates were constructed using data from the Truven database, rather than from external databases (such as CMS or AHRF files at zip code level). This approach seeks to identify any valid causal relationship between the variables and volume, the outcome of interest, and to minimise the risk of bias. The variables included were: age, gender, and the relationship to the main employee (e.g. spouse or child).

10.2.3 Analysis 3: Descriptive comparison of price, volume and coding patterns across settings

A number of descriptive comparisons were conducted. I compared the mean price of each procedure between ASCs and other settings. I compared the volume of procedures that are provided in each type of setting. The results were visualised using box plots.

The primary CPT codes of interest are often billed alongside other codes for the same patient, on the same day and with the same provider. For this analysis I examined the number of codes billed on the same day and for the same patient as the primary CPT. For each of the three forms of organisational setting I compared the mean number of codes billed alongside the primary surgical CPT.

Chapter 11

Results and Discussion

11.1 Results - Price Regression

Price regressions were conducted for a set of 12 procedures that are performed often in an ASC setting. These procedures are specified by CPT code, as shown in Table 11.1.

The CPTs were selected based on their ranking in terms of annual spending in the Truven dataset each year from 2007 - 2011. The top 30 CPTs in terms of spending and volume during these years are presented in Tables E.26 and E.27 in Appendix E. The top six CPTs in terms of spending were included in the analyses, and these remained the top six CPTs in 2011, although the order had altered slightly (see Table E.26).

The other CPTs selected for analysis were high-spending CPTs relative to other CPTs in their clinical specialties. For example, among all procedures the spinal injection procedure (CPT code 62311) ranked tenth in 2007, and cystoscopy (code 52000) ranked twenty-first, yet these were the most costly CPTs in neurology and urology respectively.

Figure 11.1 summarises the results of the price regression analyses. In this figure, the results of each econometric model are represented by two bars. The first bar represents the number of results that are statistically significant in which the coefficient is positive, and the second bar represents significant results whose coefficient is negative. The figure does not include non-statistically significant

results.

The first set of columns are labelled "CPT FE base". This refers to the main econometric model with a fixed effect specification and the following covariates: poverty levels, ethnicity, age, and wage index. The next pair of columns are labelled "CPT FE + hosp". This is identical to the preceding model but also includes the number of short-term general hospitals as a covariate. The next pair of columns is labelled "CPT RE", and this is identical to the first set of columns but with a random effects rather than fixed effects specification. In the next two columns labelled "CPT FE start", a fixed effects model is specified including only the number of ASCs as a predictor variable, with a geographic area fixed effect and a series of dummy variables for time. The final pair of columns pertain to the E&M comparator analysis.

Tables 11.2 to 11.4 depict the results for the individual regression analyses in the primary econometric model (based on a fixed effects specification). In total, five sets of regression analyses were conducted, and the individual results of the other four models are depicted in Appendix E.

The intraclass correlation coefficient quantifies the proportion of total variance that is attributable to geographic variation. This is denoted by "rho" in regression tables in this chapter and in Appendix E. Rho ranged from 0.542 to 0.889 in the random effects models of price, and from 0.659 to 0.908 in the fixed effects models of price. This implies that geographic variation accounted for more than half of the variance in price in these models, while the remaining variables accounted for less than half of the variance.

For the base case fixed effects model of CPTs, market entry of ASCs was associated with a significant negative effect on price for five of the twelve CPTs, while none had a significant positive association. This is depicted in the first section of the bar chart in Figure 11.1. When short term general hospitals were added as a covariate to the econometric model (see Tables E.1 to E.3 in Appendix E), a similar pattern of results emerged (as shown in the second section of Figure 11.1).

For the random effects specification, there were six significant negative results and one positive result (see Tables E.7 to E.9, and the third section of Figure 11.1). A basic model included the price outcome, the ASC predictor variable, a

CPT	description
29826	Shoulder arthroscopy/ surgery
29880	Knee arthroscopy/ surgery
29881	Knee arthroscopy/ surgery
43239	Upper gi endoscopy biopsy
45378	Diagnostic colonoscopy
45380	Colonscopy and biopsy
45385	Lesion removal colonoscopy
52000	Cystoscopy
62311	Inject spine 1/s (cd)
64483	Inj foramen epidural 1/s
66984	Cataract surg w/iol 1stage
69436	Create eardrum opening

Table 11.1: The list of Current Procedural Terminology codes for analysis

fixed effect at the geographic area, and a dummy variable for year. This model resulted in four significant negative results and no significant positive results (see Tables E.10 to E.12 in the appendix, and the fourth pair of bars in Figure 11.1).

The comparator analysis involved E&M codes. The results are shown in Tables E.16 to E.18 in the appendix, and are summarised in the final section of the bar chart in Figure 11.1. There were no significant effects for any of the ten E&M codes.

Of note, the coefficients in a fixed effects model are interpreted in the same manner as ordinary least square regression. In the base case, for the five CPTs for which a significant result was observed, the reduction in price ranged from $27.99 to $82.25 per unit change in the predictor variable. A unit change in the predictor variable corresponds to a net increase of one ASC per 100,000 population.

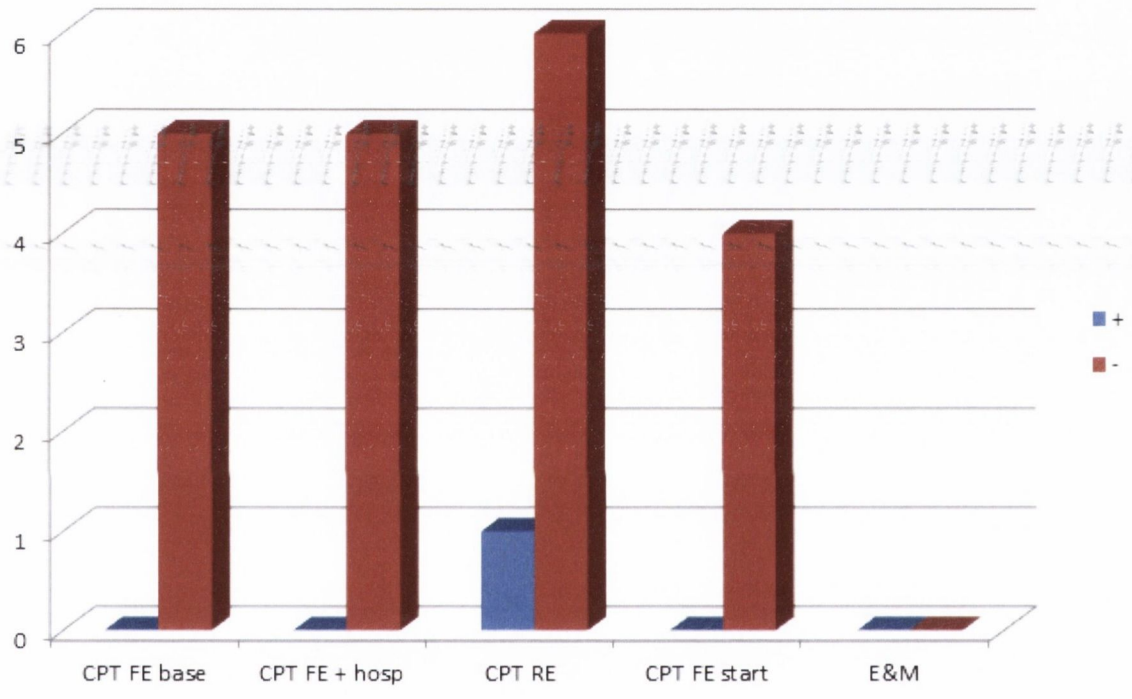

Figure 11.1: Summary of price regression results

Table 11.2: Price CPT Fixed Effects Excl. Hosp. Part 1

	CPT 29826	CPT 29880	CPT 29881	CPT 43239
ASC	-16.85	-139.0	-84.41	-40.30*
	(0.902)	(0.226)	(0.224)	(0.045)
Poverty rate	698.2	-2667.4	1781.0	749.6
	(0.854)	(0.404)	(0.355)	(0.180)
White ethnicity	4083.4**	3123.0*	2147.3**	-407.4
	(0.009)	(0.017)	(0.007)	(0.075)
65 years and older	23069.2	7935.9	-7567.5	308.2
	(0.078)	(0.470)	(0.254)	(0.873)
Wage Index	-723.1	2042.6	-1112.4	451.8*
	(0.609)	(0.089)	(0.120)	(0.030)
2008bn.year	368.1**	245.5*	132.9*	87.83***
	(0.002)	(0.013)	(0.025)	(0.000)
2009.year	913.3***	482.4***	391.8***	203.7***
	(0.000)	(0.000)	(0.000)	(0.000)
2010.year	1200.0***	617.7***	633.3***	247.3***
	(0.000)	(0.000)	(0.000)	(0.000)
2011.year	1506.4***	797.7***	782.6***	377.8***
	(0.000)	(0.000)	(0.000)	(0.000)
Constant	2592.3	618.7	5649.1***	2072.2***
	(0.297)	(0.767)	(0.000)	(0.000)
Observations	1818	1802	1819	1819
rho	0.770	0.659	0.837	0.899

p-values in parentheses

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table 11.3: Price CPT Fixed Effects Excl. Hosp. Part 2

	CPT 45378	CPT 45380	CPT 45385	CPT 52000
ASC	-27.99*	-54.43***	-76.01***	-82.25*
	(0.018)	(0.001)	(0.000)	(0.034)
Poverty rate	362.2	-418.1	-509.4	2798.9**
	(0.271)	(0.357)	(0.305)	(0.009)
White ethnicity	542.9***	427.4*	444.3*	841.7
	(0.000)	(0.022)	(0.029)	(0.056)
65 years and older	619.3	3428.6*	87.71	-15308.0***
	(0.585)	(0.028)	(0.959)	(0.000)
Wage Index	86.65	262.1	88.36	-124.2
	(0.479)	(0.121)	(0.632)	(0.756)
2008bn.year	48.19***	68.87***	49.26**	179.1***
	(0.000)	(0.000)	(0.001)	(0.000)
2009.year	100.3***	161.9***	106.3***	279.6***
	(0.000)	(0.000)	(0.000)	(0.000)
2010.year	167.9***	215.9***	170.5***	439.0***
	(0.000)	(0.000)	(0.000)	(0.000)
2011.year	198.8***	282.0***	197.7***	683.7***
	(0.000)	(0.000)	(0.000)	(0.000)
Constant	908.3***	1134.8***	1795.7***	2227.7**
	(0.000)	(0.000)	(0.000)	(0.002)
Observations	1819	1819	1819	1819
rho	0.908	0.906	0.890	0.780

p-values in parentheses

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table 11.4: Price CPT Fixed Effects Excl. Hosp. Part 3

	CPT 62311	CPT 64483	CPT 66984	CPT 69436
ASC	-7.746	34.87	-61.90	-15.96
	(0.816)	(0.188)	(0.065)	(0.742)
Poverty rate	-1597.3	-930.4	932.2	-998.5
	(0.084)	(0.205)	(0.316)	(0.459)
White ethnicity	-48.01	207.9	-388.3	435.2
	(0.899)	(0.489)	(0.308)	(0.430)
65 years and older	3055.9	-4955.0	2247.7	7484.8
	(0.336)	(0.050)	(0.482)	(0.107)
Wage Index	-549.7	-538.3*	259.6	124.6
	(0.109)	(0.048)	(0.452)	(0.804)
2008bn.year	21.49	1.061	8.085	94.40*
	(0.450)	(0.963)	(0.778)	(0.023)
2009.year	21.35	35.04	-31.21	337.9***
	(0.511)	(0.176)	(0.340)	(0.000)
2010.year	110.6*	25.26	-27.12	443.7***
	(0.011)	(0.466)	(0.536)	(0.000)
2011.year	131.8**	-60.59	33.46	514.3***
	(0.003)	(0.082)	(0.447)	(0.000)
Constant	1667.7**	2436.5***	3115.5***	1697.1
	(0.006)	(0.000)	(0.000)	(0.054)
Observations	1819	1816	1819	1818
rho	0.760	0.825	0.879	0.738

p-values in parentheses

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

11.2 Results - Volume Regression

A number of econometric models examined the association between ASC market structure and the utilisation rates of surgical procedures. The results are summarised in Figure 11.2. This bar chart can be interpreted in the same manner as Figure 11.1. The chart does not depict non-statistically significant results. The first pair of bars, labelled "FE", refer to the fixed effects model for the CPTs of interest. The next pair of bars, labelled "E&M", refer to the E&M comparator group. The final pair of bars, labelled "DRG", refer to the DRG comparator group of procedures. The regression results for individual procedures are shown in Tables 11.5 to 11.7 for the primary analysis, in which the 12 CPTs were examined using a fixed effects specification.

ASC market structure was not associated with a significant change in volume for any of the 12 CPTs (see the first section of Figure 11.2). Similarly, there was no significant effect on volume for the E&M procedure codes (see Tables E.13 to E.15 in Appendix E, and the second section of Figure 11.2). However, there was a significant effect for a number of DRGs (see Tables E.19 to E.21 in Appendix E). For each unit increase in the number of ASCs per capita there was a statistically significant increase in volume for two DRGs, and a significant decrease in volume for three DRGs, as shown in the third pair of bars in Figure 11.2.

Rho ranged from 0.651 to 0.910 in the fixed effects model of volume, which is broadly comparable to the rho values in the price regressions in Section 11.1. This signifies that geographic variation accounted for more than half of variance in relation to utilisation rates, while the remaining variables accounted for less than half of the variance.

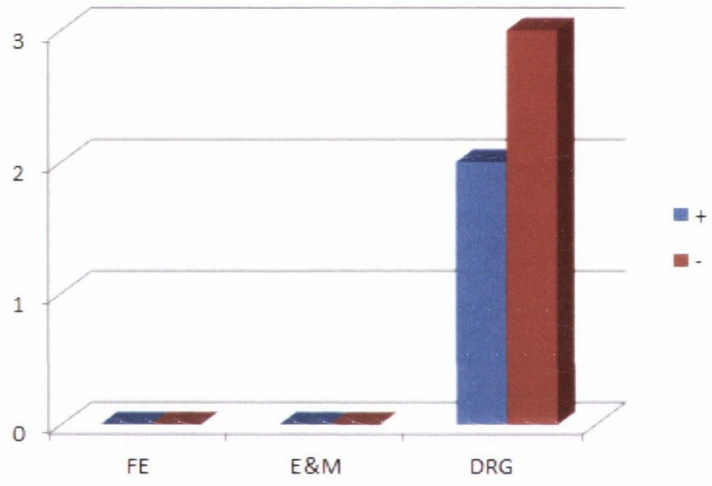

Figure 11.2: Summary of volume regression results

Table 11.5: Volume CPT Fixed Effects Part 1

	CPT 29826	CPT 29880	CPT 29881	CPT 43239
TotASClagPop	-0.0000239	-0.0000154	0.0000159	0.000176
	(0.545)	(0.544)	(0.748)	(0.172)
agegrp2_mean	-0.00257	-0.0000997	-0.00404	-0.000453
	(0.142)	(0.930)	(0.066)	(0.937)
agegrp3_mean	0.00283	-0.00181	-0.00166	-0.00204
	(0.256)	(0.260)	(0.596)	(0.802)
agegrp4_mean	0.00206	-0.00123	0.00333	0.0189***
	(0.225)	(0.264)	(0.118)	(0.001)
agegrp5_mean	0.00604***	0.00146	0.00468**	0.0168***
	(0.000)	(0.113)	(0.009)	(0.000)
emprel2_mean	0.00123	0.00142	-0.000180	0.00773
	(0.426)	(0.159)	(0.926)	(0.125)
emprel3_mean	0.00351*	-0.00227*	0.00541**	0.00406
	(0.016)	(0.017)	(0.003)	(0.394)
sex_mean	-0.00278	0.000646	-0.000284	0.0176**
	(0.102)	(0.559)	(0.894)	(0.002)
2008bn.year	0.000184***	0.0000212	0.0000302	0.000626***
	(0.000)	(0.334)	(0.479)	(0.000)
2009.year	0.000341***	0.0000457	0.0000325	0.00157***
	(0.000)	(0.057)	(0.488)	(0.000)
2010.year	0.000368***	0.0000406	-0.00000871	0.00162***
	(0.000)	(0.112)	(0.861)	(0.000)
2011.year	0.000430***	0.0000753	0.0000135	0.00217***
	(0.000)	(0.089)	(0.875)	(0.000)
Constant	0.000398	0.00138	0.00117	-0.00628
	(0.773)	(0.123)	(0.500)	(0.164)
Observations	1813	1799	1815	1815
rho	0.741	0.651	0.669	0.910

p-values in parentheses

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table 11.6: Volume CPT Fixed Effects Part 2

	CPT 45378	CPT 45380	CPT 45385	CPT 52000
TotASClagPop	-0.000212	0.0000619	-0.000113	0.000122
	(0.243)	(0.629)	(0.266)	(0.055)
agegrp2_mean	-0.0189*	-0.00208	-0.00308	0.00403
	(0.018)	(0.713)	(0.491)	(0.153)
agegrp3_mean	-0.0287*	-0.0132	-0.00109	-0.00235
	(0.012)	(0.102)	(0.864)	(0.559)
agegrp4_mean	0.0297***	0.0178**	0.0155***	0.00672*
	(0.000)	(0.001)	(0.000)	(0.014)
agegrp5_mean	0.0393***	0.0272***	0.0214***	0.0102***
	(0.000)	(0.000)	(0.000)	(0.000)
emprel2_mean	-0.00171	-0.00100	0.00223	0.0108***
	(0.810)	(0.841)	(0.573)	(0.000)
emprel3_mean	0.00764	0.00888	-0.000279	-0.00198
	(0.256)	(0.061)	(0.941)	(0.401)
sex_mean	0.0203**	0.00768	-0.00150	0.00455
	(0.009)	(0.162)	(0.731)	(0.097)
2008bn.year	-0.000487**	0.000619***	0.000130	0.0000378
	(0.002)	(0.000)	(0.135)	(0.491)
2009.year	-0.000772***	0.000776***	0.0000396	0.0000362
	(0.000)	(0.000)	(0.678)	(0.548)
2010.year	-0.00205***	0.000861***	-0.0000585	-0.000145*
	(0.000)	(0.000)	(0.564)	(0.023)
2011.year	-0.00274***	0.00143***	0.000438*	0.0000684
	(0.000)	(0.000)	(0.012)	(0.536)
Constant	0.00181	-0.00135	0.00229	-0.00323
	(0.776)	(0.762)	(0.518)	(0.148)
Observations	1815	1815	1815	1815
rho	0.805	0.892	0.839	0.808

p-values in parentheses

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table 11.7: Volume CPT Fixed Effects Part 3

	CPT 62311	CPT 64483	CPT 66984	CPT 69436
TotASClagPop	0.0000399	0.00000401	-0.0000428	0.00000167
	(0.730)	(0.967)	(0.544)	(0.971)
agegrp2_mean	-0.00758	-0.00911*	0.000788	-0.00737***
	(0.137)	(0.031)	(0.800)	(0.000)
agegrp3_mean	0.000225	-0.00874	0.00145	-0.00771**
	(0.975)	(0.147)	(0.744)	(0.008)
agegrp4_mean	0.00172	0.000986	-0.00569	-0.0164***
	(0.728)	(0.810)	(0.059)	(0.000)
agegrp5_mean	0.0141***	0.0123***	0.0223***	-0.0116***
	(0.001)	(0.000)	(0.000)	(0.000)
emprel2_mean	0.00452	-0.00107	0.000858	0.00463*
	(0.317)	(0.775)	(0.755)	(0.011)
emprel3_mean	0.00273	0.00825*	-0.000852	-0.00469**
	(0.522)	(0.020)	(0.744)	(0.006)
sex_mean	0.0169***	-0.00681	0.000459	0.00714***
	(0.001)	(0.098)	(0.879)	(0.000)
2008bn.year	-0.0000292	0.000583***	0.0000741	0.0000964*
	(0.769)	(0.000)	(0.221)	(0.016)
2009.year	-0.00000817	0.00103***	0.000113	0.0000569
	(0.940)	(0.000)	(0.090)	(0.192)
2010.year	-0.000110	0.00124***	0.000140*	0.000201***
	(0.342)	(0.000)	(0.047)	(0.000)
2011.year	0.000174	0.00134***	0.000241*	0.000151
	(0.385)	(0.000)	(0.048)	(0.060)
Constant	-0.00545	0.00613	0.000393	0.00720***
	(0.178)	(0.067)	(0.873)	(0.000)
Observations	1815	1811	1815	1813
rho	0.897	0.838	0.695	0.835

p-values in parentheses

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

11.3 Results - Other

The annual net change in the main predictor variable, the number of ASCs per 100,000 population in each MSA, is depicted in Figure E.2 in Appendix E. This illustrates significant variability in the pattern of ASC market entry and exit between markets. In addition there is temporal variation, with fewer ASCs entering markets in 2011 compared to previous years. This variability in the main predictor variable is expected to boost the signal strength of any causal relationship that may exist with price or volume, and this should increase the statistical power of this study, *ceteris paribus* [302].

As shown in Figure 11.3, the CPTs under analysis are performed in three different settings: ASCs, HOPDs, and office-based surgery facilities. The relative proportion in each setting is estimated based on a number of variables in the Truven database, as discussed in Chapter 10.

The estimate of the proportion of services provided in ASCs versus other settings varies depending on the definition of a "unit of service". One definition assumes that a unit of service comprises only the principal surgical procedure of interest, and omits any other billing codes on the same day for the same patient. Based on this classification, a majority of the procedures conducted (for each of the twelve CPTs) would be classified as occurring in an office-based surgery setting (see Figure 11.3).

By comparison, another definition specifies a unit of service as a "patient day". This includes all billing codes for a patient that occur on the same day as the primary surgical CPT of interest. Based on this classification, a higher proportion of services are provided in the ASC setting. Moreover, the proportion of services provided in office-based settings is estimated to be lower than in ASCs or HOPDs for all but three of the twelve CPTs (see Figure E.3 in Appendix E).

Using the definition of a patient/ day as the unit of service, for every ASC entering a market per 100,000 population the proportion of services delivered in ASCs increases between 3 - 5% in a statistically significant manner for nine of the twelve CPTs. For the other three CPTs (64483, 52000, 29880) there is not a significant change.

By contrast, when the unit of service is defined as solely the primary surgical

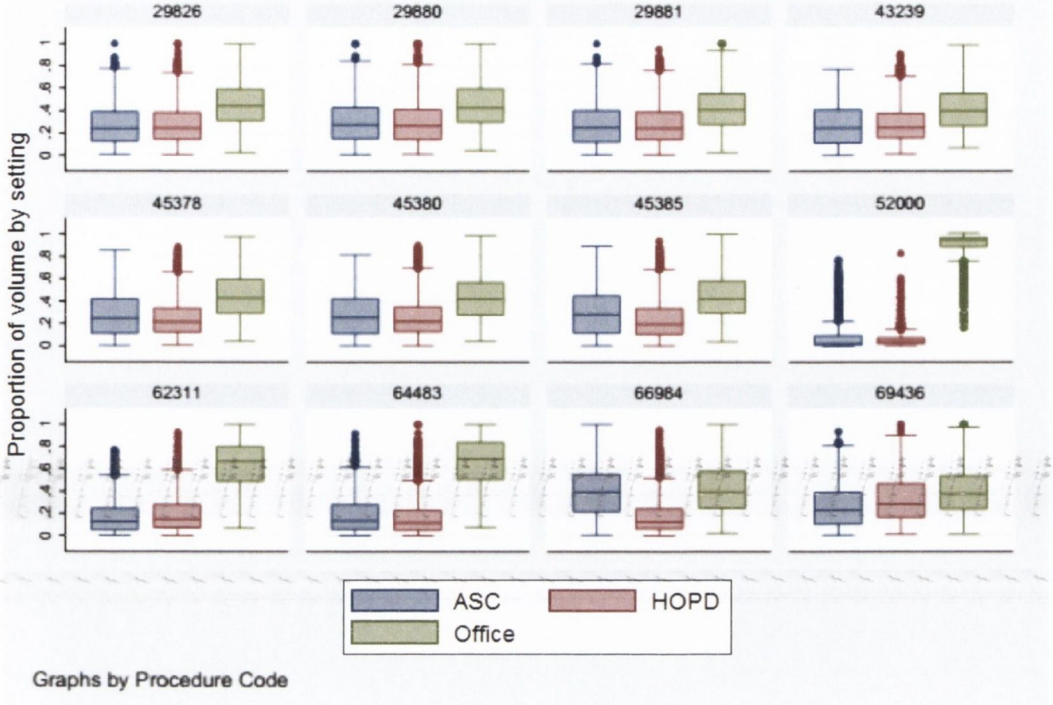

Figure 11.3: Proportion of services in each setting (procedure level)

CPT code of interest (i.e. excluding other codes on the same patient / day), there is a significant increase of 2 - 4% for eight CPTs, while four CPTs experience no significant change (66984 and the three aforementioned CPTs).

The mean price of each procedure by setting is depicted in Figure 11.4. For each procedure, the mean price is highest in the HOPD setting, followed by the ASC and then the office-based surgery setting. Figure E.5 presents the mean price per CPT when the unit of analysis is specified as the patient / day (Appendix E). The price per unit of service is higher in Figure E.5, as it includes additional codes billed alongside the main surgical CPT of interest.

The price of each of the twelve surgical CPTs varied from year to year. The percentage price increase for each year was modest for all twelve. To illustrate this, the percentage price increase from 2007 to 2008 is depicted in Figure E.1 in Appendix E. Although this is but one change, it is characteristic of the magnitude

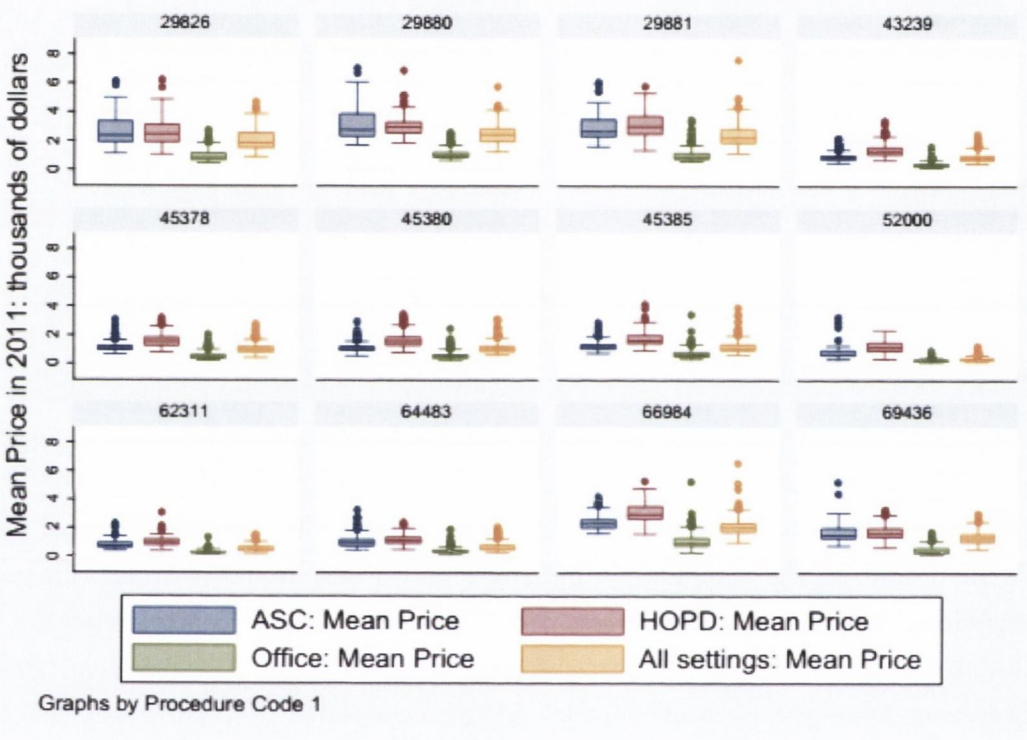

Figure 11.4: Mean Price per CPT (specified at the procedure level)

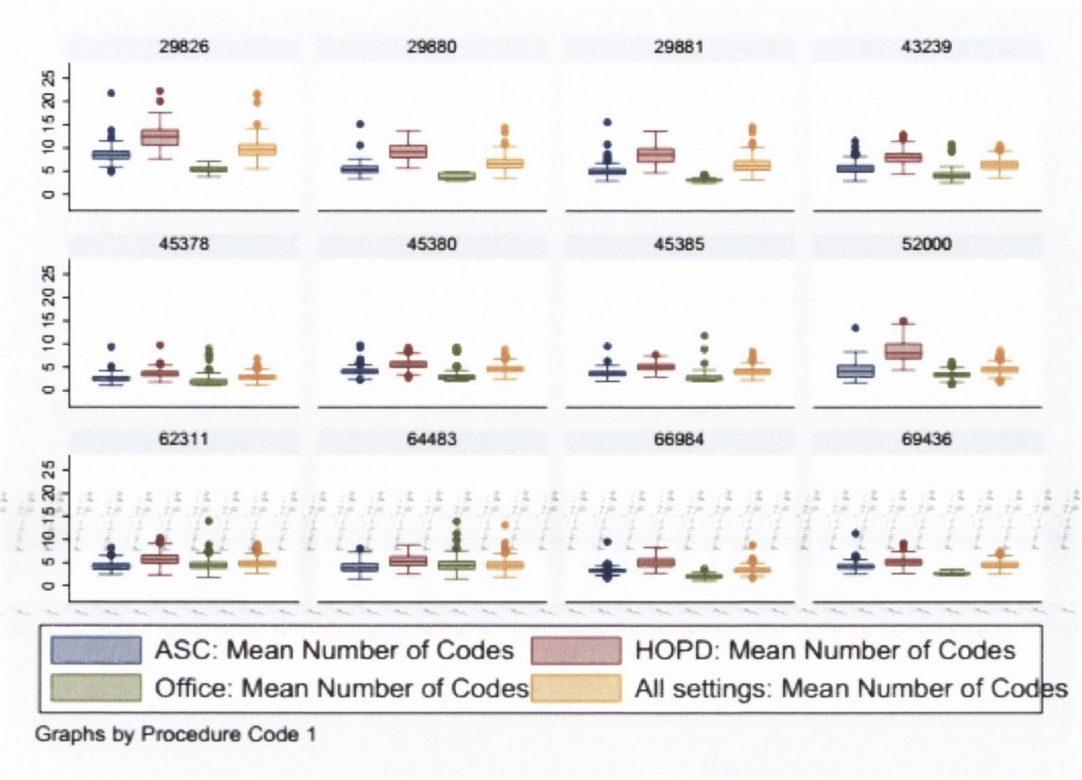

Figure 11.5: Mean number of codes alongside the primary CPT code

of change occurring in other years.

The pattern of coding by setting was analysed. This involved comparing the number of codes billed alongside the primary surgical CPT code of interest. Some selected examples of billing are presented in Tables 11.8 and E.24 (the latter in Appendix E). Each row represents an individual code, and in each example all codes apply to the same patient / day. The dollar amounts are omitted from each row; however, each row (code) is associated with a charge to the insurer. In some cases a facility payment (for a HOPD or ASC) is uncategorised, as it is not associated with a CPT or revenue code. Of the total spending on codes billed alongside the twelve CPTs of interest, less than 2% was on CPTs that were "uncategorised", and among these CPTs the code accounting for the most spending was less than 0.2% of total spending.

Example 1:			
Facility/ Professional	**CPT**	**revcode**	**description**
P	45380	-	Colonoscopy, flexible, proximal to splenic flexure; diagnostic, with or without collection of specimen(s) by brushing or washing, with or without colon decompression (separate procedure) with biopsy, single or multiple
P	43250	-	Upper gastrointestinal endoscopy including esophagus, stomach, and either the duodenum and/or jejunum as appropriate; diagnostic, with or without collection of specimen(s) by brushing or washing (separate procedure) with removal of tumor(s), polyp(s), or other lesion(s) by hot biopsy forceps or bipolar cautery
P	43239	-	Upper gastrointestinal endoscopy including esophagus, stomach, and either the duodenum and/or jejunum as appropriate; diagnostic, with or without collection of specimen(s) by brushing or washing (separate procedure) with biopsy, single or multiple
F	-	-	-
Example 2:			
Facility/ Professional	**CPT**	**Revenue code**	**description**
P	88305	-	Level 4 Surgical Pathology, gross and microscopic examination
P	45385	-	Colonoscopy, flexible, proximal to splenic flexure; diagnostic, with or without collection of specimen(s) by brushing or washing, with or without colon decompression (separate procedure) with removal of tumor(s), polyp(s), or other lesion(s) by snare technique
F	-	312	Laboratory pathological-histology
F	-	750	Gastro-intestinal services-general classification
F	-	250	Pharmacy-general classification
F	-	258	Pharmacy-IV solutions
F	-	272	Medical/surgical supplies-sterile supply

Table 11.8: Examples of codes occurring during a single "patient day" of care

11.4 Discussion

In Chapter 9, the arguments in favour of ASCs were noted. Proponents argue that ASCs can result in reduced length of stay and a lower unit cost per surgical patient, and this may free up inpatient facilities for the care of more complex and acutely ill patients. ASCs may increase the flexibility of clinicians to redesign care processes, enabling a reduction in perioperative times and increased levels of patient satisfaction.

But even if these assertions are valid, a shift from inpatient to ambulatory surgery may not result in lower aggregate spending. Such a reduction is only likely to be achieved if some hospital beds are closed. If hospital beds are used for the treatment of additional patients this may increase aggregate spending. A critical mass of hospital beds must be closed in order to enable a reduction in staffing levels and net savings [289].

This analysis did not uncover evidence that ASC market structure is associated with a change in the volume of surgical procedures. There was a significant association with volume for a number of DRGs however. For three DRGs, ASC market entry was associated with a decrease in volume, while for two DRGs there was an increase in volume. It is plausible that ASC market structure has consequences for the production of DRGs, even though ASCs do not carry out these interventions. For example, hospitals may respond to ASC market entry by increasing the volume of certain DRGs to compensate for a loss in volume of profitable services. Alternatively, hospitals may lose the ability to cross-subsidise unprofitable DRGs, and therefore may lower production of certain DRGs.

There was a significant increase in volume for chest pain (DRG 313) and major joint replacement (DRG 470). It is plausible that hospitals increase the admission rates of patients who present to an emergency department with chest pain, if there is an increase in spare capacity in the hospital following ASC market entry. Similarly, hospitals may conduct a higher rate of major joint replacement to compensate for loss of patients (and revenue) to ASCs.

A statistically significant reduction in the level of production occurred for three DRGs: "Other skin, subcutaneous tissue, and breast procedure with major complications or comorbidities" (DRG 579); Mastectomy for malignancy (DRG 583);

Cesarean section with complications or comorbidities (DRG 765). It is implausible that ASC market structure would impact on the population rates of breast cancer and pregnancy. Nonetheless, hospitals may respond to ASC market entry by changing the intensity of interventions for pregnant individuals or those with breast cancer, or by up-coding DRGs to increase revenue.

However, caution is warranted in interpreting these results. There is significant potential for spurious findings due to the conduct of multiple regression tests. This increases the likelihood of false positive results. Consequently, there is not a strong case for interpreting these changes to be a result of ASC market structure.

By contrast, ASC market entry was associated with price reductions for multiple CPT surgical procedures. The CPTs are shown below, together with the mean reduction in price for an increase of one ASC per 100,000 population:

I Upper gastrointestinal endoscopy and biopsy (CPT 43239), a reduction of $40.30

II Diagnostic colonoscopy (CPT 45378), a reduction of $27.99

III Colonoscopy and biopsy (CPT 45380), a reduction of $54.43

IV Lesion removal colonoscopy (CPT 45385), a reduction of $76.01

V Cystoscopy (CPT 52000), a reduction of $82.25

This observed pattern of price reductions could have arisen for a number of reasons. The results could be spurious, arising as an result of the large number of regression tests that were conducted. However the observed results could also reflect downward pressure on prices instilled by ASC market entry. ASC market entry can increase the level of competition in a market, and enhance the negotiating position of insurers *vis-a-vis* hospitals. This could enable insurers to extract improved value from hospitals.

Patients in the USA frequently encounter out-of-pocket payments for surgery, and these payments can be substantial for patients enrolled in certain health plans (e.g. high-deductible health plans). These payments can be of greater magnitude for care provided in hospitals than in ASCs. This instils incentives for patients

to undergo treatment in an ASC rather than a hospital, which could augment competitive pressure on hospitals.

It bears emphasis that ASC market entry may reduce the ability of hospitals to cross-subsidise less-profitable forms of care, and this could instil upward pressure on hospital prices for procedures that are not provided in ASCs. This thesis paper did not uncover evidence to support this hypothesis. To address this question, future research could investigate price effects for DRG admissions.

The quality of ambulatory surgery in Ireland

In many Irish settings there is evidence of sub-optimal quality in the provision of ambulatory surgery. This is related in part to issues of skill mix and interprofessional teamwork.

For patients scheduled to undergo day surgery, pre-operative assessment is important to identify risk factors that might render ambulatory surgery clinically inappropriate. This form of assessment is perceived to reduce the risk of procedure cancellation. The Health Service Executive (HSE) advises that assessment should be conducted by nurses, with oversight from consultant physicians. Protocols should be in place to ensure appropriate input from consultants such as anaesthetists. However, many Irish hospitals routinely fail to align the skills of team member with patients in this recommended manner [305].

Clinical guidelines in Ireland also recommend that nurses lead the process of patient discharge and communication with primary care physicians, while adhering to clearly specified criteria for intervention by a physician. However, in around 50% of cases in Irish hospitals, nurses failed to assume responsibility for discharge. In two thirds of cases, discharged patients were not provided with information relating to pain relief, while in half of cases patients were not provided with emergency contact details [305]. Figure 11.6 depicts the steps in a recommended patient pathway in the Irish context, and this illustrates some of the scope for multidisciplinary workflows in ambulatory surgery.

After recognising the uneven quality of certain aspects of ambulatory surgery in Ireland, the HSE is seeking to improve the levels of teamwork and care processes, in partnership with the Royal College of Surgeons of Ireland. There has been no

scientific evaluation of this programme [305].

The improvement of ambulatory surgery in Ireland will require multidisciplinary skills. A transition to novel organisational forms is insufficient to optimise quality. For instance, nurses must be well-trained in tasks such as pre-operative assessment, liaising with primary care physicians, and in managing various processes of the surgical intervention. This requires multifaceted change management [289].

But there is a case for experimenting with novel organisational forms including ASCs in the Irish context, as this added degree of specialisation could plausibly facilitate improvement in quality. In addition, in comparison with ambulatory surgery in a hospital (or in an ASC co-located with a hospital), free-standing ASCs can have a lower risk of hospital acquired infections [289].

While this thesis paper has not uncovered strong evidence in favour of the introduction of ASCs, it has uncovered evidence that is suggestive of potential benefits of ASCs. Specifically, there is limited evidence that ASCs may instil downward pressure on procedure prices in the USA.

However, even if these findings were proven to be valid, they may have limited applicability in the Irish context. As noted in Section 1.3 of this thesis, there are marked differences between the Irish and American health systems. The USA is a pluralistic environment of competing payers, whereas the bulk of financing in Ireland is channelled through the public sector HSE. Ambulatory surgery patients in the USA may be more sensitive to price signals than patients in Ireland, due to the comparatively high level of out-of-pocket payments for surgery associated with many health plans in the USA. Therefore, caution should be exercised when generalising any findings to Ireland. Nonetheless, there may be a case for implementing a limited number of ASCs in Ireland and subjecting this innovation to careful evaluation.

Another organisational form for the provision of ambulatory surgery is office-based surgery. In this setting, the intervention is provided in a surgical annex in a clinician's premises. The evidence in favour of this surgery is less favourable than ASCs. Evidence is scant, but one study in the USA found that these settings have been associated with a ten-fold greater risk of mortality or serious adverse event compared to an ambulatory surgery centre. A system of regulation and accreditation is not in place for office-based surgery in the USA [306]. In some office

settings there may be poor quality facilities, insufficient monitoring of patients, safety breaches such as the absence of a specialist anaesthetist, and clinicians undertaking procedures for which they are poorly trained [289].

11.4.1 Limitations

This study has some limitations. First, office-based providers may exert a competitive effect in the market for ambulatory surgery. Due to the absence of rigorous data it was not feasible to include as a covariate the number of office-based providers.

The Truven dataset includes utilisation data from three settings: HOPDs, ASCs and office-based surgeries. This dataset does not enable the identification of any individual provider organisations, but it is possible to infer the type of setting based on the value of a number of variables. The second limitation of this study relates to the classification of care into these three provider forms. It was assumed that surgery was conducted in an office setting if the payment did not include a facility fee. However, payment mechanisms can vary between insurers therefore this may not be universally accurate. This limitation applies to the descriptive comparison of price and volume by setting. It does not impact the price or volume regressions, as these analysed price and volume collectively across all forms of providers within a MSA to gauge the overall impact of ASC market entry.

Third, although the number of hospitals was included as a covariate in a sensitivity analysis, it was not possible to specify whether these were members of multi-hospital systems. A previous study found that such hospitals can extract higher prices from insurers (34% versus 17% price growth over 1997 to 2003) [307].

Fourth, an assumption is that inclusion of comparator groups (DRG and E&M codes) can isolate the impact of ASCs on CPT price and volume. However this assumption is vulnerable to criticism.

Fifth, it was not possible to discern the ownership status of ASCs. The CMS Provider of Service dataset contains a variable to indicate whether an ASC is "freestanding", but this variable can be interpreted in multiple ways. It may imply that an ASC is located on separate premises to a hospital, rather than implying that an ASC is or is not owned by a hospital. Of note, there may be differences

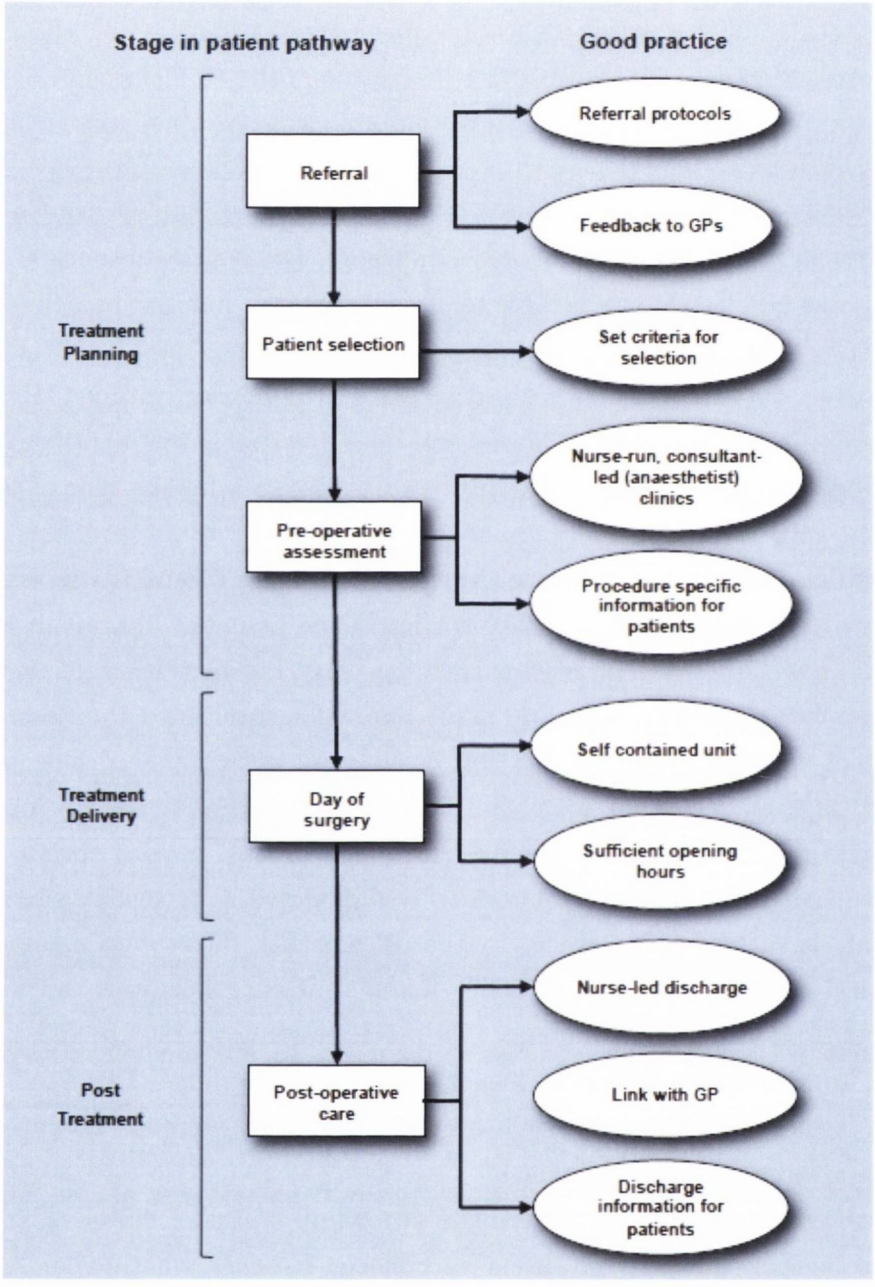

Figure 11.6: Day surgery patient pathway

in the negotiating power of ASCs *vis-a-vis* insurers depending on the ownership status of ASCs, and this may impact price and volume. For example, ASCs that are jointly owned by hospital systems may be able to leverage higher prices from insurers. However, as a majority of ASCs are entirely physician-owned, this is not a major limitation of this study. The sixth limitation is that it was not possible to discern the specific services provided by each ASC in the Provider of Service dataset.

Part V
Conclusions

Chapter 12

Conclusions

12.1 Outcomes of this thesis

The problems of modern healthcare systems are varied. Some common criticisms of the systems in Ireland and the USA include uneven quality of care, failure to tailor care to the individualised needs of patients, inequitable access, and wasteful spending. It may be possible to alleviate these problems by reconfiguring service providers to meet the needs of patients. These changes can comprise implementation of new organisational forms and the adjustment of skill mix.

Changes to the skill and provider mix often occur in an ad-hoc manner, determined partly by local availability of skills, resources, and leadership capacity. An example is the management of warfarin therapy by pharmacists and nurses in the Boston area (see Chapters 3 - 5), which arose due to the idiosyncratic characteristics of healthcare provision in these provider institutions, notably the availability of trained personnel. Of note, this variability in context means that caution is required in extrapolating findings to other settings. Research studies do not necessarily generate transferable solutions for widespread implementation, but rather generate insights which must be interpreted and modified in light of local conditions. The issue of generalisability is examined further in the following pages.

In other cases, changes to the provider mix occur through systematic policy intervention. An example is the administration of influenza vaccination by phar-

macists across the Republic of Ireland. This innovation is underpinned by national legislation, support from a range of policy bodies, and a centralised and standardised approach to training. This policy is evaluated in Chapters 6 to 8.

The configuration of providers varies frequently across geographic areas. It is sometimes possible to exploit this variation, using statistical techniques, to ascertain the effects of alternative provider configurations on performance. An example of regional variation in the provider mix is presented in the ASC study in Chapters 9 - 11.

Changes to the provider mix can potentially impact the level of clinical quality, efficiency, access and patient-centredness. There is need for a vast number of empirical studies to investigate these changes. However, difficulties in obtaining rigorous and reliable data render it difficult to evaluate many changes, and this leads to gaps in our understanding. This thesis expands the evidence base, by gathering and analysing data on performance indicators for three forms of change to the provider mix. Although these papers address but a small fraction of the diverse changes occurring to the configuration of providers, this adds to our understanding of this evolving area, and can potentially inform policy decisions.

Due to the persistent and iterative nature of changes in health care delivery, the findings of research studies may be valid only for a limited time. For example, changes in educational standards, provider reimbursement mechanisms and information technology may render study results obsolete. The dynamic nature of organisational change creates persistent need for evaluation. But the relationship between research and policy change is interdependent and dynamic: the publication of research findings can spur policy changes, and policy changes create a need for further evaluation.

The empirical findings of this thesis should be considered in light of the published literature relating to skill mix and provider configuration. Collectively, these findings support the view that in certain circumstances, changing the mix of provider organisations and personnel is a viable policy instrument, which may be an effective mechanism to improve performance in certain dimensions.

In some cases, changes to the provider mix will not impact on quality, and in these circumstances it is appropriate to implement the lower cost option. The lowering of costs, *ceteris paribus*, frees up resources for investment in other parts

of the healthcare system. Whilst the primary goal of health care is to alleviate suffering and enhance longevity, it is also important to manage resources efficiently in order to improve access to services and enhance population outcomes.

The question arises, to what extent are the findings of this thesis generalisable to the wider health system? This depends on a variety of factors, including the execution skills and commitment of policy makers, clinical leaders, managers, and other frontline personnel, the availability of local resources, and the presence of well-developed systems of care management and quality assurance. Furthermore, interventions such as influenza vaccination and anticoagulation management are relatively well-characterised clinical areas, with protocols that are amenable to adoption by multiple categories of clinicians. These protocols reduce the need for expert clinical judgement to an extent. By contrast, the management of other clinical areas may be less well-characterised and less amenable to changes in skill mix.

Consequently, the findings of this thesis are not necessarily applicable to all clinical areas and provider settings. But this thesis demonstrates that in some contexts, given an appropriate blend of culture, training, and managerial and quality oversight, provider reconfiguration can be an effective policy instrument.

12.1.1 Changes to skill mix: implications for chronic disease management

There has been a dramatic increase in the amount of knowledge in the health care domain. As a consequence, there is increased diversification of healthcare professionals into areas of specialised knowledge and skills. This offers advantages as well as challenges for clinical teams. These changes can improve the ability of providers to manage the care of chronically ill patients, by aligning the skills of team members with the needs of patients over time. But there are challenges in modifying skill mix and achieving cohesive teamwork. These issues warrant scrutiny and are the focus of this sub-section.

Multidisciplinarity increases the range of knowledge, skills and abilities available to a clinical team. This can lead to improved capabilities for specific tasks and novel insights that lead to superior outcomes, compared to homogeneously staffed

teams [308]. The future performance of chronic disease management will depend significantly on the functioning of multidisciplinary teams, notably the ability of these teams to divide labour and to communicate effectively.

The burden on primary care physicians may continue to increase due to demographic changes, the introduction of new forms of interventions, and increasing public expectations. Therefore, developing the role of other healthcare professionals such as pharmacists and nurses is a key tool to supplement the role of physicians. This can free up the time of physicians for more complex tasks such as the management of patients with chronic co-morbidities, and thereby enhance the efficiency of resource allocation.

The literature shows that team-based care is important for the care of patients with a range of clinical conditions. Team-based care may be particularly important for patients suffering from multiple morbidities, as these patients may require a diverse spectrum of clinical interventions, education, and motivational counselling [309, 310]. Teams constitute a mechanism to align clinical expertise with the multifaceted needs of patients. As noted in Chapters 3 to 5 of this thesis, in the management of warfarin therapy in certain sites, the bulk of care is delegated to pharmacists or nurses. Physicians are responsible for more complex clinical cases, for example patients with co-morbidities whose care requires more sophisticated clinical judgement.

The nursing profession is the largest segment of the health care workforce. Evidence shows that the quality of care of nurses in the management of chronic illness is equivalent to physicians in some circumstances [311, 312]. Moreover, nurse practitioners may reduce costs and maintain quality in the management of certain minor ailments, which may free up the time of physicians for more complex aspects of chronic care [313]. There is a risk that the evidence base is distorted due to publication bias, as studies with favourable findings may be more likely to be published. Nonetheless, on balance the evidence indicates that in some clinical contexts, nurses can reach levels of performance that are at least equivalent to physicians. This has important implications for skill mix and the care of chronic conditions, particularly in light of projected demographic changes.

Similarly, pharmacists can play an effective role in a number of clinical areas. Pharmacists are extensively trained in the use of medicines, typically encounter

patients more frequently than other clinicians, and consequently may be suitably placed for an increased role in the management of various chronic illnesses. There is evidence to suggest that pharmacists can provide effective care for patients with asthma [314], hypertension [315–318], and elevated cholesterol levels [319, 320].

The potential role of pharmacists in anticoagulation management is illustrated in the first paper of this thesis. The administration of influenza vaccine is another example of aligning the skills of pharmacists with the needs of patients. Influenza vaccination is a component of high quality care for many chronically ill patients, such as those with chronic obstructive pulmonary disease.

In some instances, the benefits of expanded roles for pharmacists have been less than anticipated and there may be adverse consequences [321]. This highlights the need for careful oversight of any changes in skill mix. On the whole the evidence base is mixed, but there appears to be a beneficial role for pharmacists in some aspects of team-based care of chronic illness [321].

Evidence on skill mix from Ireland

Internationally, there has been major expansion in the number of specialist and advanced practice roles for nurses and midwives. In Ireland, professional authorities have developed rigorous practice frameworks and credentialling processes for these posts [322]. Nurse and midwife specialists in Ireland require at least five years of post-registration experience, including two years in the selected area of specialist practice, while advanced practitioners require at least seven and five years respectively [323].

The body of evidence on these roles in Ireland is modest but growing. Of note, a national evaluation of clinical nurse and midwife specialists (CNS/ CMS) and advanced nurse and midwife practitioners (ANP / AMP), known as the SCAPE study, assessed the role and outcome of these clinicians [324].

The key duties of these roles pertain to case management and provision of services. According to the SCAPE study, clinicians in these roles are perceived to exert superior impact on readmission rates, waiting lists and waiting times, collaborative decision-making, continuity of care, and management of workload. The increased autonomy of these roles, compared to non-postholders, is perceived

to enhance the transition of patients throughout the health system. For each role there is evidence of a high level of satisfaction with physical care, practical advice and emotional support [324].

SCAPE uncovered evidence that clinical specialists and advanced practitioners provide a higher level of care relative to non-postholders in comparable sites [324]. Evidence shows that clinical specialists engage in audit, evidence-based practice and research, to a greater extent than non-specialist nurses in comparable sites [323]. Of note, compared to nurse specialists, advanced practitioners have greater diagnostic responsibility, engage in more research activities, and may exhibit superior clinical leadership [324].

The SCAPE study found four mediating factors that moderate a practitioner's leadership capacity. The four factors are an explicit framework for professional development, creation of opportunities to act as leaders, tools to sustain leadership, and the individual qualities of practitioners. This conceptual framework can aid leaders and managers in stimulating leadership potential in an evidence-based manner [325].

In Ireland, the provision of maternity care is predominantly hospital-based and consultant-led. Since 2004, however, midwife-led care has been available to some women in a hospital setting. The impact of this model of care in Ireland was assessed by the MIDU trial. The trial randomised 1,653 pregnant women, all at low risk of complications, to receive midwife-led or consultant-led care [326].

In MIDU, no significant difference emerged between study arms for the seven primary outcomes: caesarean section, episiotomy, induction, instrumental birth, Apgar scores, postpartum haemorrhage, and breastfeeding initiation. But midwife-led care was associated with less intense interventions, as the rates of continuous electronic foetal monitoring and augmentation of labour were significantly less in this arm. The generalisability of this study may be high, as participating sites appear comparable to many birthing units in the United Kingdom and other countries [326].

In general, strict criteria are needed for appropriate transfer of patients from nurse- or midwife-led care to consultant physician-led care, to minimise the risk of complications and to match clinical skills to patients' needs [327]. In Ireland, during a five year period after the MIDU study (2008-2012), an observational

study found that the antenatal transfer rate from midwife-led care to consultant-led care was 38.5%, while 13.2% of women transferred to a consultant-led unit during labour and birth. This suggests that criteria are established to transfer women from midwife-led care to consultant-led care in the Irish setting [328].

Psychosocial impact

Section 2.2.2 discussed the challenges of fulfilling the psychosocial needs of patients. These needs include dignity and autonomy, and are the subject of a growing body of literature (e.g. [329–331]). Patients are more than the sum of their clinical conditions, and clinicians should consider the effect of medical intervention on the goals, aspirations, and social wellbeing of patients. The priorities of patients may differ from clinicians, as noted in a paper on "goal-oriented patient care" by Reuben and Tinetti [332]. The paper describes a hypothetical elderly patient with Parkinson's Disease whose priorities include maintaining contact with relatives via the Internet, whereas the clinician's priority may focus on reducing clinical manifestations of illness. Such divergent goals may conflict, and this can pose problems for medical decision-making.

When clinicians' priorities diverge from patients, dialogue is required to reconcile these priorities and to optimise the patient's well-being. For example, a patient with Parkinson's Disease may prioritise the maximisation of mobility, even when a trade-off exists against medication-related dyskinesia and mild confusion [332]. A process of shared decision making may facilitate this collaborative process, to reach the optimal outcome for patients' clinical and psychosocial needs [333].

It is important to ascertain the effect of skill mix changes on psychosocial aspects of care. There is evidence that the communication style of nurses, for example, may be superior to physicians in some circumstances [131]. Superior communication may be linked to a more satisfying experience of care, and to decision-making processes that support patients' integrity and autonomy [331]. As noted in Section 2.2.2, respect for patients' psychosocial needs may also be linked to medication adherence [331, 334, 335].

Whilst not the primary focus of this thesis, this research has added to our understanding of the degree of satisfaction and "patient-centredness" associated

with nurse-led and pharmacist-led warfarin services (Chapters 3 to 5). Similarly, the implementation of pharmacist vaccination and expansion of ASCs is motivated in part by the goal of convenience and satisfaction for patients. The research in Chapters 6 to 11 has assessed the economic effects of these policy changes, which can complement future research into the accompanying psychosocial effects.

The challenges of teamwork

Despite the potential for improved quality for chronically ill patients, there are challenges in achieving high-performing, team-based health care. For instance, a body of literature on diversity indicates that multidisciplinarity is not always beneficial for a team's performance. The relationship between multidisciplinarity and team performance is not necessarily linear and positive, and the relationship appears contingent upon a number of factors [308].

According to research and theory on social identity and self-categorisation, many teams may be unable to capitalise on the potential benefits of multidisciplinarity. Humans have a tendency to simplify the world and sort themselves and others into heuristical, social categories to bolster their sense of identity, based on dimensions such as age, gender or professional affiliation. To improve their self-image, people often develop positive judgements about their own category and more critical views of members of other categories. A positive bias towards one's own category can exist alongside distancing from other categories. This can offset the potential benefits of multidisciplinary teams [308].

Accordingly, a research study showed that people with a strong identification to their functional background made less contribution to team performance, in settings where individuals from their functional background formed a minority. The authors concluded that a multidisciplinary team composition, in which clinical skills are well matched to the needs of patients, may be necessary but insufficient for high performance [336]. Effort is required to ensure that the authority gradient in clinical teams is not excessively steep, that team members feel valued and respected, and that team leaders adopt a clear manner of communication. Collectively, these strategies may bolster team cohesion and performance [6].

One empirical study hypothesised that multidisciplinarity only improves team

outcomes if the standard of team processes is high. The study used the quantity and quality of innovation as the outcome variable. The study argued that high quality team processes are characterised by frequent interactions, trust, reflexivity and the pursuit of a shared vision, and moreover that these processes can offset the limitations of multidisciplinarity that are suggested by the literature on social identity and self-categorisation. Commitment to a shared, superordinate goal serves as an integrating force to enable teams to overcome these limitations. The study found that team processes significantly moderated the quality of innovations, but there was a non-significant effect of team processes on the quantity of innovations [308].

Increased interdependence among different health care professions can raise cultural tension that may negatively impact the quality of care. The formation of high-performing teams in healthcare can be impeded by allegiances to professional groups, and there may be latent tension, resentment or mistrust between different categories of clinicians [337]. There may be sensitivities around traditional professional duties and accountability, and in some settings active and passive resistance may interfere with team cohesion and clinical care [338, 339].

Team-based care requires planning and management. In some instances the members of clinical teams may be unaware of their precise roles and duties, which can dampen quality of care. Clinicians may compensate for ambiguity by seeking to cover all information areas for a patient, and this may increase the vulnerability of clinicians to burnout or feelings of being undervalued. The risk of conveying contradictory information to patients is elevated in this context, and important information may be overlooked [340–342]. One study found that certain team members frequently engage in major discussions with patients without the knowledge of other team members [340].

Consequently, when implementing changes in skill mix and team-based care, it is important to be conscious of the risk of discontinuity of care and sub-optimal communication. In Ireland, pharmacists must notify the PCRS authorities when each influenza vaccination is administered. This system seeks to mitigate the risk of discontinuity of care between pharmacists and physicians. More generally, continuity of care can be enhanced by process mapping and clear allocation of roles and responsibilities within teams. Periodic team meetings in which participation

by all team members is encouraged may also improve communication between team members, and improve the coordination of care. The term "social capital" is a euphemism for bonds of trust, reciprocity, shared values and norms between individuals, teams and communities, and this may contribute to the cohesiveness of clinical teams. A set of strategies to enable clinicians to increase the quality of "social capital" in teams has been set out. These strategies include allowing clinicians to work at the "top of their license", whereby clinical skills are used appropriately, and adopting a direct and clear manner of communication [343].

According to one study, 39% of senior oncology nurses and a quarter of physicians reported "communication with colleagues" as one of the most difficult and stressful aspects of their work [344]. A number of studies found deficits in communication standards within multidisciplinary teams. One study of team meetings in a London hospital found that occupational therapists, social workers, physiotherapists and nurses were rarely asked for opinions, and rarely contributed their opinions. Physicians, and in particular consultants, tended to adopt more dominant roles within a team. This lack of input may result in excessive conformity and missed opportunities to enhance care [345].

Another challenge in implementing changes to skill mix may be confusion regarding hierarchy. As a simple example, there may be disagreement about whether a physician team leader or a senior nurse (who is not a team member) should assume responsibility for managing the performance of a nurse [337].

Researchers have argued that in some settings, a mediating factor in team performance and culture may be gender. In a study that uncovered evidence of poor communication, 90% of nurses were female, and all occupational therapists and care managers were female. These categories of caregivers contributed relatively infrequently in team meetings [345]. In another study, male nurses stated that the hierarchy with physicians was less steep, compared to the experience of female nurses [346].

Evidently, multidisciplinary care can improve quality but is associated with a number of challenges. It is important to note that communication and teamwork are almost ubiquitous challenges, even in monodisciplinary contexts without innovation in skill mix or provider configuration. Alterations to skill mix can improve or worsen the level of communication and quality. These elements of care must be

carefully managed in all contexts.

Lessons from outliers

It is possible to learn pertinent lessons, of both a positive and negative nature, from outlier teams. Some outlier teams perform at sub-standard levels (negative deviants), whilst others achieve particularly high levels of performance (positive deviants). Investigation of the reasons for this variation away from the median can lead to actionable insight [37].

Whilst there may be more variation in performance within individual organisations than between organisations, a number of provider institutions have achieved a reputation for attaining a critical mass of high quality care across teams and specialties. An example is Intermountain Healthcare in Utah, where a number of teams are considered to have achieved high levels of cohesion and performance. The execution of numerous, carefully crafted patient pathways plays a central role in assuring quality. A team of statisticians and other researchers continuously analyses variation in process and outcomes, to draw inferences on how to improve care, which feeds back into the refinement of care protocols.

This is underpinned by a focus on cohesive teamwork across the spectrum of health care workers. For example, administrators are given clearly defined roles in tasks such as recording patient information and vital statistics (such as weight and blood pressure), and team members from the level of administrators to physicians are rewarded collectively with financial incentives to encourage teamwork [327].

A lesson emerging from the first paper of this thesis (Chapters 3 to 5) is the potential importance of performance measurement in achieving and sustaining high quality care. Performance metrics serve as a tool to detect outlier teams. To combat wide variability in the quality of warfarin management, the four centres in this paper have participated in quality improvement collaboratives in which performance is monitored routinely, and providers share strategies for enhancing quality. If one centre is a "positive deviant" in a certain aspect of care, other centres can examine this behaviour and assimilate lessons for improvement. Rapid cycles of feedback from performance measurement enable clinicians and managers to identify sub-optimal care, and to take steps to improve teamwork and care

processes.

Across the four warfarin centres, this is reflected in clinical quality that exceeds that of numerous other observational studies. In the absence of performance measurement it appears unlikely that changes to skill mix would have reached this level of effectiveness. Reconfiguration of providers is important, but this is only one aspect of a multifaceted improvement strategy that must incorporate diligent oversight of performance.

Nonetheless, the drawbacks of performance measurement bear emphasis, as noted in Section 2.2.1. Performance measurement imposes an opportunity cost, and the time that clinicians spend auditing performance could have been spent on direct patient care. Excessive performance measurement can have unintended, negative consequences, and performance metrics should be selected judiciously [41].

12.1.2 Ambulatory surgery

Changes to skill mix can occur in traditional settings such as hospitals, or in alternative provider models such as the ASC. This thesis illustrated the potential for innovative organisational forms to impact on performance. It is argued that specialised organisational forms may be more effective at leveraging the potential benefits of multidisciplinary care. The impact of the ASC organisational form was explored in Chapters 9 to 11.

Proponents argue that ASCs permit greater flexibility to refine skill mix arrangements to meet patients' needs. This flexibility may enable streamlined care processes, in which nurses adopt a more active role in pre-operative assessment and post-operative discharge. The creation of ASCs tends to lower market concentration, and competition in the market for episodic care may be a useful countervailing force to provider market consolidation, which is often associated with higher rates of spending growth.

Chapter 11 explored the empirical impact of ASC market entry on price and volume. As discussed, the intraclass correlation coefficient (ICC) compares the degree of variance between and within geographic market areas, and this is done by quantifying the correlation between units of analysis within and between market areas. The ICC represents the degree of "nesting" in the data hierarchy [347].

In Chapter 11, the ICC indicates that a significant degree of variation in the two outcomes of interest, price and volume, is attributable to nesting effects. Essentially, the geographic market area parameter exerts an important effect on price and volume, and this higher level parameter significantly outweighs the measured impact of other variables in the model.

Accordingly, it is clear that geographic variation is a dominant driver of variation in price and volume. Whilst this analysis provides insight into the effect of ASCs on market entry, a deeper understanding of the characteristics and causes of variation in price and volume by region requires further empirical analysis that lies beyond the scope of this Ph.D. thesis. In future analysis it may be helpful to model the effect of additional variables that underpin this regional variation, and the inclusion of additional variables in a larger research project may explain a greater proportion of total variance. On the other hand, much regional variation may arise from idiosyncratic market features for which data are limited or unavailable. In Section 12.1.4, I discuss potential explanations for the substantial degree of regional variation.

Evidence indicates that ambulatory surgery is a safe approach when staff members are adequately trained, supervised, and adhere to recommended guidelines and principles. Minor adverse events are quite common during the post-operative period and these include pain, nausea, vomiting, fatigue, headache, and drowsiness. There is a link between the effectiveness of regulation and quality of care, as ambulatory surgery has been associated with elevated rates of more serious adverse events where regulation or accreditation are limited [6, 348–350].

The active participation of all staff members is important for high quality ambulatory surgery. A cohesive team should include nurses, surgeons, anaesthetists and managers. According to some analysts, the efficiency and effectiveness of ambulatory surgery units are optimised when management and staff are exclusive to the service, and when there is dedicated administrative infrastructure to deal with patient flows and scheduling [289]. The degree of success of different countries in achieving this goal is discussed in the next subsection.

Varying success in the transition to ambulatory surgery

There is wide variation in the degree to which countries have shifted from inpatient surgery to ambulatory surgery. Similarly, there has been a variable degree of evolution from the traditional organisational setting for surgery, the hospital, to new organisational forms. In the USA, perceived systemic problems include under-investment in primary care services, and a disproportionate spend on hospital services relative to other industrialised countries. But there has been significant shift in the setting of care to organisations such as the ASC.

The proportion of surgeries provided on an ambulatory basis appears to vary widely across countries. For a bundle of procedures, the proportion of day cases varied from under 10% (Poland) to over 80% (USA and Canada). There was much variation for individual procedures, ranging from 0% to over 90%. Some of this perceived variation may be attributable to data inaccuracies and inconsistent definitions, or to the treatment of less severe cases in certain countries (potentially related to supplier-induced demand). It appears implausible that inaccurate data could explain all of the variation.

Potential reasons for this variation, and some of the barriers to increased rates of ambulatory surgery, are as follows:

- Regulation: national or state regulations and legislation may prohibit a shift to ambulatory surgery

- Economic incentives for inpatient surgery: reimbursement patterns may incentivise providers to prolong length of stay and conduct surgery on an inpatient basis. It is important to harmonise financial incentives with policy goals. In Slovenia, following the implementation of a fixed payment system that did not differentiate between ambulatory and inpatient surgery, there was a reported 70% increase in ambulatory surgery rates [289]

- Economic incentives for ambulatory surgery: reimbursement patterns may incentivise providers to reduce length of stay in order to bolster revenues. Providers may increase the number of profitable procedures and the treatment of low-severity conditions, and may exploit asymmetrical information to induce unnecessary demand for services (see Section 2.3.1)

- Preferences and habits of clinicians: a lack of emphasis on ambulatory surgery in clinical education may dampen awareness of its potential benefits
- Facility design: health care facilities may not be configured for ambulatory surgery (e.g. poor patient flow)
- Community services and home support: a lack of external support may preclude some patients from undergoing ambulatory surgery
- Organisational capacity: poor teamwork and managerial competencies may impede implementation [289]

Ambulatory surgery in Ireland

In Ireland, a number of problems around skill mix, teamwork and organisational capacity appear to have hindered the transition to ambulatory surgery in some settings. Innovative organisational forms such as the ASC may have a role to play in accelerating the transition to high quality, high value ambulatory surgery.

In Irish hospitals, approximately 247,000 surgical procedures were conducted during 2012. Elective surgery comprised 198,000 of these procedures, and 69% of these elective surgery cases were conducted on an ambulatory basis. The increase in the volume and proportion of ambulatory surgery cases between 2006 and 2012 is shown in Figure 12.1. The Health Service Executive (HSE) estimated that day cases are on average 60% less expensive to perform than inpatient cases [305].

From 2006, the HSE requested hospitals to submit annual data on the proportion of ambulatory surgery (versus inpatient surgery) for 24 surgical procedures. These procedures cover the major surgical specialties. For acute hospitals from 2009 to 2012, the target was for ambulatory surgery to comprise 75% of these procedures. The HSE did not specify a target during 2013 and 2014 [305].

Although rates of ambulatory surgery are increasing in Ireland, they are considered less than optimal. Indeed, the proportion of "non-target" procedures performed on an ambulatory basis has increased at a faster rate than targeted procedures. From 2006 to 2012 targeted procedures increased by 3% compared to a 39% increase for non-targeted procedures [305], as shown in Figure 12.2.

In Appendix E, Figure E.6 depicts the proportion of care provided on an inpatient and day case basis for the 24 officially targeted procedures, in 2006 and 2012. There is considerable variation by procedure. For laparoscopic cholecystectomy, tonsillectomy, and bunion removal, hospitals provided over 75% of cases on an inpatient basis in 2006, and there were modest increases per procedure between 2006 and 2012. By contrast, for myringotomy, reduction of nasal fracture, and excision of ganglion, hospitals provided more than 75% of interventions on an ambulatory basis in each of these years, and there were modest increases from 2006 and 2012.

Figure E.7 depicts the trend from 2006 to 2012 in more detail for six common procedures. The proportion of day cases fell for some procedures in a number of years, illustrating the difficulties in achieving change, but on aggregate the proportion increased for each procedure between 2006 and 2012. Figure E.8 examines the level of variation between hospitals regarding the proportion of services provided as day cases versus inpatient cases, for laparoscopy and the repair of inguinal hernia. There is significant variation between upper and lower quartile hospitals in terms of the proportion of day cases. The greatest increase between 2006 and 2012 occurred in hospitals that were in the lowest quartile.

There is considerable variation across providers. For one hospital, the day case rate was approximately 100% for the 24 selected procedures, whereas the poorest performing hospital recorded slightly over 50%. In maternity hospitals the ambulatory case rate was 86%, compared to 75% in paediatric hospitals, 78% in orthopaedic hospitals, and 82% in ophthalmic hospitals. The organisational arrangements to support ambulatory surgery appear less than optimal. In 60% of Irish hospitals there are no dedicated ambulatory surgery theatres, 25% of hospitals have separate dedicated ambulatory surgery theatres for specific specialties, and 15% of hospitals have separate units with dedicated ambulatory surgery theatres [305]. This situation may be ameliorated by organisational forms such as the ASC, but this would require careful planning and data collection to assure that quality is of high standard, and to avoid inappropriate utilisation of services.

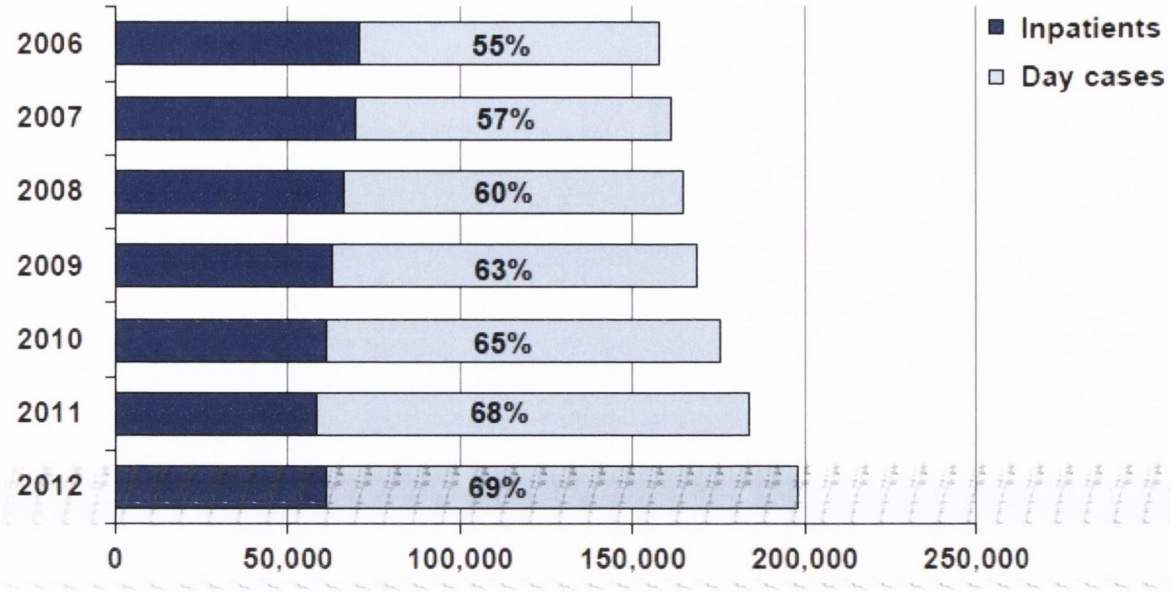

Figure 12.1: Elective inpatient and elective day surgery ratio, 2006 to 2012

12.1.3 Changes in skill mix: lessons for influenza vaccine uptake

As noted in Chapter 6, there is much evidence of disparities in influenza vaccination by geographic area, and by socioeconomic and ethnic groups. These disparities are a result of barriers at the community, provider and patient level. Each layer of barriers may be mitigated by adjusting skill mix arrangements, such as by expanding access to influenza vaccination in primary care settings such as community pharmacies.

Community barriers include the ability to pay for healthcare consultations or the capability to enrol in government-run schemes such as the general medical services or GP visit card schemes. The impact of these barriers is linked to a patient's education level, literacy and language. Another potential barrier is an undersupply of clinicians in certain geographic areas. These factors influence the frequency of consultations in primary care [254]. Allowing pharmacists to administer influenza vaccine mitigates these barriers by increasing the availability of providers and potentially lowering financial hurdles to care.

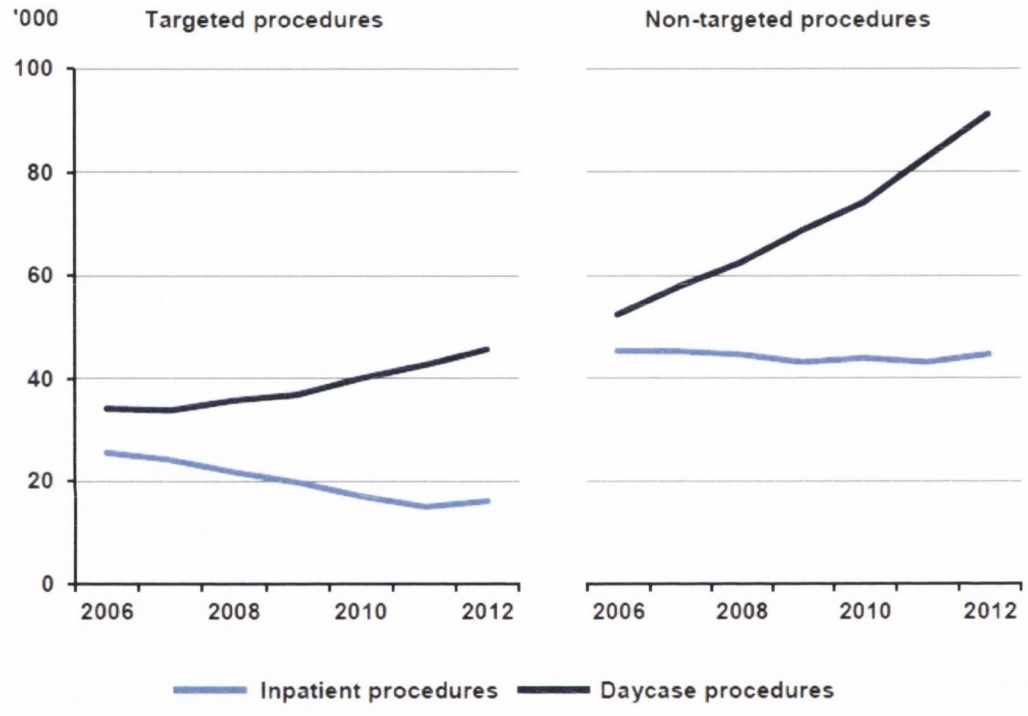

Figure 12.2: Elective surgery volumes for targeted and non-targeted procedures, 2006 to 2012

When a patient attends a provider, the likelihood of vaccination is determined by a potentially complex interaction with the care team. This interaction is influenced by patient preferences, values and beliefs, health literacy, and cultural background, as well as the preferences, priorities and organisational attributes of the primary care office. Nonetheless, evidence from the USA suggests that patients' attitudes are often mutable if there is a clear recommendation for vaccination from a clinician [254].

As primary care physicians typically face a heavy burden of care, they may be unable to optimise vaccination levels alone, due to time and logistical constraints. Yet it may be possible to optimise vaccination rates through a team-based approach. The research base on improving teamwork and uptake rates offers guidance. First, influenza vaccination of at risk groups should be established as a shared goal among all staff. Regular staff meetings that incorporate progress reports provide an arena to discuss changes in strategy. It can be helpful if a single staff member assumes primary responsibility for orchestration of the vaccination campaign [254].

Second, alerts embedded in electronic health records can remind clinicians that a patient has not been vaccinated. Alerts have been shown to improve vaccination rates in some circumstances, although there is a risk of alert fatigue when clinicians encounter an excessive frequency of alerts, which may limit their effectiveness. The benefits of a multidisciplinary team can be realised by coupling alerts with "standing orders". Standing orders delegate responsibility to a team member for the discussion of trade-offs between risks and benefits, and for the administration of a vaccine. The feasibility of a standing order mechanism is influenced by staff qualifications, national or state regulations, and the level of teamwork in an organisation. A third innovation is outreach to patients to increase attendance to primary care clinics for vaccination. The sending of reminders via text message can be a cost-effective intervention [254].

Patients tend to attend pharmacists more frequently than other health care providers, therefore there is intuitive appeal for deploying pharmacists to increase vaccination in under-served subpopulations. The research study in Chapters 6 to 8 offers insight into the potential for pharmacists to enhance vaccine uptake in Ireland. This study indicates that such changes in care delivery may take time

to embed, and the effects may be modest, therefore a multifaceted intervention strategy to enhance vaccine uptake may be needed. From October 2010 to January 2011 pharmacists administered fewer than 5,000 vaccinations. By the 2012-2013 season this had increased to over 19,000 vaccinations, and in the 2013-2014 influenza season to over 41,000 vaccinations. This gradual change may reflect cultural challenges in redefining the professional identity of pharmacists away from the traditional roles of dispensing prescriptions, medicines management, and patient counselling. The gradual change may also reflect logistical challenges in the scaling of training programmes and developing pharmacy capacity.

12.1.4 Changing the provider mix: choices between market and planning interventions

It is evident that changes to skill mix and provider configuration can impact on performance. But what is the best approach to the modification of skill mix? Policy makers in Ireland and the USA have pursued a number of strategies, and these can be broadly categorised as market-based and planning-based.

The introduction to this thesis discussed arguments for and against a market-based approach, in which forces of supply and demand dictate service configuration. Unfettered markets function poorly in the context of healthcare, for reasons such as patients' limited ability to judge the quality or appropriateness of care, and the unpredictable and often catastrophic nature of health care needs and expenditures. Competition may lead to market failures such as cream-skimming of profitable patients and induced demand. Chapters 9 - 11 present empirical evidence on the effects of competition in ambulatory surgery on volume and price.

Therefore competition has to date been a poor instrument with which to address skill mix. For instance, the profit motive may instil incentives to implement a low cost skill mix arrangement, to the extent that patient safety is compromised, as patients are generally incapable of assessing the level of safety of a provider. Competition must be subject to careful regulation to mitigate market failures [287, 351, 352].

Rather than seek to instil competitive market forces, policy makers may micromanage skill mix arrangements. For instance, Californian legislation stipulates

a minimum ratio of nurses to patients for hospitals, informed by the findings of a number of research studies that correlated clinical quality with staffing ratios [353].

At present, two schools of thought guide much of health policy in the USA, each of which has implications for skill mix and the blend of organisational forms. The first is that horizontal and vertical integration of provider organisations can encourage multidisciplinary cooperation, teamwork, and appropriateness of care, and thereby improve quality and costs. There is evidence that certain forms of integration may accomplish these aims [354], but there are concerns that provider consolidation has the potential to facilitate rent-seeking behaviour and unwarranted spending growth. A second strategy is fostering of competitive provider markets to improve performance. As noted, although more competitive provider markets have been associated with a lower rate of price growth, concerns exist over care fragmentation and the effects of a variety of market failures [287].

There are intermediate approaches to the management of skill mix. One possibility is to instil financial incentives to encourage high quality and efficient care, and to give providers flexibility to execute skill mix in accordance with local culture, resources, and patient needs. These incentives could involve diagnosis related group payment for hospitals, where the payment rate is benchmarked against the national mean cost of care delivery for comparable organisations, in conjunction with outcomes measurement.

In the USA, an alternative trend is to pay provider organisations a global budget for managing the care of a defined patient population, known as "accountable care", where the budget is risk-adjusted to reflect the predicted spending levels for different categories of patients, and to discourage cream-skimming (selection of favourable risks) by providers. For example, payment levels are higher for elderly patients and for patients with multiple morbidities. A "shared savings" component means that providers retain a proportion of unspent budget if spending is less than projected. In addition, payment levels are tied to indicators of clinical quality through pay-for-performance arrangements, to limit deficiencies in quality. In an evaluation of an accountable care payment system in Massachusetts, the average quarterly spending per enrollee was $15.51 less for enrolled patients relative to similar but non-enrolled patients. This was associated with increased multidisciplinary care in primary care settings, and this change in skill mix may

have contributed to tempered spending [354].

Markets and geographic variation

A key finding of Chapter 11 is that a high proportion of variance in volume and price is attributable to geographic variation, rather than to other variables included in the models. A rich stream of literature documents the extent of geographic variation in health care utilisation in the USA, but research into the causes of this variation is less conclusive. Payment and regulatory policies in the USA have attempted to temper this variation, whilst retaining predominantly market-based provision of health care, but these policies have had limited success [355]. In England, by contrast, policy makers have pursued more systematic and extensive efforts to link funding and provision to local need. The following paragraphs present some data on the extent of regional variation in the USA, and discuss efforts to curtail unwarranted regional variation in England.

In the USA, much analysis of geographic variation occurs at the level of the 306 hospital referral regions (HRRs) defined by the Dartmouth Atlas. In 2007-2009, Medicare spending was 1.43 times greater for the mean beneficiary in an HRR at the 90th percentile of spending as for the mean beneficiary in an HRR at the 10th percentile, after adjustment for regional levels of rents, wages, and prices for utilities and other services. Most geographic variation arises in the realm of inpatient services and post-acute care [355]. In 2008-2010, the rates of coronary bypass surgery, hip replacement, prostatectomy and numerous other major procedures varied at least four-fold to five-fold across HRRs [356].

Research also reveals substantial variation in health care spending across smaller geographic areas in the USA. Across 3,436 geographic areas (hospital service areas (HSAs)), the ratio of spending on pharmaceuticals at the 75th percentile to that of the 25th percentile was 1.21. Around 43% of adjusted variation in pharmaceuticals spending is between HRRs, and 57% is within HRRs. Many high-spending HSAs are located inside the borders of low-spending HRRs, while many low-spending HSAs are inside high-spending HRRs. This intra-HRR variation indicates that targeting of policies at the HRR level to reduce variation is unlikely to be effective [357]. This extensive variation is likely related to the finding of a high degree

of geographic variation uncovered in Chapter 11.

In an effort to disentangle the sources of geographic variation, Finkelstein et al. exploited data on patient migration across the USA. Around 40-50% of variation in spending is due to patient demand, whilst the remainder is due to specific local supply factors such as medical decision-making and the number of hospital beds [358].

In England there is also evidence of regional variation in health care utilisation that appears to be unexplained by clinical need [356, 359]. However, policy makers in England seek to mitigate unwarranted variation by linking supply of services with measures of population need. By contrast, market forces play a more pronounced role in dictating the level of supply of services in much of the USA.

A number of other high-income countries seek to allocate resources by region on the basis, at least in part, of clinical need. A review of funding allocation formulae in seven high-income settings found distinct differences in formula composition [360]. However, the formulae incorporated, to varying degrees, the following common categories of predictors of clinical need:

- demographics
- health status adjusters
- normative adjustment for unmet need to promote equity
- compensation for care costs not related directly to need (such as geographic wage differentials, additional costs of teaching hospitals, and hospitals in remote areas).

In England, a research team developed and tested over 200 predictive models of hospital costs, based on both individual-level and area-level parameters. The models were developed on a random sample of five million people, and tested on another two samples of five million people. The most powerful predictor variables were person-level age, gender, and ICD-10 diagnostic codes from inpatient admissions. The most effective models predict around 77% of practice-level cost variation and 12% of person-level variation [361]. The implementation of resource

allocation models such as this in the USA could plausibly lower the degree of regional variation in utilisation.

The results in Chapter 11 appear to conform to existing evidence on regional variation, considering the extensive role of market forces in the provision of health care in the USA. Given the explicit efforts of policy makers in numerous other settings to link supply to local levels of clinical need, these results are perhaps unlikely to generalise to other contexts.

Steps forward

In sum, a range of policy options can be adopted to influence skill mix, ranging from *laissez-faire* approaches reliant on market mechanisms, to micromanagement, to intermediate methods such as accountable care incentives. This should be integrated with consideration of local resources and needs, a focus on cultivating clinical leadership, and a culture of collaboration and improvement.

There are challenges in surmounting obsolete but firmly entrenched professional demarcations. This may require reform of regulation, policy, financial incentives, and explicit attempts to reshape culture. Such a multifactorial approach may succeed in extending the roles of disparate health care professionals, achieving collaborative care across disciplines, and reconfiguring providers for high quality.

For example, it is important to ensure that clinicians can practice to the complete extent of their education and training. In the USA, regulations specifying scope of practice limitations differ widely across states. Some regulations contain vague provisions that are open to multiple interpretations, while others are highly detailed. Scope of practice regulations should keep pace with developments in the science of health care delivery, and with the level of training and education of nurses and other professions, for example in prescribing of medications and the management of chronic conditions. However, regulatory regimes in a majority of states do not accomplish this. Although it is important to safeguard patients from an excessively broad scope of clinical practice, overly stringent restrictions may undermine efforts to achieve equitable access to high quality care [131].

Another important ingredient for reform is strong clinical leadership. This is needed to achieve collaborative care and support for care redesign. Professions

such as nursing, pharmacy and physiotherapy must produce leaders to advance practice and act as partners with physicians [131].

In addition, the focus of educational curricula should be updated to ensure appropriate clinical competencies. Innovative educational strategies, such as online education and simulation, may facilitate learning throughout the lifespan of the clinician [131]. Failure to fulfil any of these criteria may result in failure to achieve effective reconfiguration of service providers.

12.2 The PhD as a learning process

The process of preparing this thesis has fulfilled a number of objectives. First, this thesis has generated evidence to enhance our understanding of the impact of changes to the health care provider mix. But another important function of this thesis has been to develop the research skills of the student.

These skills include practical tasks such as data collection, data storage, cleaning, management, encryption, and data quality assurance. The student also developed skills in project planning and management, and gained experience in securing and sustaining the engagement of clinicians and other stakeholders for a research project. Analytical skills include the methods of biostatistics for survey analysis, econometric methods for the analysis of panel data, the conduct of a cost of illness study using primary and secondary data sources, cost-effectiveness analysis, and infectious disease modelling to project the impact of different intervention strategies on morbidity, mortality and costs. More generally, this process has enhanced the student's critical thinking abilities.

But rather than reflect uncritically on the creation of this thesis, it is opportune to reflect on ways in which this work could be improved. There is scope for improvement of the three papers. For the influenza paper, a limitation was the reliance on routinely collected data on the incidence of influenza like illness (ILI). These data are collected in sentinel general practice (GP) settings, selected to be representative of GP settings across Ireland. A number of specimens from each sentinel practice are periodically tested in a laboratory to ascertain the proportion of ILI cases that are genuinely influenza, and this system serves as a useful foundation for assessing the burden of influenza across Ireland.

It may be possible to improve the standard of this research by gathering primary survey data on the incidence of ILI across a wider sample of the population. Particular emphasis could be placed on influenza incidence among individuals who may be less likely to seek formal care, such as individuals residing in areas of comparatively low socioeconomic status and with a lower number of clinicians per capita. Ideally, this would be supplemented by laboratory confirmation of the presence of the influenza virus.

Chapters 3 to 5 addressed anticoagulation management. This project could be expanded by assessing the relationship between medicines adherence and the standard of clinical management as measured using the time in the therapeutic range (TTR). There is no ideal method to measure adherence, and a combination of methods may be best such as medical event monitoring systems, and a self reporting scale such as the Morisky Medicines Adherence Scale. This would shed light on the role of medicines adherence as a mediating factor between patient experience, patient satisfaction, and the surrogate outcome (TTR).

Another way to improve this study would be to gather rigorous data on outcomes of care such as stroke and bleeding, rather than on a surrogate outcome. As noted in Chapter 3, there is a significant body of evidence demonstrating correlation between TTR and harder outcomes such as stroke. Nonetheless, this correlation has a significant idiosyncratic element, and there is limited evidence on how the relationship between TTR and other outcomes varies between patient subpopulations. It was not possible to obtain these data within the constraints of this thesis project.

The third paper addressed the impact of ASCs, an institutional setting that exclusively provides ambulatory surgery and associated activities such as preoperative planning. Future research could improve on this study by assessing the appropriateness of care, for example by examining whether the clinical criteria for necessity are fulfilled, and whether the tenets of shared decision making were reflected in the decision making process. This could incorporate digital recordings of consultations, which may be regarded as the gold standard for assessment of decision making processes, in addition to analysis of electronic medical record (EMR) data. Patient surveys may also have a role to play in discerning clinical appropriateness.

Another method to improve this study would be to identify ASCs that are owned by hospitals and those owned wholly by physicians. The main predictor variable (ASC numbers) could be subdivided on this basis, on the assumption that physician-owned ASCs may exert more forceful competitive effects on hospitals. However, these data were not available for this study.

In summation, this thesis adds to our understanding of the impact of changes in the configuration of providers, but this occurred in the context of data and resource constraints. A more heavily resourced programme of research could overcome some of these constraints. This could potentially alter or refine some research findings. Nonetheless, this thesis has generated new evidence on a number of innovations relating to the mix of providers.

Concluding comments

Policy makers in Ireland and other countries have specified major health policy objectives. In Ireland, these objectives include a system which makes care universally accessible, promotes health and prevents illness, and reliably achieves high quality and compassionate care. The attainment of these goals shall require the advancement of new professional roles, interprofessional collaboration and coordination, and redrawing of professional demarcations. These reforms should be guided by evidence where possible.

This thesis has conducted three relevant and opportunistic studies to investigate changes in the configuration of providers. These studies illustrate the potential benefits of reform as well as the associated challenges. The effectiveness of planning and change management play a significant role in determining whether reform is effective or harmful. The evidence in this thesis can potentially serve to inform policy-making and the process of adjusting provider form. Ultimately, this can serve as one component of a broader research programme that facilitates effective change to provider configuration, and the attainment of high quality, equitable and efficient health care.

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Appendix A

Acronyms

ASC: Ambulatory surgery centre
CMS: Centres for Medicare and Medicaid Services
CON: Certificate of Need
CPT: Current Procedural Terminology
DPS: Drug Payment Scheme
DRG: Diagnosis related group
GMS: General Medical Services scheme
GP: General Practitioner
GPRD: General Practice Research Database
HIPAA: Health Insurance Portability and Accountability Act
HIPE: Hospital Inpatient Enquiry Scheme
HOPD: Hospital Outpatient Department
HRQoL: Health related quality of life
HSE: Health Service Executive
ICD-10: International Statistical Classification of Diseases and Related Health Problems, 10th Revision
ICC: Intraclass Correlation Coefficient
ICER: Incremental Cost Effectiveness Ratio
ILI: Influenza like illness
INR: International Normalisation Ratio
LAIV: Live Attenuated Influenza Vaccine

OBS: Office-based surgery
PCC: Primary care centre
PCRS: Primary care reimbursement service
PCT: Primary care team
POS: Provider of services
QALY: Quality adjusted life year
RCT: Randomised controlled trial
TIV: Trivalent Inactivated Vaccine
TTR: Time in the therapeutic range
UK: United Kingdom
USA: United States of America

Appendix B

Anticoagulation: Survey questions

Warfarin Questionnaire

We would like information on your Warfarin treatment. Please check the best answer for you.

Section 1: Understanding your medicines

Question 1: In the last 12 months, how often did your Warfarin medical team give you all the information you wanted about your health?

- Never
- Sometimes
- Usually
- Always

Question 2: In the last 12 months, how often did your Warfarin medical team encourage you to talk about all your health questions or concerns?

- Never
- Sometimes
- Usually

- Always

Question 3: In the last 12 months, how often did your Warfarin medical team ask you to tell them how you were going to follow these instructions?

- Never
- Sometimes
- Usually
- Always

Question 4: In the last 12 months, how often were the results of your blood test easy to understand?

- Never
- Sometimes
- Usually
- Always

Question 5: In the last 12 months, how often were these instructions about how to take your medicines easy to understand?

- Never
- Sometimes
- Usually
- Always

Section 2: General health questions

Describing your health TODAY

Please check the ONE box that best describes your health TODAY

Question 6: Mobility (walking around)

- I have no problems walking around
- I have some problems walking around
- I have a lot of problems walking around

Question 7: Taking care of myself

- I have no problems taking a bath or shower by myself or getting dressed by myself
- I have some problems taking a bath or shower by myself or getting dressed by myself
- I have a lot of problems taking a bath or shower by myself or getting dressed by myself

Question 8: Doing usual activities (for example, going to school, hobbies, sports, playing, doing things with family or friends)

- I have no problems doing my usual activities
- I have some problems doing my usual activities
- I have a lot of problems doing my usual activities

Question 9: Having pain or discomfort

- I have no pain or discomfort
- I have some pain or discomfort
- I have a lot of pain or discomfort

Question 10: Feeling worried, sad, or unhappy

- I am not worried, sad, or unhappy
- I am a little worried, sad, or unhappy

- I am very worried, sad, or unhappy

Question 11: How good is your health TODAY

- We would like to know how good or bad your health is TODAY.
- This line is numbered from 0 to 100.
- 100 means the best health you can imagine. 0 means the worst health you can imagine.
- Please mark an X on the line to show how good or bad your health is TODAY.

Section 3: Satisfaction with Warfarin

Please check the best answer for you. If a question is not relevant for you, then check the box under "not at all".

Warfarin makes some people bleed or bruise more easily. People might do less of some things because of this.

Question 12: Does the possibility of bleeding or bruising stop you from:

- traveling?
- doing physical activities (for example, housework, gardening, dancing, sports, or anything else you would usually do)?
- getting the medical care you need (for example, visiting a dentist, chiropractor, or doctor of your choice)?
- working for pay?

Please tick the appropriate answer:

- 1 (not at all)

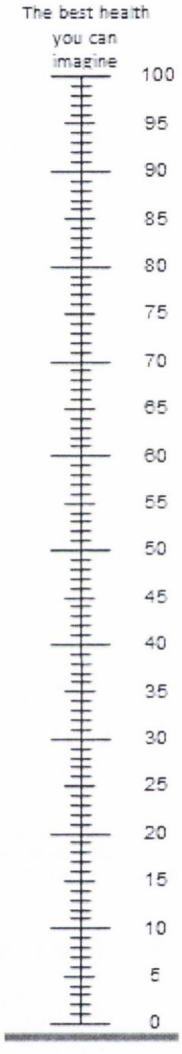

Figure B.1: Quality of life scale: 0 to 100

- 2 (a little)
- 3
- 4
- 5
- 6
- 7 (lots)

Question 13: Overall, how much does the possibility of bleeding or bruising affect your daily life?

- 1 (not at all)
- 2 (a little)
- 3
- 4
- 5
- 6
- 7 (lots)

Being on Warfarin treatment may mean changing some other things as well.

Question 14: How much does Warfarin stop you from:

- eating some foods?
- drinking alcohol?
- from taking medicines you can buy in a pharmacy without seeing a doctor (for example, aspirin, ibuprofen, vitamins)?

- 1 (not at all)
- 2 (a little)
- 3
- 4
- 5
- 6
- 7 (lots)

Question 15: Overall, how much does Warfarin affect your daily life?

- 1 (not at all)
- 2 (a little)
- 3
- 4
- 5
- 6
- 7 (lots)

Being on Warfarin means doing lots of things, some every day and some less often.

Every day things could be things like: remembering to take your medicine at the right time, taking the right dose of your medicine, not drinking much alcohol, eating the right foods, avoiding bruising and bleeding.

Things you do less often could be things like: traveling to the clinic for blood tests, contacting the clinic because of bleeding or other important things.

Question 16: How much of a hassle are the daily things you do for Warfarin treatment?

- 1 (not at all)
- 2 (a little)
- 3
- 4
- 5
- 6
- 7 (lots)

Question 17: How much of a hassle are the things you do less often for Warfarin treatment?

- 1 (not at all)
- 2 (a little)
- 3
- 4
- 5
- 6
- 7 (lots)

Thinking about all of your Warfarin treatment (that is, both the daily things and things you do less often), please answer these questions.

Question 18: How complicated do you find your Warfarin treatment?

- 1 (not at all)
- 2 (a little)

- 3
- 4
- 5
- 6
- 7 (lots)

Question 19: How much of your time does your Warfarin treatment take?

- 1 (not at all)
- 2 (a little)
- 3
- 4
- 5
- 6
- 7 (lots)

Question 20: How frustrating (annoying) or painful is your Warfarin treatment?

- 1 (not at all)
- 2 (a little)
- 3
- 4
- 5
- 6
- 7 (lots)

Question 21: Overall, how hard do you find it being on Warfarin treatment?

- 1 (not at all)
- 2 (a little)
- 3
- 4
- 5
- 6
- 7 (lots)

Question 22: Overall, how confident are you about handling your Warfarin treatment

- 1 (not at all)
- 2 (a little)
- 3
- 4
- 5
- 6
- 7 (lots)

These last questions ask what you know and feel about your Warfarin treatment.

Question 23: How well do you feel that you understand the medical reason for your Warfarin treatment?

- 1 (not at all)

- 2 (a little)
- 3
- 4
- 5
- 6
- 7 (lots)

Question 24: How much do you feel safer because of your Warfarin treatment?

- 1 (not at all)
- 2 (a little)
- 3
- 4
- 5
- 6
- 7 (lots)

Question 25: How much do you worry about bleeding and bruising?

- 1 (not at all)
- 2 (a little)
- 3
- 4
- 5
- 6

- 7 (lots)

Question 26: Overall, how much has Warfarin treatment been good for your life?

- 1 (not at all)
- 2 (a little)
- 3
- 4
- 5
- 6
- 7 (lots)

Question 27: Overall, how much has Warfarin treatment been bad for your life?

- 1 (not at all)
- 2 (a little)
- 3
- 4
- 5
- 6
- 7 (lots)

Question 28: Overall, how satisfied (happy) are you with your Warfarin treatment?

- 1 (not at all)

- 2 (a little)
- 3
- 4
- 5
- 6
- 7 (lots)

Question 29: Compared with other treatments you have had, how hard is it for you to manage your Warfarin treatment?

- 1 (not at all)
- 2 (a little)
- 3
- 4
- 5
- 6
- 7 (lots)

Question 30: Would you recommend Warfarin treatment to someone else with your disease or medical condition?

- 1 (not at all)
- 2 (a little)
- 3
- 4
- 5
- 6
- 7 (lots)

Appendix C

Anticoagulation: Ethics forms

Template script for Phone Contact for Patient of the Anticoagulation Management Service

Hello, this is XXX, from the Anticoagulation Management Service at XXX Hospital and the Value Report Card For Anticoagulation Study. May I speak with XXX?

I'm calling about a study organized by Dr. XXX, examining the quality of care in the Anticoagulation Management Service. We are letting many patients on Warfarin treatment know about this research project, in case they would like to participate. The full title of this study is "Developing a value report card to reflect the quality of anticoagulation management services".

Do you have a couple of minutes to talk right now? (If not, when is a better time for me to reach you?)

We are asking you to answer a survey for a research study. We plan for this survey to be answered by over 260 patients using Anticoagulation Management Services in two hospitals.

The Purpose of the Study is to learn about patients' views on communication standards in Warfarin care, satisfaction, quality of life, and access to services.

Can I tell you about what the study involves? If you are satisfied with all of this information, you can answer the survey.

Taking part would involve answering up to 35 questions. It takes around twenty to thirty minutes to complete this survey, but you can stop at any time and finish

it another time. Taking part is voluntary and can stop at any time. Deciding not to take part won't affect medical care you receive at XXX now or in the future, or any benefits you receive now or have a right to receive. We will also be looking at your medical records as part of this study. We obtained your name and contact information from hospital records. You will not receive any personal health benefits as a result of your participation in this research study. We hope that your answers will help us to better understand warfarin therapy, and will benefit patients using warfarin in the future.

There are less than minimal physical risks to you for being in the study. Some people may feel uncomfortable answering questions about personal information but you may skip any questions that you don't feel comfortable answering. To assure privacy, you will be assigned a study ID number. All study documents will be labeled with your study ID number. Your name will be deleted from the questionnaires and will not appear directly on the records of your information. Research information will be kept on a password protected and encrypted computer in XXX's research office.

Do you have any questions?

If you are satisfied with all of this information, you can answer the survey questions now. [Researcher reads questions from survey in earlier Appendix, records the responses]

I appreciate the time you've taken to talk with me today. If you think of any other questions, please call me at XXX-XXX-XXXX.

Patient Information Statement for RedCAP survey website

Dear Patient,

I am writing to tell you about a research study being conducted by myself, Dr. XXX of the Anticoagulation Management Service at XXX Hospital. We are letting many patients on Warfarin treatment know about this research project, in case they would like to participate.

We are studying patients' views on communication standards in Warfarin care, satisfaction, quality of life, and access to services. The title of this study is "Developing a value report card to reflect the quality of anticoagulation management

services". Participation would involve answering up to 35 questions in a survey. This page provides information on this research study. If you are satisfied with all of this information, you can click the button at the bottom of this screen to answer the questions.

It takes around twenty to thirty minutes to complete this survey, but you can stop at any time and come back to finish it. Participation is voluntary and can stop at any time. Deciding not to participate won't affect medical care you receive at XXX now or in the future, or any benefits you receive now or have a right to receive. You may also be approached by study staff via email, telephone, letter, or at regular clinic visits, to discuss participation. We will also be looking at your medical records as part of this study.

We obtained your name and contact information from hospital records. Over two hundred patients are expected to answer this questionnaire. You will not receive any personal health benefits as a result of your participation in this research study. We hope that your answers will help us to better understand warfarin therapy, and will benefit patients using warfarin in the future.

Please contact my co-investigator XXX, at XXX-XXX-XXXX or myself Dr. XXX at XXX-XXX-XXXX if you would like to learn more about the study. If you'd like to speak to someone not involved in this research about your rights as a research subject, or any concerns or complaints you may have about the research, contact the XXX Hospital Human Research Committee at XXX-XXX-XXXX.

We are required by the Health Insurance Portability and Accountability Act (HIPAA) to protect the privacy of health information obtained for research. This is an abbreviated notice, and does not describe all details of this requirement (see XXX Hospital Privacy Notice*). During this study, identifiable information about you or your health will be collected and shared with the researchers conducting the research. In general, under federal law, identifiable health information is private. However, there are exceptions to this rule. In some cases, others may see your identifiable health information for purposes of research oversight, quality control, public health and safety, or law enforcement. We share your health information only when we must, and we ask anyone who receives it from us to protect your privacy. *Hospital Privacy Notice for Use and Sharing of Protected Health Information. URL: XXX

Thank you in advance for considering this research study.
To answer this survey, click the button below.

Sincerely,

P.I. SIGNATURE
P.I. PRINTED NAME QUALIFICATION
P.I. POSITION

CO-INVESTIGATOR SIGNATURE
CO-INVESTIGATOR PRINTED NAME QUALIFICATION
CO-INVESTIGATOR POSITION

Appendix D

Influenza: Supplementary tables and figures

D.1 Descriptive data on vaccinations, influenza like illness, influenza related spending

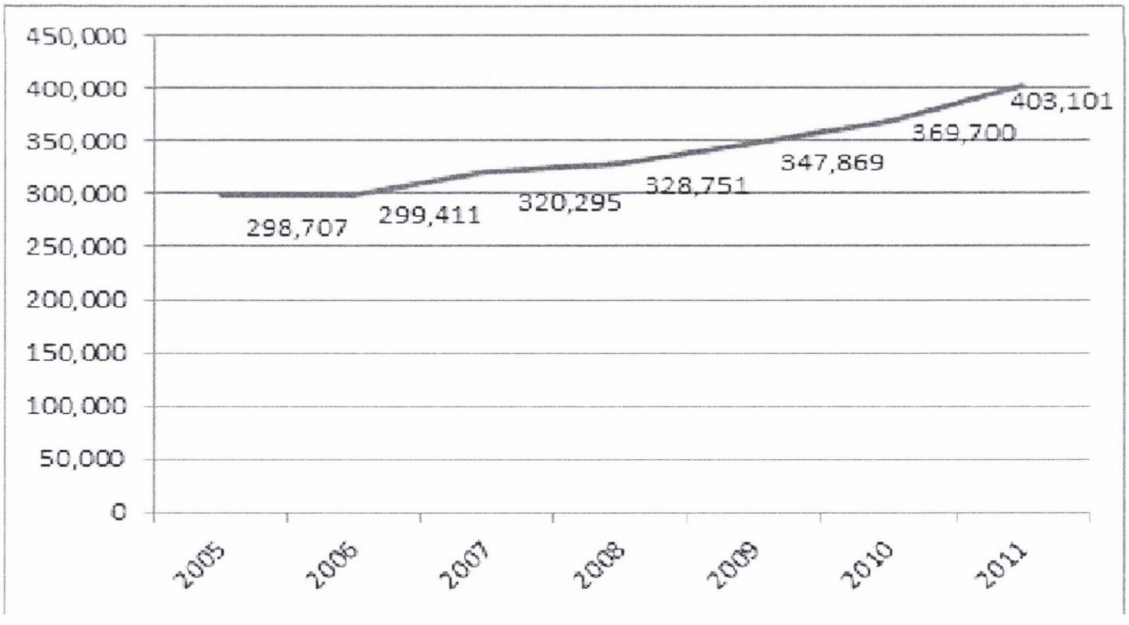

Figure D.1: Influenza vaccinations per year

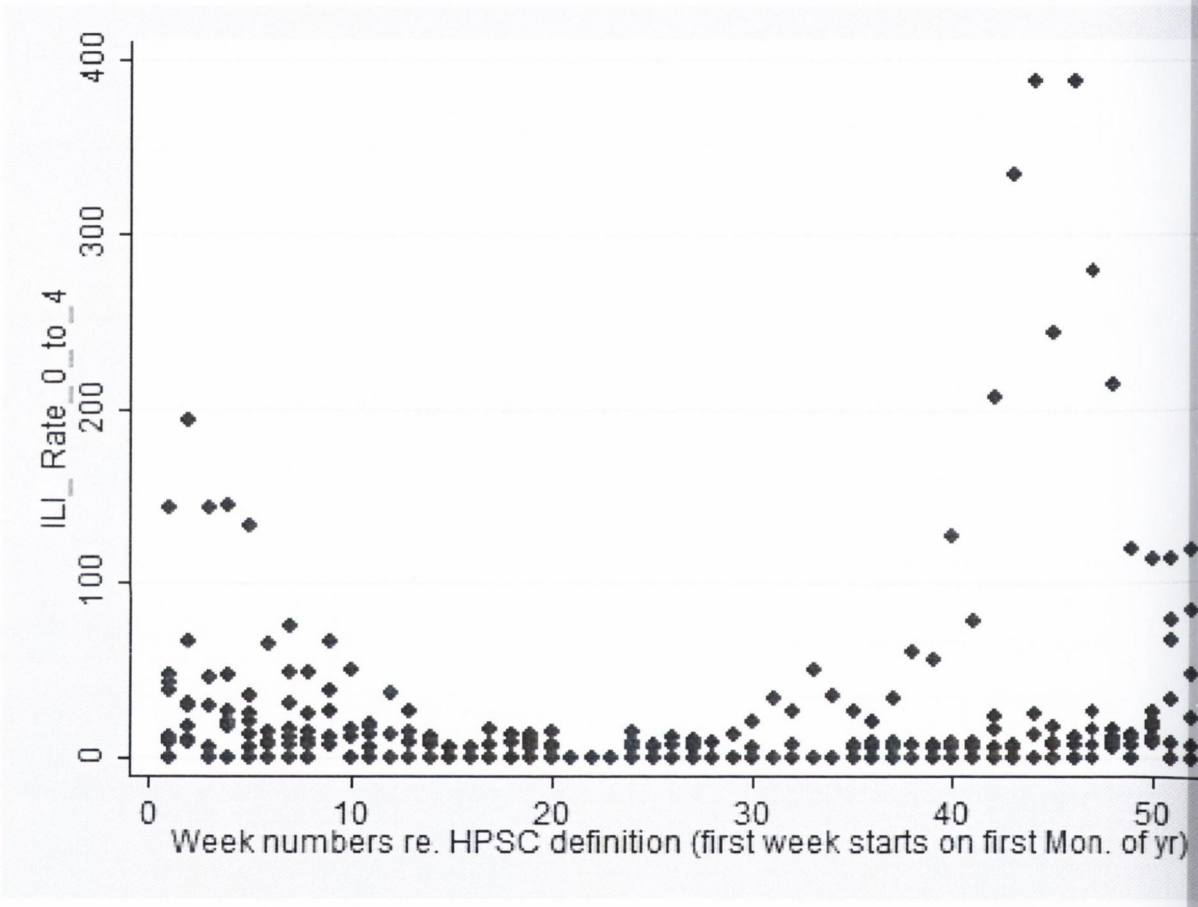

Figure D.2: ILI weekly rate: 0 - 4 years

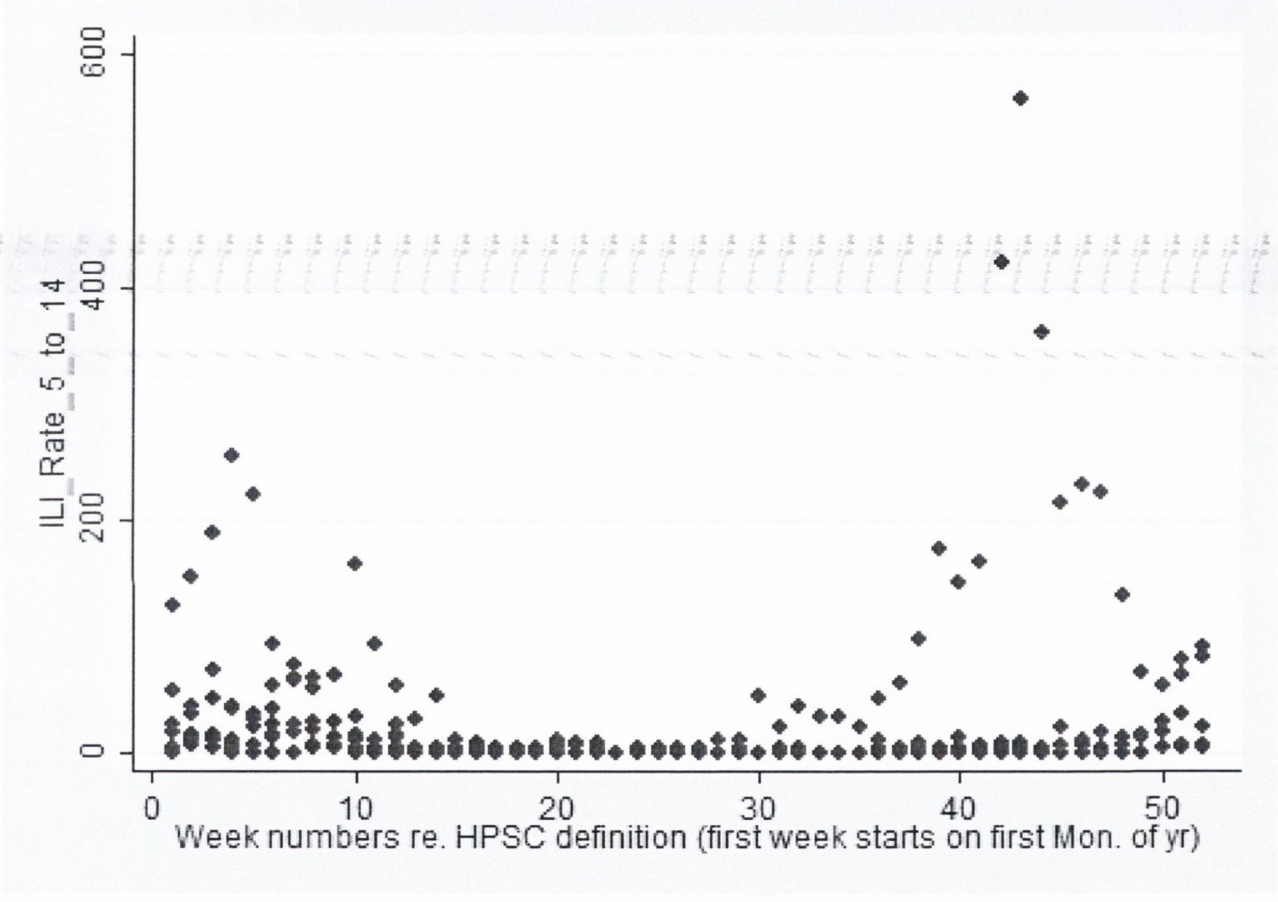

Figure D.3: ILI weekly rate: 5 - 14 years

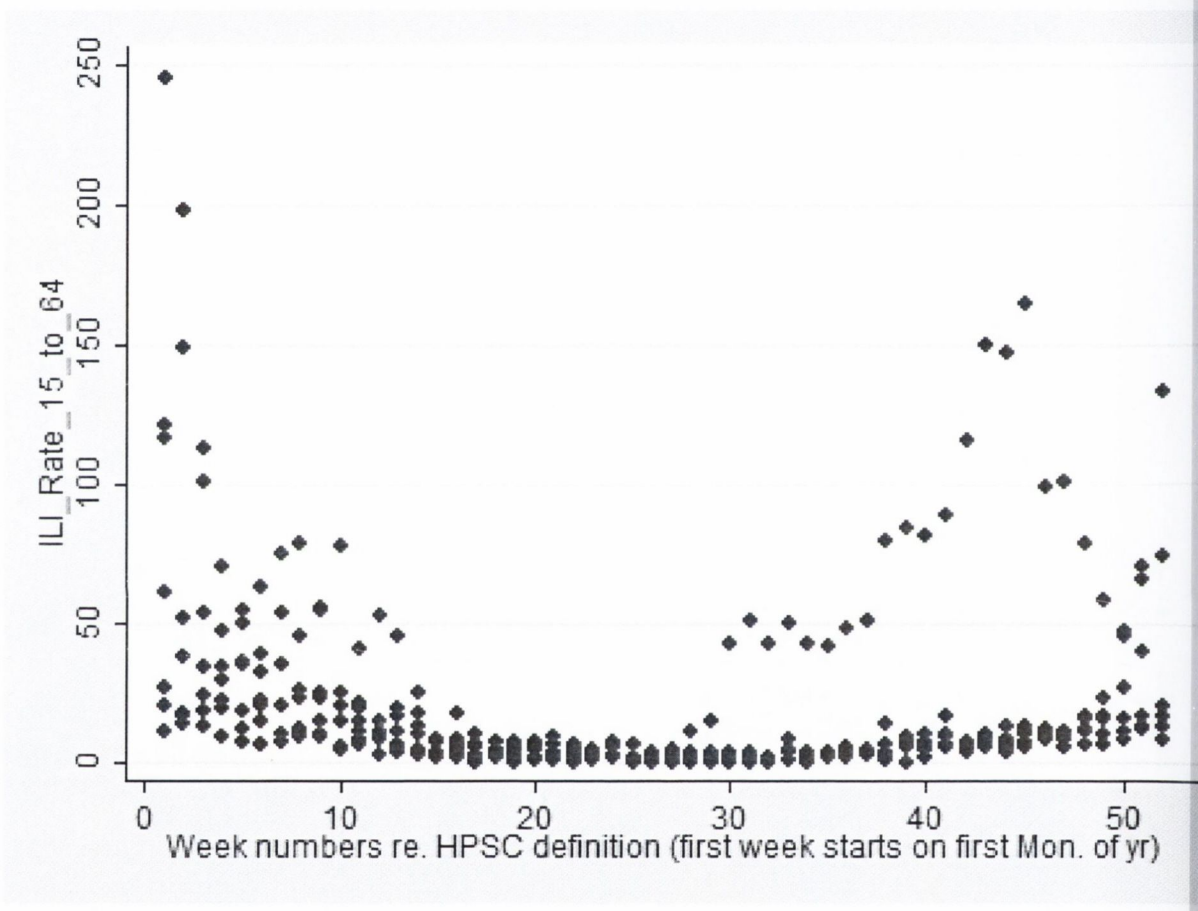

Figure D.4: ILI weekly rate: 15 - 64 years

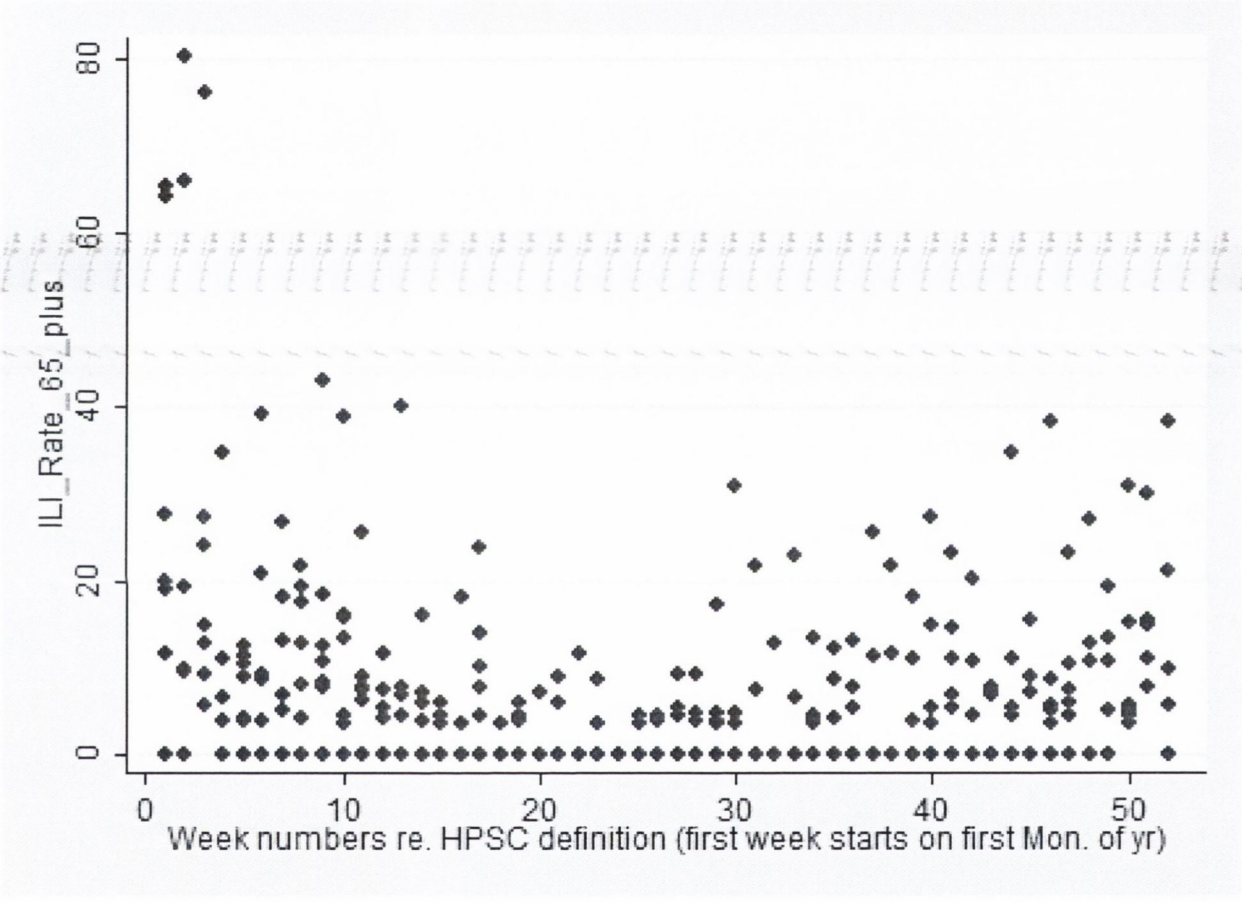

Figure D.5: ILI weekly rate: 65 years and above

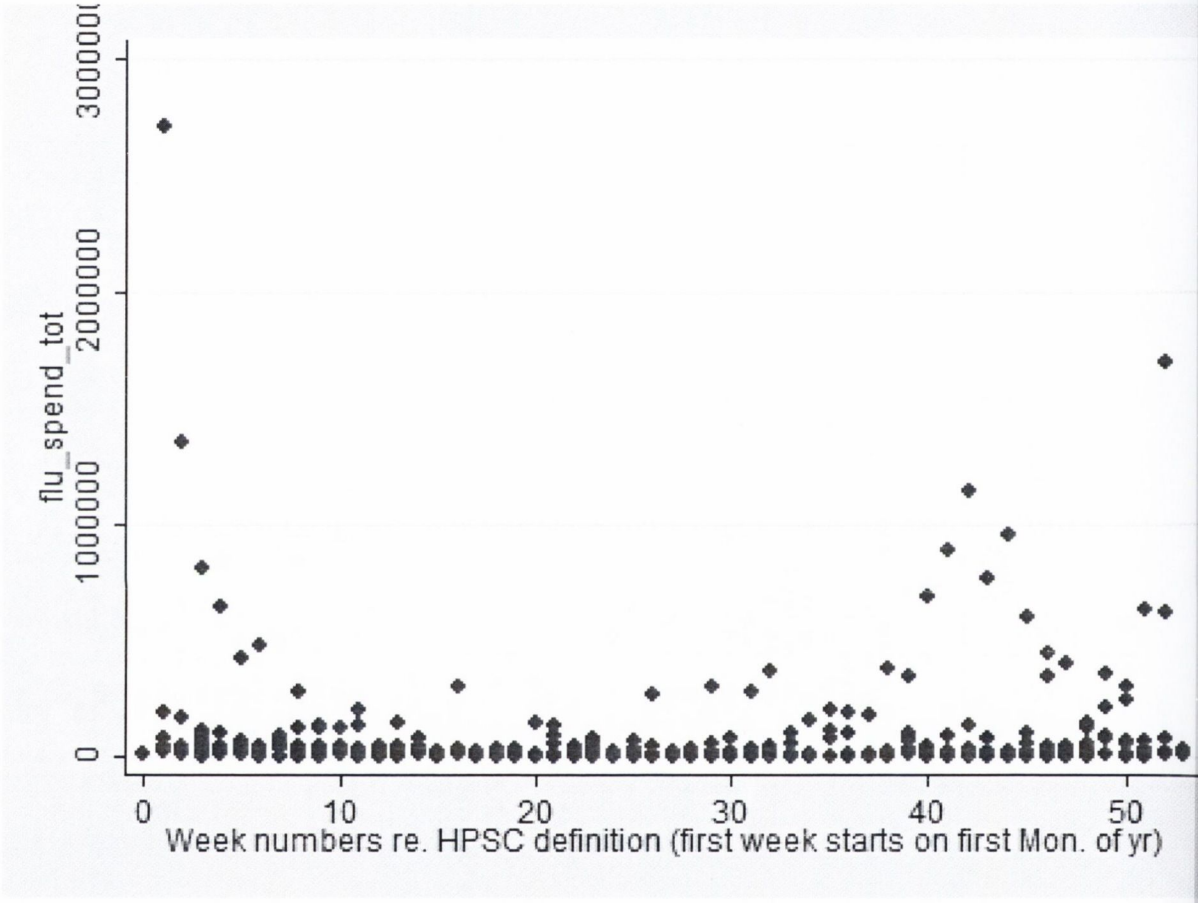

Figure D.6: Spending per week: total influenza related hospitalisations

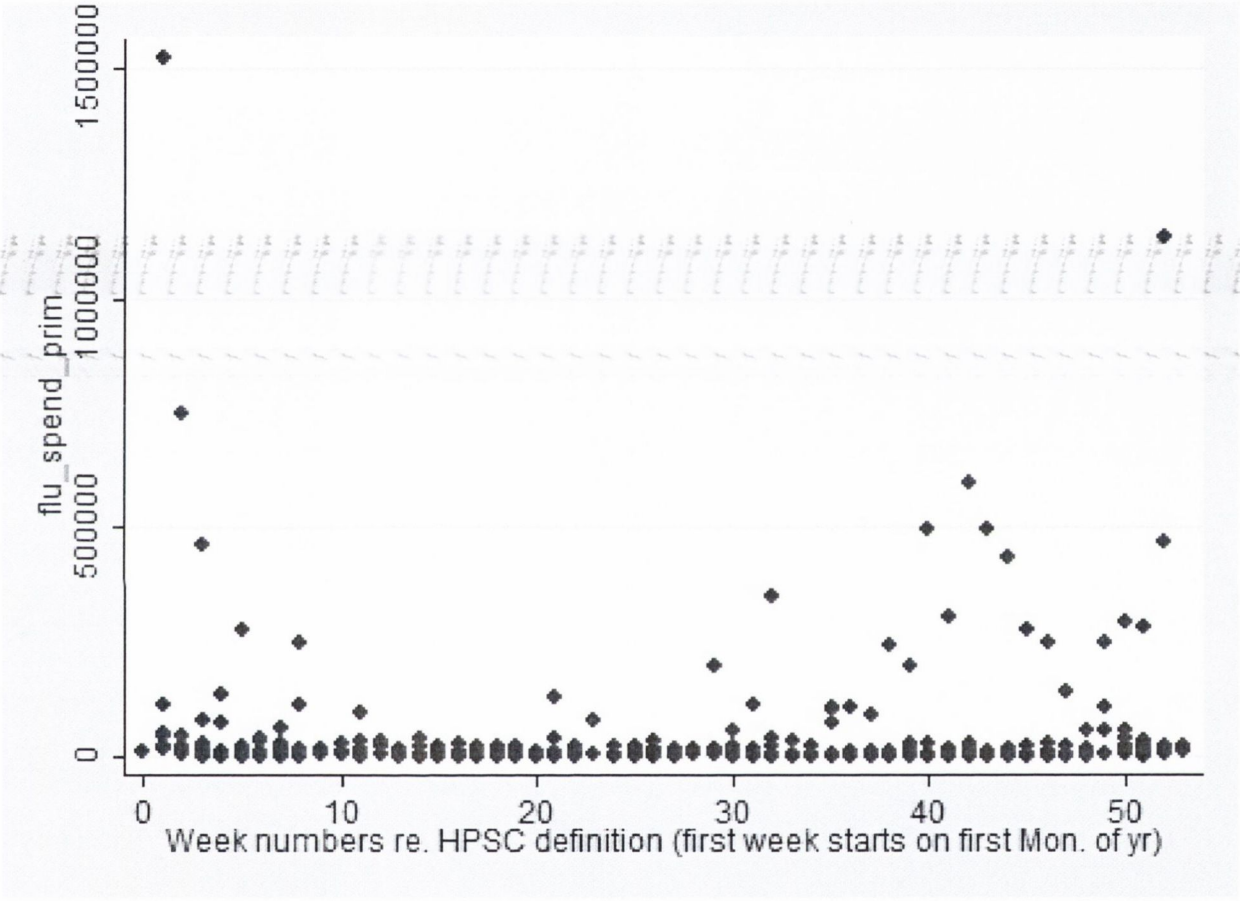

Figure D.7: Spending per week: primary diagnosis influenza hospitalisations

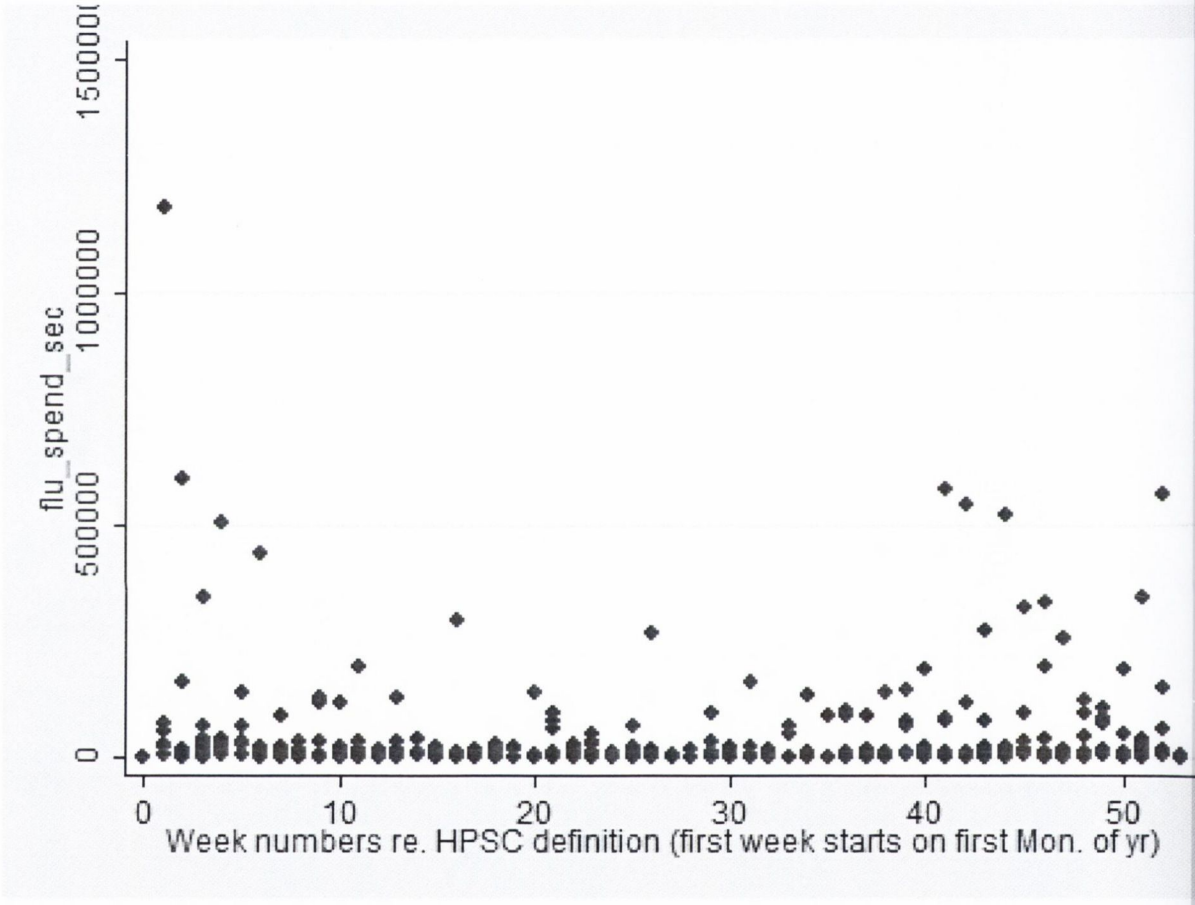

Figure D.8: Spending per week: secondary diagnosis influenza hospitalisations

Table D.1: Influenza Hospital Costs: Gender breakdown

	Hospital Spending: Influenza		
Influenza Season	**Male**	**Female**	**Total**
2005 - 2006	669,876	599,299	1,269,176
2006 - 2007	341,142	296,833	637,974
2006 Summer	255,121	141,123	396,243
2007 - 2008	208,658	315,980	524,638
2007 Summer	200,071	26,597	226,669
2008 - 2009	284,664	407,278	691,942
2008 Summer	114,688	139,354	254,042
2009 - 2010	4,124,221	3,881,105	8,005,326
2009 Summer	1,412,218	1,397,957	2,810,175
2010 - 2011	5,512,759	5,354,165	10,866,924
2010 Summer	144,390	425,896	570,286
2011 Summer	49,270	71,374	120,644
Total	13,317,079	13,056,961	26,374,039

Source: Tabout.dta

D.2 Sensitivity Analyses

Table D.2: Mortality: 75% Vaccinated in Week 1

	Mortalities - Sensitivity Analysis			
Influenza Season	**0 - 14**	**15 - 64**	**65 plus**	**Total**
2005 - 2006	0	46	229	275
2006 - 2007	0	40	203	243
2006 Summer	0	2	18	20
2007 - 2008	0	40	161	201
2007 Summer	0	2	17	19
2008 - 2009	0	57	351	408
2008 Summer	0	3	18	21
2009 - 2010	0	101	375	476
2009 Summer	0	39	202	241
2010 - 2011	0	71	317	388
2010 Summer	0	4	34	38
2011 Summer	0	3	21	24
Total	0	408	1,946	2,354

Source: .dta

Table D.3: Influenza Costs: 75% Vaccinated in Week 1

	Sensitivity Analysis - Costs (Euro)					
Influenza Season	**Indirect**	**ILI - Public**	**ILI - Private**	**Pharma**	**Hospital**	**Total**
2005 - 2006	2,052,961	433,647	392,336	227,298	778,804	3,885,046
2006 - 2007	1,774,295	342,953	306,404	121,331	390,704	2,935,687
2006 Summer	130,367	25,660	22,299	11,684	238,456	428,465
2007 - 2008	1,758,846	337,145	308,176	174,683	313,407	2,892,256
2007 Summer	106,842	20,641	17,524	15,876	136,978	297,862
2008 - 2009	2,508,794	508,245	445,193	504,006	407,463	4,373,700
2008 Summer	143,022	29,663	26,311	20,347	148,688	368,031
2009 - 2010	4,448,967	1,150,212	1,082,434	3,038,201	5,239,162	14,958,975
2009 Summer	1,735,707	365,858	329,468	1,219,421	1,639,991	5,290,444
2010 - 2011	3,542,321	779,538	716,506	2,008,287	6,396,907	13,443,560
2010 Summer	175,766	36,101	29,849	950,738	322,221	1,514,676
2011 Summer	146,395	28,077	24,165	56,141	70,531	325,308
Total	18,524,283	4,057,740	3,700,665	8,348,011	16,083,311	50,714,010

Source: .dta

Table D.4: Cost Effectiveness: Comparator, 75% Vaccinated in Week 1

Influenza Season	NHB	NMB	CE ratio
2005 - 2006	-2,702	-54,034,044	42,952
2006 - 2007	-3,007	-60,149,324	46,994
2006 Summer	-298	-5,955,811	-7,676
2007 - 2008	-3,484	-69,675,784	52,877
2007 Summer	-433	-8,667,467	-30,214
2008 - 2009	-1,755	-35,100,384	30,168
2008 Summer	-519	-10,370,086	-28,879
2009 - 2010	-1,608	-32,152,408	31,325
2009 Summer	-3,085	-61,709,688	-1,956
2010 - 2011	-1,410	-28,193,372	31,198
2010 Summer	-805	-16,091,981	-15,257
2011 Summer	-634	-12,687,366	-34,861
Aggregate	-8,191	-163,822,928	29,824

Source: .dta

Table D.5: Mortality: 75% Vaccinated by End of Season

	Mortalities - Sensitivity Analysis			
Influenza Season	**0 - 14**	**15 - 64**	**65 plus**	**Total**
2005 - 2006	0	28	139	167
2006 - 2007	0	45	225	270
2006 Summer	0	1	8	9
2007 - 2008	0	26	107	133
2007 Summer	0	2	17	19
2008 - 2009	0	70	430	500
2008 Summer	0	1	10	11
2009 - 2010	0	93	346	439
2009 Summer	0	41	212	253
2010 - 2011	0	100	442	542
2010 Summer	0	3	29	32
2011 Summer	0	4	29	33
Total	0	414	1,994	2,408

Source: .dta

Table D.6: Influenza Costs: 75% Vaccinated by End of Season

	Sensitivity Analysis - Costs (Euro)					
Influenza Season	**Indirect**	**ILI - Public**	**ILI - Private**	**Pharma**	**Hospital**	**Total**
2005 - 2006	1,243,595	262,685	237,660	137,687	471,765	2,353,392
2006 - 2007	1,968,117	380,417	339,875	134,585	433,385	3,256,378
2006 Summer	61,941	12,192	10,595	5,551	113,297	203,576
2007 - 2008	1,168,251	223,937	204,695	116,027	208,170	1,921,079
2007 Summer	104,896	20,265	17,205	15,587	134,482	292,434
2008 - 2009	3,071,704	622,282	545,083	617,092	498,888	5,355,048
2008 Summer	82,247	17,058	15,131	11,701	85,505	211,641
2009 - 2010	4,109,303	1,062,397	999,793	2,806,244	4,839,169	13,816,906
2009 Summer	1,827,489	385,204	346,890	1,283,902	1,726,712	5,570,198
2010 - 2011	4,927,068	1,084,272	996,600	2,793,357	8,897,555	18,698,851
2010 Summer	150,374	30,885	25,537	813,387	275,670	1,295,854
2011 Summer	196,233	37,635	32,391	75,253	94,541	436,053
Total	18,911,216	4,139,229	3,771,454	8,810,372	17,779,138	53,411,410

Source: .dta

Table D.7: Cost Effectiveness: Comparator, 75% Vaccinated by End of Season

Influenza Season	NHB	NMB	CE ratio
2005 - 2006	-4,411	-88,211,272	43,034
2006 - 2007	-2,202	-44,042,504	44,069
2006 Summer	-312	-6,245,808	40,801
2007 - 2008	409	8,189,611	19,300
2007 Summer	-5,725	-114,509,840	698,222
2008 - 2009	538	10,769,632	17,591
2008 Summer	-1,656	-33,118,398	125,336
2009 - 2010	3,381	67,618,424	9,778
2009 Summer	-2,800	-56,001,192	47,581
2010 - 2011	369	7,378,221	20,487
2010 Summer	-717	-14,348,091	56,931
2011 Summer	-1,310	-26,204,494	247,841
Aggregate	-14,436	-288,725,728	35,390

Source: .dta

Table D.8: Mortality: Lower Vaccine Effectiveness, 75% Vaccinated in Week 1

	Mortalities - Sensitivity Analysis			
Influenza Season	**0 - 14**	**15 - 64**	**65 plus**	**Total**
2005 - 2006	0	67	329	396
2006 - 2007	0	58	291	349
2006 Summer	0	4	27	31
2007 - 2008	0	59	236	295
2007 Summer	0	3	25	28
2008 - 2009	0	85	521	606
2008 Summer	0	4	27	31
2009 - 2010	0	138	512	650
2009 Summer	0	59	304	363
2010 - 2011	0	107	473	580
2010 Summer	0	6	53	59
2011 Summer	0	5	32	37
Total	0	595	2,830	3,425

Source: .dta

Table D.9: Influenza Cost: Lower Vaccine Effectiveness, 75% Vaccinated in Week 1

	Sensitivity Analysis - Costs (Euro)					
Influenza Season	**Indirect**	**ILI - Public**	**ILI - Private**	**Pharma**	**Hospital**	**Total**
2005 - 2006	2,945,757	622,233	562,957	326,145	1,117,492	5,574,584
2006 - 2007	2,549,878	492,866	440,339	174,367	561,490	4,218,941
2006 Summer	190,423	37,480	32,572	17,066	348,304	625,845
2007 - 2008	2,577,948	494,155	451,694	256,033	459,363	4,239,193
2007 Summer	155,800	30,100	25,554	23,150	199,744	434,348
2008 - 2009	3,720,065	753,630	660,137	747,344	604,190	6,485,366
2008 Summer	213,908	44,365	39,352	30,432	222,382	550,439
2009 - 2010	6,073,395	1,570,183	1,477,657	4,147,523	7,152,109	20,420,865
2009 Summer	2,610,809	550,315	495,578	1,834,224	2,466,835	7,957,760
2010 - 2011	5,274,276	1,160,680	1,066,829	2,990,203	9,524,561	20,016,549
2010 Summer	270,627	55,585	45,959	1,463,851	496,123	2,332,146
2011 Summer	220,427	42,276	36,385	84,531	106,198	489,817
Total	26,803,313	5,853,865	5,335,013	12,094,871	23,258,791	73,345,853

Source: .dta

Table D.10: Cost Effectiveness: Comparator, Lower Vaccine Effectiveness, 75% Vaccinated in Week 1

Influenza Season	NHB	NMB	CE ratio
2005 - 2006	-4,388	-87,769,656	113,586
2006 - 2007	-4,549	-90,988,696	124,708
2006 Summer	-167	-3,335,914	-23,035
2007 - 2008	-4,948	-98,966,672	140,341
2007 Summer	-324	-6,477,646	-83,019
2008 - 2009	-4,392	-87,847,472	79,637
2008 Summer	-384	-7,679,393	-79,624
2009 - 2010	-4,510	-90,209,280	80,870
2009 Summer	-1,420	-28,404,190	-7,821
2010 - 2011	-4,335	-86,705,960	79,902
2010 Summer	-523	-10,465,793	-45,942
2011 Summer	-487	-9,747,532	-95,236
Aggregate	-23,819	-476,377,248	77,635

Source: .dta

Table D.11: Mortality: Higher Vaccine Effectiveness, 75% Vaccinated in Week 1

	Mortalities - Sensitivity Analysis			
Influenza Season	**0 - 14**	**15 - 64**	**65 plus**	**Total**
2005 - 2006	0	40	199	239
2006 - 2007	0	35	176	211
2006 Summer	0	2	16	18
2007 - 2008	0	34	139	173
2007 Summer	0	2	14	16
2008 - 2009	0	49	301	350
2008 Summer	0	2	15	17
2009 - 2010	0	90	334	424
2009 Summer	0	33	171	204
2010 - 2011	0	61	271	332
2010 Summer	0	3	29	32
2011 Summer	0	2	18	20
Total	0	353	1,683	2,036

Source: .dta

Table D.12: Influenza Cost: Higher Vaccine Effectiveness, 75% Vaccinated in Week 1

	Sensitivity Analysis - Costs (Euro)					
Influenza Season	**Indirect**	**ILI - Public**	**ILI - Private**	**Pharma**	**Hospital**	**Total**
2005 - 2006	1,787,534	377,581	341,611	197,910	678,112	3,382,750
2006 - 2007	1,543,716	298,385	266,585	105,563	339,930	2,554,179
2006 Summer	112,512	22,145	19,245	10,083	205,798	369,785
2007 - 2008	1,515,329	290,466	265,508	150,497	270,015	2,491,816
2007 Summer	92,288	17,830	15,137	13,713	118,318	257,285
2008 - 2009	2,148,687	435,292	381,291	431,662	348,977	3,745,909
2008 Summer	121,948	25,292	22,434	17,349	126,779	313,802
2009 - 2010	3,966,029	1,025,356	964,935	2,708,402	4,670,447	13,335,168
2009 Summer	1,475,541	311,019	280,084	1,036,642	1,394,172	4,497,459
2010 - 2011	3,027,416	666,226	612,356	1,716,366	5,467,065	11,489,430
2010 Summer	147,564	30,308	25,060	798,191	270,520	1,271,643
2011 Summer	124,386	23,856	20,532	47,700	59,927	276,400
Total	16,062,950	3,523,757	3,214,778	7,234,079	13,950,060	43,985,625

Source: .dta

Table D.13: Cost Effectiveness: Comparator, Higher Vaccine Effectiveness, 75% Vaccinated in Week 1

Influenza Season	NHB	NMB	CE ratio
2005 - 2006	-2,200	-44,004,512	36,352
2006 - 2007	-2,549	-50,980,904	39,733
2006 Summer	-337	-6,734,704	-6,241
2007 - 2008	-3,048	-60,967,704	44,704
2007 Summer	-466	-9,318,491	-25,280
2008 - 2009	-971	-19,418,882	25,545
2008 Summer	-559	-11,170,021	-24,137
2009 - 2010	-745	-14,892,259	26,695
2009 Summer	-3,581	-71,611,304	-1,409
2010 - 2011	-540	-10,797,677	26,647
2010 Summer	-888	-17,764,626	-12,390
2011 Summer	-678	-13,561,374	-29,220
Aggregate	-3,545	-70,901,432	25,357

Source: .dta

Table D.14: Cost Effectiveness: €15 per vaccination, 75% Vaccinated in Week 1

Influenza Season	NHB	NMB	CE ratio
2005 - 2006	652	13,043,075	16,825
2006 - 2007	393	7,858,952	18,249
2006 Summer	-242	-4,849,684	-1,995
2007 - 2008	136	2,722,640	20,525
2007 Summer	-272	-5,447,880	-10,683
2008 - 2009	1,953	39,057,024	11,870
2008 Summer	-329	-6,588,191	-10,109
2009 - 2010	2,272	45,438,284	12,999
2009 Summer	-2,818	-56,359,280	213
2010 - 2011	2,369	47,386,616	13,184
2010 Summer	-583	-11,662,530	-3,907
2011 Summer	-386	-7,711,103	-12,530
Aggregate	12,406	248,125,264	12,140

Source: .dta

Table D.15: Cost Effectiveness: higher vaccination price, 75% Vaccinated in Week 1

Influenza Season	NHB	NMB	CE ratio
2005 - 2006	-4,102	-82,043,968	53,861
2006 - 2007	-4,427	-88,548,088	58,997
2006 Summer	-321	-6,417,705	-10,048
2007 - 2008	-4,995	-99,907,784	66,386
2007 Summer	-501	-10,011,897	-38,370
2008 - 2009	-3,303	-66,066,888	37,808
2008 Summer	-597	-11,949,323	-36,716
2009 - 2010	-3,228	-64,552,588	38,977
2009 Summer	-3,197	-63,943,900	-2,862
2010 - 2011	-2,988	-59,753,920	38,721
2010 Summer	-897	-17,941,624	-19,997
2011 Summer	-738	-14,765,344	-44,187
Aggregate	-16,792	-335,843,456	37,209

Source: .dta

Table D.16: Influenza Cost: Increased absenteeism and 75% Vaccinated in Week 1

	Sensitivity Analysis - Costs (Euro)					
Influenza Season	**Indirect**	**ILI - Public**	**ILI - Private**	**Pharma**	**Hospital**	**Total**
2005 - 2006	3,158,401	433,647	392,336	227,298	778,804	4,990,486
2006 - 2007	2,729,684	342,953	306,404	121,331	390,704	3,891,076
2006 Summer	200,565	25,660	22,299	11,684	238,456	498,663
2007 - 2008	2,705,917	337,145	308,176	174,683	313,407	3,839,327
2007 Summer	164,373	20,641	17,524	15,876	136,978	355,392
2008 - 2009	3,859,683	508,245	445,193	504,006	407,463	5,724,589
2008 Summer	220,034	29,663	26,311	20,347	148,688	445,043
2009 - 2010	6,844,565	1,150,212	1,082,434	3,038,201	5,239,162	17,354,573
2009 Summer	2,670,318	365,858	329,468	1,219,421	1,639,991	6,225,056
2010 - 2011	5,449,725	779,538	716,506	2,008,287	6,396,907	15,350,964
2010 Summer	270,410	36,101	29,849	950,738	322,221	1,609,319
2011 Summer	225,223	28,077	24,165	56,141	70,531	404,136
Total	28,498,897	4,057,740	3,700,665	8,348,011	16,083,311	60,688,624

Source: .dta

Table D.17: Cost Effectiveness: Increased absenteeism and 75% vaccination in Week 1

Influenza Season	NHB	NMB	CE ratio
2005 - 2006	-2,667	-53,338,004	43,223
2006 - 2007	-2,977	-59,544,676	47,249
2006 Summer	-300	-6,002,261	-7,438
2007 - 2008	-3,452	-69,037,480	53,162
2007 Summer	-435	-8,705,137	-29,986
2008 - 2009	-1,708	-34,157,228	30,400
2008 Summer	-521	-10,424,654	-28,608
2009 - 2010	-1,544	-30,887,582	31,623
2009 Summer	-3,119	-62,376,560	-1,686
2010 - 2011	-1,343	-26,860,522	31,516
2010 Summer	-808	-16,164,844	-15,070
2011 Summer	-637	-12,743,375	-34,610
Aggregate	-7,870	-157,408,672	30,099

Source: .dta

Table D.18: Influenza related mortalities: Reduced mortality rate, 75% Vaccinated in Week 1

	Mortalities - Sensitivity Analysis			
Influenza Season	**0 - 14**	**15 - 64**	**65 plus**	**Total**
2005 - 2006	0	5	90	95
2006 - 2007	0	5	79	84
2006 Summer	0	0	7	7
2007 - 2008	0	4	63	67
2007 Summer	0	0	6	6
2008 - 2009	0	7	138	145
2008 Summer	0	0	7	7
2009 - 2010	0	12	147	159
2009 Summer	0	4	79	83
2010 - 2011	0	8	124	132
2010 Summer	0	0	13	13
2011 Summer	0	0	8	8
Total	0	45	761	806

Source: .dta

Table D.19: Cost Effectiveness: Reduced mortality rate, 75% Vaccinated in Week 1

Influenza Season	NHB	NMB	CE ratio
2005 - 2006	-3,918	-78,356,136	84,291
2006 - 2007	-4,169	-83,373,264	95,181
2006 Summer	-199	-3,984,978	-15,432
2007 - 2008	-4,583	-91,657,360	107,481
2007 Summer	-354	-7,070,202	-59,485
2008 - 2009	-3,760	-75,199,136	61,581
2008 Summer	-420	-8,392,768	-57,702
2009 - 2010	-3,421	-68,425,344	56,805
2009 Summer	-1,920	-38,403,988	-3,280
2010 - 2011	-3,434	-68,688,352	62,841
2010 Summer	-598	-11,953,722	-32,727
2011 Summer	-522	-10,439,721	-71,641
Aggregate	-19,273	-385,454,208	58,959

Source: .dta

Table D.20: Mortality: Dynamic Modelling, 75% Vaccinated in Week 1

	Mortalities - Sensitivity Analysis			
Influenza Season	**0 - 14**	**15 - 64**	**65 plus**	**Total**
2005 - 2006	0	4	19	23
2006 - 2007	0	3	16	19
2006 Summer	0	0	1	1
2007 - 2008	0	11	47	58
2007 Summer	0	0	4	4
2008 - 2009	0	3	23	26
2008 Summer	0	0	0	0
2009 - 2010	0	55	206	261
2009 Summer	0	0	0	0
2010 - 2011	0	3	16	19
2010 Summer	0	0	0	0
2011 Summer	0	0	0	0
Total	0	79	332	411

Source: .dta

Table D.21: Influenza Costs: Dynamic Modelling, 75% Vaccinated in Week 1

	Sensitivity Analysis - Costs (Euro)					
Influenza Season	**Indirect**	**ILI - Public**	**ILI - Private**	**Pharma**	**Hospital**	**Total**
2005 - 2006	177,095	37,408	33,844	19,607	67,182	335,136
2006 - 2007	140,542	27,165	24,270	9,611	30,948	232,535
2006 Summer	11,221	2,209	1,919	1,006	20,524	36,878
2007 - 2008	519,158	99,515	90,964	51,561	92,508	853,707
2007 Summer	29,228	5,647	4,794	4,343	37,471	81,482
2008 - 2009	167,322	33,897	29,692	33,614	27,175	291,701
2008 Summer	0	0	0	0	0	1
2009 - 2010	2,452,207	633,980	596,622	1,674,613	2,887,751	8,245,172
2009 Summer	0	0	0	0	0	0
2010 - 2011	180,478	39,717	36,505	102,320	325,916	684,936
2010 Summer	0	0	0	0	0	0
2011 Summer	0	0	0	0	0	0
Total	3,677,250	879,537	818,611	1,896,675	3,489,476	10,761,549

Source: .dta

Table D.22: Cost Effectiveness: Dynamic Modelling, Comparator 75% Vaccinated in Week 1

Influenza Season	NHB	NMB	CE ratio
2005 - 2006	1,202	24,032,072	18,087
2006 - 2007	570	11,397,895	19,608
2006 Summer	-586	-11,725,899	-2,379
2007 - 2008	-1,042	-20,830,744	26,292
2007 Summer	-627	-12,541,505	-13,701
2008 - 2009	3,867	77,336,736	13,341
2008 Summer	-821	-16,425,388	-11,219
2009 - 2010	2,327	46,543,964	17,789
2009 Summer	-6,807	-136,140,576	78
2010 - 2011	4,926	98,528,248	14,519
2010 Summer	-1,387	-27,745,358	-4,948
2011 Summer	-964	-19,285,142	-13,874
Aggregate	23,044	460,872,000	13,986

Source: .dta

Table D.23: Mortality: Dynamic Modelling, Lower Vaccine Effectiveness

	Mortalities - Sensitivity Analysis			
Influenza Season	**0 - 14**	**15 - 64**	**65 plus**	**Total**
2005 - 2006	0	13	64	77
2006 - 2007	0	12	60	72
2006 Summer	0	1	8	9
2007 - 2008	0	33	133	166
2007 Summer	0	2	16	18
2008 - 2009	0	23	141	164
2008 Summer	0	0	0	0
2009 - 2010	0	101	374	475
2009 Summer	0	0	1	1
2010 - 2011	0	25	111	136
2010 Summer	0	0	0	0
2011 Summer	0	0	0	0
Total	0	210	908	1,118

Source: .dta

Table D.24: Influenza Cost: Dynamic Modelling, Lower Vaccine Effectiveness

	Sensitivity Analysis - Costs (Euro)					
Influenza Season	**Indirect**	**ILI - Public**	**ILI - Private**	**Pharma**	**Hospital**	**Total**
2005 - 2006	578,573	122,212	110,570	64,058	219,485	1,094,899
2006 - 2007	529,163	102,282	91,381	36,186	116,523	875,535
2006 Summer	62,735	12,348	10,731	5,622	114,750	206,186
2007 - 2008	1,451,480	278,227	254,321	144,156	258,638	2,386,822
2007 Summer	102,834	19,867	16,866	15,280	131,838	286,686
2008 - 2009	1,011,765	204,969	179,541	203,259	164,325	1,763,859
2008 Summer	5,209	1,080	958	741	5,415	13,404
2009 - 2010	4,440,261	1,147,961	1,080,316	3,032,255	5,228,909	14,929,701
2009 Summer	9,326	1,966	1,770	6,552	8,811	28,425
2010 - 2011	1,239,456	272,760	250,705	702,698	2,238,274	4,703,894
2010 Summer	1,083	222	184	5,858	1,985	9,332
2011 Summer	2,025	388	334	777	976	4,501
Total	9,433,910	2,164,283	1,997,677	4,217,442	8,489,930	26,303,242

Source: .dta

Table D.25: Cost Effectiveness: Dynamic Modelling, Lower Vaccine Effectiveness

Influenza Season	NHB	NMB	CE ratio
2005 - 2006	547	10,941,328	19,975
2006 - 2007	44	887,010	21,403
2006 Summer	-538	-10,767,237	-2,788
2007 - 2008	-1,106	-22,127,924	26,642
2007 Summer	-634	-12,670,668	-13,445
2008 - 2009	3,061	61,220,252	14,465
2008 Summer	-705	-14,104,483	-14,838
2009 - 2010	2,358	47,164,656	17,731
2009 Summer	-4,927	-98,535,256	-529
2010 - 2011	3,854	77,085,464	15,845
2010 Summer	-1,073	-21,465,474	-8,423
2011 Summer	-799	-15,986,860	-20,032
Aggregate	17,435	348,700,768	15,371

Source: .dta

Table D.26: Mortality: Dynamic Modelling, Higher Vaccine Effectiveness

	Mortalities - Sensitivity Analysis			
Influenza Season	**0 - 14**	**15 - 64**	**65 plus**	**Total**
2005 - 2006	0	3	17	20
2006 - 2007	0	2	14	16
2006 Summer	0	0	1	1
2007 - 2008	0	9	37	46
2007 Summer	0	0	3	3
2008 - 2009	0	3	20	23
2008 Summer	0	0	0	0
2009 - 2010	0	49	183	232
2009 Summer	0	0	0	0
2010 - 2011	0	3	14	17
2010 Summer	0	0	0	0
2011 Summer	0	0	0	0
Total	0	69	289	358

Source: .dta

Table D.27: Influenza Cost: Dynamic Modelling, Higher Vaccine Effectiveness

	Sensitivity Analysis - Costs (Euro)					
Influenza Season	**Indirect**	**ILI - Public**	**ILI - Private**	**Pharma**	**Hospital**	**Total**
2005 - 2006	157,427	33,253	30,086	17,430	59,721	297,917
2006 - 2007	124,323	24,030	21,469	8,502	27,376	205,700
2006 Summer	7,119	1,401	1,218	638	13,022	23,399
2007 - 2008	408,248	78,255	71,531	40,546	72,745	671,326
2007 Summer	20,178	3,898	3,310	2,998	25,869	56,253
2008 - 2009	142,886	28,947	25,356	28,705	23,207	249,101
2008 Summer	0	0	0	0	0	0
2009 - 2010	2,171,336	561,365	528,286	1,482,805	2,556,993	7,300,785
2009 Summer	0	0	0	0	0	0
2010 - 2011	156,074	34,346	31,569	88,485	281,847	592,323
2010 Summer	0	0	0	0	0	0
2011 Summer	0	0	0	0	0	0
Total	3,187,592	765,497	712,824	1,670,109	3,060,781	9,396,804

Source: .dta

Table D.28: Cost Effectiveness: Dynamic Modelling, Higher Vaccine Effectiveness

Influenza Season	NHB	NMB	CE ratio
2005 - 2006	3,429	68,582,648	13,760
2006 - 2007	2,085	41,702,064	15,831
2006 Summer	-752	-15,049,677	-1,419
2007 - 2008	-1,760	-35,192,768	30,789
2007 Summer	-501	-10,028,775	-21,407
2008 - 2009	5,443	108,866,104	11,601
2008 Summer	-1,510	-30,197,232	-4,074
2009 - 2010	504	10,070,988	22,097
2009 Summer	-20,290	-405,804,192	1,064
2010 - 2011	7,738	154,763,792	12,020
2010 Summer	-3,793	-75,864,144	607
2011 Summer	-2,157	-43,139,280	-3,752
Aggregate	46,444	928,876,160	10,351

Source: .dta

Table D.29: Cost Effectiveness: Dynamic Modelling, 15 euro per vaccination

Influenza Season	NHB	NMB	CE ratio
2005 - 2006	4,555	91,109,192	7,428
2006 - 2007	3,970	79,406,168	7,899
2006 Summer	-531	-10,619,772	7
2007 - 2008	2,578	51,567,680	10,478
2007 Summer	-466	-9,321,917	-4,442
2008 - 2009	7,575	151,494,096	5,511
2008 Summer	-632	-12,643,492	-3,435
2009 - 2010	6,207	124,134,656	7,883
2009 Summer	-6,540	-130,790,144	982
2010 - 2011	8,705	174,108,272	6,880
2010 Summer	-1,166	-23,315,906	-11
2011 Summer	-715	-14,308,882	-4,598
Aggregate	43,641	872,820,224	6,144

Source: .dta

Table D.30: Cost Effectiveness: Dynamic Modelling, higher vaccination price, 75% vaccinated in week 1

Influenza Season	NHB	NMB	CE ratio
2005 - 2006	-199	-3,977,854	22,538
2006 - 2007	-850	-17,000,868	24,498
2006 Summer	-609	-12,187,793	-3,375
2007 - 2008	-2,553	-51,062,740	32,896
2007 Summer	-694	-13,885,934	-17,567
2008 - 2009	2,319	46,370,188	16,611
2008 Summer	-900	-18,004,624	-14,469
2009 - 2010	707	14,143,785	21,925
2009 Summer	-6,919	-138,374,768	-299
2010 - 2011	3,348	66,967,740	17,709
2010 Summer	-1,480	-29,595,000	-7,010
2011 Summer	-1,068	-21,363,124	-17,748
Aggregate	14,443	288,851,488	17,260

Source: .dta

Table D.31: Mortalities: Dynamic modelling, Reduced mortality rate, 75% Vaccinated in Week 1

	Mortalities - Sensitivity Analysis			
Influenza Season	**0 - 14**	**15 - 64**	**65 plus**	**Total**
2005 - 2006	0	0	7	7
2006 - 2007	0	0	6	6
2006 Summer	0	0	0	0
2007 - 2008	0	1	18	19
2007 Summer	0	0	1	1
2008 - 2009	0	0	9	9
2008 Summer	0	0	0	0
2009 - 2010	0	6	81	87
2009 Summer	0	0	0	0
2010 - 2011	0	0	6	6
2010 Summer	0	0	0	0
2011 Summer	0	0	0	0
Total	0	7	128	135

Source: .dta

Table D.32: Cost Effectiveness: Dynamic modelling, Reduced mortality rate, 75% Vaccinated in Week 1

Influenza Season	NHB	NMB	CE ratio
2005 - 2006	-2,449	-48,979,940	45,176
2006 - 2007	-2,849	-56,979,352	49,835
2006 Summer	-315	-6,296,834	-5,317
2007 - 2008	-3,689	-73,774,160	65,216
2007 Summer	-427	-8,542,447	-32,578
2008 - 2009	-1,685	-33,706,632	33,756
2008 Summer	-539	-10,783,584	-26,976
2009 - 2010	-1,817	-36,348,888	39,671
2009 Summer	-3,353	-67,069,444	864
2010 - 2011	-783	-15,667,341	36,455
2010 Summer	-857	-17,136,384	-11,921
2011 Summer	-650	-12,999,360	-33,924
Aggregate	-7,131	-142,628,288	34,622

Source: .dta

D.3 Cost of illness of related conditions

Table D.33: Ischaemic Heart Disease

	Hospital Spending: Ischaemic Heart Disease				
Influenza Season	**0 to 4 years**	**15 to 64 years**	**5 to 14 years**	**65 years and older**	**Total**
2005 - 2006	227,772	4,801	41,499,778	103,143,660	144,876,011
2006 - 2007	43,393	0	44,354,064	107,242,170	151,639,627
2006 Summer	8,257	4,783	24,926,720	57,288,323	82,228,082
2007 - 2008	163,955	1,596	44,082,603	105,373,442	149,621,596
2007 Summer	0	0	23,656,417	55,700,178	79,356,595
2008 - 2009	72,087	0	44,068,104	112,652,648	156,792,839
2008 Summer	0	5,053	24,520,064	57,938,496	82,463,613
2009 - 2010	430,536	6,406	58,167,370	136,585,946	195,190,258
2009 Summer	4,148	0	22,144,211	60,859,239	83,007,599
2010 - 2011	296,817	46,844	62,923,083	150,837,185	214,103,929
2010 Summer	0	19,976	36,226,156	83,920,522	120,166,654
2011 Summer	125,465	7,997	34,293,167	78,971,204	113,397,833
Total	1,372,429	97,456	460,861,739	1,110,513,011	1,572,844,636

Source: Tabout.dta

Table D.34: Cerebrovascular Events

	Hospital Spending: Cerebrovascular Disease				
Influenza Season	**0 to 4 years**	**15 to 64 years**	**5 to 14 years**	**65 years and older**	**Total**
2005 - 2006	558,463	239,546	24,366,753	63,486,949	88,651,710
2006 - 2007	637,486	499,971	24,947,208	66,977,509	93,062,174
2006 Summer	452,106	155,732	14,819,990	33,992,917	49,420,746
2007 - 2008	1,051,922	203,508	27,063,896	74,861,600	103,180,926
2007 Summer	528,398	120,019	12,852,799	36,539,565	50,040,781
2008 - 2009	504,447	197,593	26,379,288	85,817,567	112,898,894
2008 Summer	397,037	223,258	14,765,050	41,092,109	56,477,454
2009 - 2010	1,060,528	353,375	33,425,403	89,071,648	123,910,953
2009 Summer	1,027,589	204,302	14,593,343	43,552,905	59,378,138
2010 - 2011	1,532,639	897,481	31,886,338	88,554,977	122,871,435
2010 Summer	294,610	383,960	18,292,535	46,474,431	65,445,536
2011 Summer	961,930	561,506	16,986,960	42,206,184	60,716,580
Total	9,007,155	4,040,249	260,379,562	712,628,362	986,055,328

Source: Tabout.dta

Table D.35: Upper Respiratory Tract Infection

	Hospital Spending: Upper Respiratory Tract Infection				
Influenza Season	**0 to 4 years**	**15 to 64 years**	**5 to 14 years**	**65 years and older**	**Total**
2005 - 2006	8,850,355	2,384,324	5,514,484	1,476,689	18,225,853
2006 - 2007	7,895,008	1,940,195	6,152,351	1,578,953	17,566,508
2006 Summer	3,524,157	1,007,906	2,899,772	858,709	8,290,545
2007 - 2008	7,892,891	1,975,483	5,176,218	1,197,607	16,242,199
2007 Summer	4,033,599	891,000	2,924,436	787,842	8,636,878
2008 - 2009	7,611,523	2,285,826	5,540,539	2,551,302	17,989,190
2008 Summer	3,216,825	798,143	2,570,671	831,163	7,416,802
2009 - 2010	8,696,284	1,929,417	5,505,986	2,492,504	18,624,191
2009 Summer	3,309,088	909,603	2,992,788	636,731	7,848,210
2010 - 2011	9,482,284	2,650,025	5,836,292	2,018,533	19,987,134
2010 Summer	3,750,161	1,089,726	3,823,595	924,279	9,587,762
2011 Summer	3,848,660	1,295,485	3,192,725	949,154	9,286,024
Total	72,110,835	19,157,135	52,129,857	16,303,467	159,701,294

Source: Tabout.dta

Table D.36: Pneumonia

Influenza Season	*Hospital Spending: Pneumonia*				Total
	0 to 4 years	15 to 64 years	5 to 14 years	65 years and older	
2005 - 2006	23,391,750	5,152,237	57,592,801	123,046,524	209,183,311
2006 - 2007	20,750,912	3,356,479	63,103,952	132,800,603	220,011,946
2006 Summer	6,261,361	1,728,956	32,227,833	56,515,622	96,733,771
2007 - 2008	21,944,402	3,659,180	67,017,678	136,934,344	229,555,604
2007 Summer	6,091,549	1,313,175	31,035,475	63,161,338	101,601,537
2008 - 2009	19,168,605	3,333,064	74,551,905	162,355,718	259,409,292
2008 Summer	5,235,324	2,087,865	36,593,357	68,255,606	112,172,152
2009 - 2010	23,705,595	4,221,417	86,948,186	160,008,667	274,883,865
2009 Summer	5,374,426	1,655,395	38,878,161	68,298,203	114,206,184
2010 - 2011	25,169,431	5,150,154	83,392,954	167,248,887	280,961,425
2010 Summer	6,444,395	2,173,412	40,815,508	81,777,327	131,210,641
2011 Summer	4,708,559	1,680,714	38,738,045	75,302,878	120,430,196
Total	168,246,308	35,512,046	650,895,854	1,295,705,716	2,150,359,925

Source: Tabout.dta

Table D.37: Respiratory Disease

Influenza Season	*Hospital Spending: Respiratory Disease*				Total
	0 to 4 years	15 to 64 years	5 to 14 years	65 years and older	
2005 - 2006	16,865,971	5,653,440	42,394,913	74,126,634	139,040,959
2006 - 2007	15,324,098	3,762,988	47,234,688	77,962,063	144,283,837
2006 Summer	7,047,836	2,126,799	23,502,755	33,231,119	65,908,509
2007 - 2008	16,678,204	4,275,008	49,401,748	83,717,134	154,072,094
2007 Summer	6,617,792	1,678,718	23,506,876	39,211,289	71,014,675
2008 - 2009	13,708,679	4,287,087	57,487,274	103,738,187	179,221,227
2008 Summer	5,905,004	2,207,602	28,507,998	41,581,317	78,201,921
2009 - 2010	18,896,438	5,016,599	69,344,965	104,797,881	198,055,882
2009 Summer	6,359,389	1,994,012	30,948,182	46,450,227	85,751,810
2010 - 2011	17,256,319	6,380,989	65,775,685	108,843,728	198,256,720
2010 Summer	6,956,773	2,440,978	30,776,522	52,832,431	93,006,703
2011 Summer	5,841,682	2,206,031	28,336,752	48,084,988	84,469,452
Total	137,458,184	42,030,250	497,218,358	814,576,998	1,491,283,790

Source: Tabout.dta

Table D.38: Bronchitis

Influenza Season	*Hospital Spending: Bronchitis*				Total
	0 to 4 years	15 to 64 years	5 to 14 years	65 years and older	
2005 - 2006	341,683	48,916	98,536	136,447	625,582
2006 - 2007	273,130	19,325	108,225	138,519	539,199
2006 Summer	80,379	2,192	42,331	102,159	227,061
2007 - 2008	485,544	29,333	105,936	102,397	723,210
2007 Summer	93,257	18,580	34,261	54,841	200,939
2008 - 2009	200,748	14,336	100,340	136,617	452,041
2008 Summer	40,032	29,252	46,578	39,431	155,293
2009 - 2010	186,797	9,952	116,095	70,228	383,073
2009 Summer	204,258	3,981	33,767	37,274	279,279
2010 - 2011	355,725	37,995	103,407	119,793	616,921
2010 Summer	41,518	5,971	74,934	15,326	137,750
2011 Summer	43,223	8,185	53,965	50,147	155,520
Total	2,346,295	228,019	918,374	1,003,180	4,495,868

Source: Tabout.dta

Table D.39: Acute Bronchiolitis

Influenza Season	*Hospital Spending: Acute Bronchiolitis*				Total
	0 to 4 years	15 to 64 years	5 to 14 years	65 years and older	
2005 - 2006	11,662,909	32,034	67,516	49,184	11,811,643
2006 - 2007	9,392,028	23,119	10,809	45,094	9,471,051
2006 Summer	1,127,913	146,453	22,954	15,185	1,312,505
2007 - 2008	11,253,392	94,147	138,475	34,432	11,520,445
2007 Summer	2,115,324	6,162	20,038	4,679	2,146,204
2008 - 2009	10,253,589	32,241	93,614	93,343	10,472,787
2008 Summer	1,985,504	9,243	15,902	6,877	2,017,526
2009 - 2010	12,110,828	142,822	126,333	119,437	12,499,420
2009 Summer	1,600,266	20,985	6,310	93,599	1,721,159
2010 - 2011	14,523,055	45,139	183,165	132,874	14,884,233
2010 Summer	1,097,527	16,715	26,871	76,226	1,217,339
2011 Summer	1,245,986	18,140	54,517	15,687	1,334,331
Total	78,368,322	587,201	766,504	686,618	80,408,644

Source: Tabout.dta

Table D.40: Acute Lower Respiratory Infection

	Unspecified Acute Lower Respiratory Infection				
Influenza Season	**0 to 4 years**	**15 to 64 years**	**5 to 14 years**	**65 years and older**	**Total**
2005 - 2006	4,726,347	1,880,158	21,651,746	53,012,270	81,270,520
2006 - 2007	4,772,091	1,504,212	23,029,890	59,216,533	88,522,725
2006 Summer	1,648,734	604,237	12,780,386	25,481,373	40,514,731
2007 - 2008	3,967,936	1,251,941	23,888,437	57,821,271	86,929,585
2007 Summer	1,290,113	487,624	10,814,778	26,262,587	38,855,103
2008 - 2009	4,232,760	1,239,212	24,695,446	65,051,702	95,219,121
2008 Summer	1,392,610	600,544	11,301,335	28,805,130	42,099,618
2009 - 2010	4,729,539	1,521,919	28,323,640	61,377,841	95,952,940
2009 Summer	1,540,400	613,774	12,155,011	24,343,027	38,652,212
2010 - 2011	5,457,907	1,629,838	30,619,447	64,711,174	102,418,366
2010 Summer	2,155,811	833,576	14,656,067	31,226,608	48,872,062
2011 Summer	1,531,280	752,923	14,357,574	30,433,891	47,075,668
Total	37,445,528	12,919,959	228,273,756	527,743,407	806,382,651

Source: Tabout.dta

Table D.41: Other Respiratory Infections

	Hospital Spending: Other Respiratory Disease				
Influenza Season	**0 to 4 years**	**15 to 64 years**	**5 to 14 years**	**65 years and older**	**Total**
2005 - 2006	10,841,945	4,026,072	85,212,881	169,188,521	269,269,418
2006 - 2007	12,137,640	4,333,508	97,580,043	184,650,386	298,701,577
2006 Summer	7,177,775	1,839,511	50,814,376	87,357,250	147,188,911
2007 - 2008	15,028,613	3,804,002	106,420,828	188,230,217	313,483,660
2007 Summer	7,125,788	1,891,884	52,183,520	93,884,905	155,086,097
2008 - 2009	13,427,994	3,835,566	109,863,519	211,768,375	338,895,454
2008 Summer	6,430,800	3,093,641	59,338,126	100,629,752	169,492,319
2009 - 2010	20,894,409	8,696,406	146,764,844	236,017,244	412,372,903
2009 Summer	6,641,601	2,027,495	59,531,959	101,194,873	169,395,927
2010 - 2011	21,334,941	11,053,110	156,959,886	251,349,549	440,697,487
2010 Summer	10,721,094	6,187,615	86,542,931	134,556,927	238,008,567
2011 Summer	9,645,785	6,446,656	78,246,726	123,789,390	218,128,557
Total	141,408,384	57,235,466	1,089,459,639	1,882,617,389	3,170,720,878

Source: Tabout.dta

D.4 Cost of illness of related conditions - Gender breakdown

Table D.42: Ischaemic Heart Disease - Gender breakdown

	Hospital Spending: Ischaemic Heart Disease		
Influenza Season	**Male**	**Female**	**Total**
2005 - 2006	90,946,156	53,929,856	144,876,011
2006 - 2007	96,305,240	55,334,387	151,639,627
2006 Summer	52,022,396	30,205,686	82,228,082
2007 - 2008	95,796,500	53,825,095	149,621,596
2007 Summer	52,528,118	26,828,476	79,356,595
2008 - 2009	100,000,785	56,792,054	156,792,839
2008 Summer	51,554,517	30,909,096	82,463,613
2009 - 2010	130,389,397	64,800,861	195,190,258
2009 Summer	53,324,627	29,682,972	83,007,599
2010 - 2011	144,133,577	69,970,352	214,103,929
2010 Summer	80,016,757	40,149,897	120,166,654
2011 Summer	77,942,547	35,455,286	113,397,833
Total	1,024,960,618	547,884,018	1,572,844,636

Source: Tabout.dta

Table D.43: Cerebrovascular Events - Gender breakdown

	Hospital Spending: Cerebrovascular Disease		
Influenza Season	**Male**	**Female**	**Total**
2005 - 2006	45,106,106	43,545,605	88,651,710
2006 - 2007	47,670,955	45,391,219	93,062,174
2006 Summer	25,082,150	24,338,596	49,420,746
2007 - 2008	54,032,267	49,148,658	103,180,926
2007 Summer	26,507,841	23,532,940	50,040,781
2008 - 2009	58,033,548	54,865,346	112,898,894
2008 Summer	29,890,230	26,587,224	56,477,454
2009 - 2010	65,830,295	58,080,658	123,910,953
2009 Summer	30,682,212	28,695,926	59,378,138
2010 - 2011	66,386,308	56,485,127	122,871,435
2010 Summer	34,409,393	31,036,143	65,445,536
2011 Summer	32,290,868	28,425,712	60,716,580
Total	515,922,173	470,133,155	986,055,328

Source: Tabout.dta

Table D.44: Upper Respiratory Tract Infection - Gender breakdown

	Hospital Spending: Upper Respiratory Tract Infection		
Influenza Season	**Male**	**Female**	**Total**
2005 - 2006	9,675,229	8,550,624	18,225,853
2006 - 2007	8,821,537	8,744,970	17,566,508
2006 Summer	4,318,143	3,972,401	8,290,545
2007 - 2008	8,587,567	7,654,632	16,242,199
2007 Summer	4,841,037	3,795,841	8,636,878
2008 - 2009	9,027,582	8,961,608	17,989,190
2008 Summer	4,037,807	3,378,996	7,416,802
2009 - 2010	9,349,527	9,274,663	18,624,191
2009 Summer	4,430,046	3,418,164	7,848,210
2010 - 2011	10,376,768	9,610,365	19,987,134
2010 Summer	5,192,847	4,394,914	9,587,762
2011 Summer	4,708,104	4,577,920	9,286,024
Total	83,366,196	76,335,098	159,701,294

Source: Tabout.dta

Table D.45: Pneumonia - Gender breakdown

	Hospital Spending: Pneumonia		
Influenza Season	**Male**	**Female**	**Total**
2005 - 2006	112,554,201	96,629,110	209,183,311
2006 - 2007	117,017,735	102,994,210	220,011,946
2006 Summer	52,642,783	44,090,988	96,733,771
2007 - 2008	127,043,058	102,512,547	229,555,604
2007 Summer	55,642,147	45,959,390	101,601,537
2008 - 2009	138,590,476	120,818,816	259,409,292
2008 Summer	60,689,356	51,482,795	112,172,152
2009 - 2010	150,052,821	124,831,044	274,883,865
2009 Summer	62,717,200	51,488,984	114,206,184
2010 - 2011	153,441,049	127,520,376	280,961,425
2010 Summer	74,321,627	56,889,014	131,210,641
2011 Summer	68,755,972	51,674,224	120,430,196
Total	1,173,468,425	976,891,500	2,150,359,925

Source: Tabout.dta

Table D.46: Respiratory Disease - Gender breakdown

	Hospital Spending: Respiratory Disease		
Influenza Season	**Male**	**Female**	**Total**
2005 - 2006	75,717,558	63,323,401	139,040,959
2006 - 2007	77,476,149	66,807,688	144,283,837
2006 Summer	36,341,772	29,566,737	65,908,509
2007 - 2008	87,099,641	66,972,453	154,072,094
2007 Summer	39,759,967	31,254,708	71,014,675
2008 - 2009	95,984,203	83,237,024	179,221,227
2008 Summer	42,959,034	35,242,887	78,201,921
2009 - 2010	109,214,901	88,840,982	198,055,882
2009 Summer	47,710,115	38,041,695	85,751,810
2010 - 2011	108,344,947	89,911,774	198,256,720
2010 Summer	53,457,238	39,549,464	93,006,703
2011 Summer	48,581,740	35,887,713	84,469,452
Total	822,647,263	668,636,527	1,491,283,790

Source: Tabout.dta

Table D.47: Bronchitis - Gender breakdown

	Hospital Spending: Bronchitis		
Influenza Season	**Male**	**Female**	**Total**
2005 - 2006	320,743	304,839	625,582
2006 - 2007	336,010	203,189	539,199
2006 Summer	100,141	126,920	227,061
2007 - 2008	423,871	299,339	723,210
2007 Summer	51,965	148,973	200,939
2008 - 2009	263,255	188,785	452,041
2008 Summer	103,094	52,199	155,293
2009 - 2010	191,466	191,607	383,073
2009 Summer	233,327	45,952	279,279
2010 - 2011	119,369	497,552	616,921
2010 Summer	59,529	78,220	137,750
2011 Summer	79,920	75,599	155,520
Total	2,282,691	2,213,177	4,495,868

Source: Tabout.dta

Table D.48: Acute Bronchiolitis - Gender breakdown

	Hospital Spending: Acute Bronchiolitis		
Influenza Season	**Male**	**Female**	**Total**
2005 - 2006	7,140,375	4,671,268	11,811,643
2006 - 2007	5,569,221	3,901,830	9,471,051
2006 Summer	898,086	414,419	1,312,505
2007 - 2008	7,289,517	4,230,928	11,520,445
2007 Summer	1,116,757	1,029,447	2,146,204
2008 - 2009	6,113,264	4,359,523	10,472,787
2008 Summer	1,401,831	615,695	2,017,526
2009 - 2010	7,148,659	5,350,761	12,499,420
2009 Summer	770,493	950,666	1,721,159
2010 - 2011	8,550,063	6,334,170	14,884,233
2010 Summer	707,828	509,511	1,217,339
2011 Summer	783,946	550,384	1,334,331
Total	47,490,041	32,918,603	80,408,644

Source: Tabout.dta

Table D.49: Acute Lower Respiratory Infection - Gender breakdown

	Hospital Spending: Unspecified Acute Lower Respiratory Infection		
Influenza Season	**Male**	**Female**	**Total**
2005 - 2006	41,937,882	39,332,638	81,270,520
2006 - 2007	46,177,763	42,344,962	88,522,725
2006 Summer	21,066,135	19,448,596	40,514,731
2007 - 2008	45,644,964	41,284,621	86,929,585
2007 Summer	20,900,923	17,954,180	38,855,103
2008 - 2009	49,715,406	45,503,715	95,219,121
2008 Summer	21,686,762	20,412,856	42,099,618
2009 - 2010	49,794,624	46,158,316	95,952,940
2009 Summer	20,732,861	17,919,351	38,652,212
2010 - 2011	54,345,790	48,072,576	102,418,366
2010 Summer	26,892,550	21,979,512	48,872,062
2011 Summer	26,000,136	21,075,532	47,075,668
Total	424,895,795	381,486,856	806,382,651

Source: Tabout.dta

Table D.50: Other Respiratory Infections - Gender breakdown

	Hospital Spending: Other Respiratory Disease		
Influenza Season	**Male**	**Female**	**Total**
2005 - 2006	146,591,354	122,678,065	269,269,418
2006 - 2007	162,509,113	136,192,464	298,701,577
2006 Summer	79,623,320	67,565,591	147,188,911
2007 - 2008	173,462,706	140,020,954	313,483,660
2007 Summer	87,750,947	67,335,150	155,086,097
2008 - 2009	181,804,857	157,090,596	338,895,454
2008 Summer	91,307,362	78,184,958	169,492,319
2009 - 2010	226,808,539	185,564,364	412,372,903
2009 Summer	93,646,216	75,749,711	169,395,927
2010 - 2011	239,318,031	201,379,456	440,697,487
2010 Summer	132,980,582	105,027,985	238,008,567
2011 Summer	119,286,197	98,842,360	218,128,557
Total	1,735,089,223	1,435,631,655	3,170,720,878

Source: Tabout.dta

D.5 Cost of illness of related conditions - Primary versus Secondary diagnosis

Table D.51: Ischaemic Heart Disease - Primary versus Secondary diagnosis

	Hospital Spending: Ischaemic Heart Disease		
Influenza Season	**Primary**	**Secondary**	**Total**
2005 - 2006	37,549,867	107,326,144	144,876,011
2006 - 2007	36,538,072	115,101,555	151,639,627
2006 Summer	20,717,769	61,510,313	82,228,082
2007 - 2008	34,577,988	115,043,608	149,621,596
2007 Summer	19,780,004	59,576,590	79,356,595
2008 - 2009	29,978,284	126,814,555	156,792,839
2008 Summer	17,702,448	64,761,165	82,463,613
2009 - 2010	36,623,203	158,567,056	195,190,258
2009 Summer	16,291,230	66,716,368	83,007,599
2010 - 2011	42,730,789	171,373,140	214,103,929
2010 Summer	24,281,800	95,884,854	120,166,654
2011 Summer	25,009,652	88,388,181	113,397,833
Total	341,781,107	1,231,063,529	1,572,844,636

Source: Tabout.dta

Table D.52: Cerebrovascular Events - Primary versus Secondary diagnosis

	Hospital Spending: Cerebrovascular Disease		
Influenza Season	**Primary**	**Secondary**	**Total**
2005 - 2006	48,077,795	40,573,915	88,651,710
2006 - 2007	50,407,438	42,654,736	93,062,174
2006 Summer	27,644,307	21,776,439	49,420,746
2007 - 2008	50,171,791	53,009,135	103,180,926
2007 Summer	26,240,615	23,800,166	50,040,781
2008 - 2009	52,930,171	59,968,723	112,898,894
2008 Summer	25,295,514	31,181,940	56,477,454
2009 - 2010	50,528,226	73,382,727	123,910,953
2009 Summer	27,656,799	31,721,340	59,378,138
2010 - 2011	48,289,865	74,581,570	122,871,435
2010 Summer	26,302,869	39,142,667	65,445,536
2011 Summer	27,366,113	33,350,468	60,716,580
Total	460,911,504	525,143,824	986,055,328

Source: Tabout.dta

Table D.53: Upper Respiratory Tract Infection - Primary versus Secondary diagnosis

	Hospital Spending: Upper Respiratory Tract Infection		
Influenza Season	**Primary**	**Secondary**	**Total**
2005 - 2006	10,420,822	7,805,031	18,225,853
2006 - 2007	9,577,157	7,989,351	17,566,508
2006 Summer	4,728,074	3,562,470	8,290,545
2007 - 2008	8,851,402	7,390,797	16,242,199
2007 Summer	4,756,795	3,880,083	8,636,878
2008 - 2009	9,429,598	8,559,592	17,989,190
2008 Summer	3,905,673	3,511,130	7,416,802
2009 - 2010	9,471,434	9,152,757	18,624,191
2009 Summer	4,558,935	3,289,275	7,848,210
2010 - 2011	9,891,240	10,095,893	19,987,134
2010 Summer	4,477,024	5,110,738	9,587,762
2011 Summer	4,592,435	4,693,589	9,286,024
Total	84,660,588	75,040,706	159,701,294

Source: Tabout.dta

Table D.54: Pneumonia - Primary versus Secondary diagnosis

	Hospital Spending: Pneumonia		
Influenza Season	**Primary**	**Secondary**	**Total**
2005 - 2006	91,126,152	118,057,159	209,183,311
2006 - 2007	88,787,899	131,224,046	220,011,946
2006 Summer	35,408,750	61,325,022	96,733,771
2007 - 2008	92,008,955	137,546,650	229,555,604
2007 Summer	34,527,653	67,073,884	101,601,537
2008 - 2009	99,091,388	160,317,904	259,409,292
2008 Summer	35,421,954	76,750,197	112,172,152
2009 - 2010	92,134,098	182,749,766	274,883,865
2009 Summer	35,906,025	78,300,159	114,206,184
2010 - 2011	95,975,951	184,985,474	280,961,425
2010 Summer	36,606,856	94,603,786	131,210,641
2011 Summer	39,553,628	80,876,568	120,430,196
Total	776,549,310	1,373,810,615	2,150,359,925

Source: Tabout.dta

Table D.55: Respiratory Disease - Primary versus Secondary diagnosis

	Hospital Spending: Respiratory Disease		
Influenza Season	**Primary**	**Secondary**	**Total**
2005 - 2006	57,587,984	81,452,975	139,040,959
2006 - 2007	54,531,943	89,751,894	144,283,837
2006 Summer	24,800,780	41,107,729	65,908,509
2007 - 2008	58,703,681	95,368,413	154,072,094
2007 Summer	24,054,156	46,960,520	71,014,675
2008 - 2009	66,976,949	112,244,278	179,221,227
2008 Summer	24,502,173	53,699,747	78,201,921
2009 - 2010	65,571,670	132,484,212	198,055,882
2009 Summer	28,680,663	57,071,147	85,751,810
2010 - 2011	66,772,000	131,484,720	198,256,720
2010 Summer	27,626,738	65,379,965	93,006,703
2011 Summer	29,654,550	54,814,902	84,469,452
Total	529,463,287	961,820,503	1,491,283,790

Source: Tabout.dta

Appendix E

Ambulatory surgery: Supplementary figures

E.1 Price Regression including hospitals

Table E.1: Price CPT Fixed Effects Part 1

	CPT 29826	CPT 29880	CPT 29881	CPT 43239
ASC	-30.49	-146.7	-82.45	-40.25*
	(0.824)	(0.202)	(0.236)	(0.046)
Poverty rate	354.2	-2843.7	1829.8	750.8
	(0.926)	(0.374)	(0.343)	(0.180)
White ethnicity	4033.1**	3100.1*	2154.4**	-407.2
	(0.010)	(0.018)	(0.006)	(0.075)
65 years and older	21364.4	6894.9	-7325.4	314.0
	(0.104)	(0.532)	(0.271)	(0.871)
Hospitals: short term general	164.2	106.1	-23.45	-0.559
	(0.154)	(0.286)	(0.688)	(0.974)
Wage Index	-712.2	2025.6	-1114.2	451.7*
	(0.614)	(0.091)	(0.120)	(0.030)
2008bn.year	375.5**	250.1*	131.8*	87.80***
	(0.001)	(0.011)	(0.026)	(0.000)
2009.year	930.9***	492.6***	389.3***	203.7***
	(0.000)	(0.000)	(0.000)	(0.000)
2010.year	1219.8***	629.6***	630.5***	247.2***
	(0.000)	(0.000)	(0.000)	(0.000)
2011.year	1776.9***	968.9***	743.9***	376.9***
	(0.000)	(0.000)	(0.000)	(0.000)
Constant	2674.5	671.6	5637.9***	2072.0***
	(0.282)	(0.748)	(0.000)	(0.000)
Observations	1818	1802	1819	1819
rho	0.766	0.654	0.838	0.899

p-values in parentheses

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table E.2: Price CPT Fixed Effects Part 2

	CPT 45378	CPT 45380	CPT 45385	CPT 52000
ASC	-27.49*	-52.93**	-75.18***	-86.17*
	(0.021)	(0.001)	(0.000)	(0.027)
Poverty rate	374.6	-380.9	-488.8	2701.1*
	(0.256)	(0.403)	(0.326)	(0.012)
White ethnicity	544.7***	432.8*	447.3*	827.5
	(0.000)	(0.020)	(0.028)	(0.060)
65 years and older	680.9	3613.4*	189.7	-15792.9***
	(0.550)	(0.021)	(0.912)	(0.000)
Hospitals: short term general	-5.966	-17.90	-9.882	46.97
	(0.550)	(0.194)	(0.511)	(0.150)
Wage Index	86.20	260.7	87.62	-120.7
	(0.481)	(0.122)	(0.635)	(0.763)
2008bn.year	47.92***	68.05***	48.81**	181.3***
	(0.000)	(0.000)	(0.001)	(0.000)
2009.year	99.64***	160.0***	105.2***	284.7***
	(0.000)	(0.000)	(0.000)	(0.000)
2010.year	167.2***	213.7***	169.3***	444.7***
	(0.000)	(0.000)	(0.000)	(0.000)
2011.year	189.0***	252.6***	181.4***	761.1***
	(0.000)	(0.000)	(0.000)	(0.000)
Constant	905.4***	1126.2***	1791.0***	2250.2**
	(0.000)	(0.000)	(0.000)	(0.001)
Observations	1819	1819	1819	1819
rho	0.908	0.907	0.891	0.783

p-values in parentheses

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table E.3: Price CPT Fixed Effects Part 3

	CPT 62311	CPT 64483	CPT 66984	CPT 69436
ASC	-10.15	31.43	-61.16	-18.02
	(0.761)	(0.236)	(0.069)	(0.711)
Poverty rate	-1657.4	-1016.6	950.7	-1050.0
	(0.073)	(0.167)	(0.308)	(0.437)
White ethnicity	-56.73	195.1	-385.6	427.8
	(0.881)	(0.516)	(0.311)	(0.438)
65 years and older	2758.3	-5384.2*	2339.7	7230.5
	(0.387)	(0.034)	(0.467)	(0.121)
Hospitals: short term general	28.83	41.75	-8.909	24.70
	(0.303)	(0.061)	(0.752)	(0.545)
Wage Index	-547.6	-535.2*	259.0	126.4
	(0.111)	(0.050)	(0.454)	(0.801)
2008bn.year	22.80	3.051	7.678	95.53*
	(0.423)	(0.893)	(0.789)	(0.022)
2009.year	24.46	39.54	-32.17	340.6***
	(0.454)	(0.128)	(0.328)	(0.000)
2010.year	114.1**	30.32	-28.21	446.7***
	(0.009)	(0.382)	(0.521)	(0.000)
2011.year	179.3**	8.179	18.77	555.0***
	(0.005)	(0.871)	(0.769)	(0.000)
Constant	1681.6**	2456.3***	3111.2***	1708.8
	(0.005)	(0.000)	(0.000)	(0.053)
Observations	1819	1816	1819	1818
rho	0.759	0.827	0.879	0.736

p-values in parentheses

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table E.4: Price CPT Random Effects Part 1

	CPT 29826	CPT 29880	CPT 29881	CPT 43239
ASC	-14.63	-69.25	-40.30	-30.37*
	(0.818)	(0.132)	(0.294)	(0.033)
Poverty rate	-4286.8	-2516.6	-2286.3	-599.9
	(0.073)	(0.157)	(0.098)	(0.199)
White ethnicity	2839.8**	1577.3*	1413.3**	196.3
	(0.002)	(0.017)	(0.007)	(0.286)
65 years and older	-9598.6**	-8867.4***	-9709.7***	-411.2
	(0.005)	(0.000)	(0.000)	(0.635)
Hospitals: short term general	358.0***	315.2***	77.07	25.50
	(0.000)	(0.000)	(0.158)	(0.121)
Wage Index	5060.6***	4751.8***	3020.1***	781.4***
	(0.000)	(0.000)	(0.000)	(0.000)
2008bn.year	501.3***	305.1**	170.2**	93.71***
	(0.000)	(0.001)	(0.004)	(0.000)
2009.year	1164.8***	557.6***	473.8***	228.1***
	(0.000)	(0.000)	(0.000)	(0.000)
2010.year	1468.0***	621.4***	723.0***	321.6***
	(0.000)	(0.000)	(0.000)	(0.000)
2011.year	2466.5***	1377.0***	1046.1***	471.3***
	(0.000)	(0.000)	(0.000)	(0.000)
Constant	2396.2	834.0	2880.9***	1469.3***
	(0.058)	(0.372)	(0.000)	(0.000)
Observations	1818	1802	1819	1819
rho	0.641	0.542	0.736	0.870

p-values in parentheses

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table E.5: Price CPT Random Effects Part 2

	CPT 45378	CPT 45380	CPT 45385	CPT 52000
ASC	-28.65**	-43.06***	-59.09***	5.659
	(0.001)	(0.000)	(0.000)	(0.742)
Poverty rate	-236.8	-989.1*	-1180.4**	445.7
	(0.399)	(0.010)	(0.004)	(0.496)
White ethnicity	514.5***	600.0***	554.6***	307.5
	(0.000)	(0.000)	(0.001)	(0.208)
65 years and older	123.4	178.3	-795.0	-2588.0**
	(0.820)	(0.806)	(0.295)	(0.005)
Hospitals: short term general	8.529	7.677	15.54	48.51
	(0.380)	(0.568)	(0.285)	(0.087)
Wage Index	386.4***	555.2***	447.8**	-186.6
	(0.000)	(0.000)	(0.001)	(0.348)
2008bn.year	52.46***	78.64***	53.18***	141.9***
	(0.000)	(0.000)	(0.000)	(0.000)
2009.year	112.6***	184.1***	119.1***	240.3***
	(0.000)	(0.000)	(0.000)	(0.000)
2010.year	185.9***	257.4***	197.8***	385.4***
	(0.000)	(0.000)	(0.000)	(0.000)
2011.year	234.6***	338.2***	248.5***	704.1***
	(0.000)	(0.000)	(0.000)	(0.000)
Constant	777.8***	1176.2***	1505.0***	1141.5***
	(0.000)	(0.000)	(0.000)	(0.001)
Observations	1819	1819	1819	1819
rho	0.889	0.879	0.867	0.602

p-values in parentheses

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table E.6: Price CPT Random Effects Part 3

	CPT 62311	CPT 64483	CPT 66984	CPT 69436
ASC	12.77	32.90*	-106.7***	-50.09*
	(0.417)	(0.026)	(0.000)	(0.020)
Poverty rate	-1290.6*	-1110.7*	-644.6	-2214.2**
	(0.028)	(0.036)	(0.381)	(0.007)
White ethnicity	215.9	-129.1	153.5	53.90
	(0.329)	(0.523)	(0.592)	(0.860)
65 years and older	-3087.1***	-3066.5***	-4650.7***	-926.6
	(0.000)	(0.000)	(0.000)	(0.425)
Hospitals: short term general	43.86	42.67*	47.00	82.87*
	(0.075)	(0.038)	(0.083)	(0.019)
Wage Index	1131.1***	1071.6***	1228.4***	2214.6***
	(0.000)	(0.000)	(0.000)	(0.000)
2008bn.year	47.50	9.052	39.26	136.6***
	(0.084)	(0.682)	(0.166)	(0.001)
2009.year	53.15	39.90	37.45	410.3***
	(0.064)	(0.087)	(0.216)	(0.000)
2010.year	161.6***	13.33	97.47**	518.7***
	(0.000)	(0.632)	(0.009)	(0.000)
2011.year	248.7***	0.697	231.4***	757.2***
	(0.000)	(0.987)	(0.000)	(0.000)
Constant	465.4	878.3**	2866.8***	1196.0**
	(0.135)	(0.002)	(0.000)	(0.006)
Observations	1819	1816	1819	1818
rho	0.653	0.754	0.822	0.611

p-values in parentheses

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

E.2 Random Effects: Price Regression Base Case

Table E.7: Price CPT Random Effects Excl. Hosp. Part 1

	CPT 29826	CPT 29880	CPT 29881	CPT 43239
ASC	4.139	-55.33	-37.11	-29.14*
	(0.949)	(0.241)	(0.342)	(0.042)
Poverty rate	-3628.4	-2113.8	-2074.2	-492.6
	(0.134)	(0.245)	(0.137)	(0.292)
White ethnicity	3127.2***	1845.9**	1486.2**	185.2
	(0.001)	(0.006)	(0.005)	(0.316)
65 years and older	-9219.1**	-8659.6***	-9665.9***	-319.1
	(0.009)	(0.001)	(0.000)	(0.717)
Wage Index	4653.0***	4396.7***	2857.8***	757.9***
	(0.000)	(0.000)	(0.000)	(0.000)
2008bn.year	491.5***	295.9**	167.5**	92.79***
	(0.000)	(0.002)	(0.004)	(0.000)
2009.year	1141.7***	541.4***	467.7***	225.3***
	(0.000)	(0.000)	(0.000)	(0.000)
2010.year	1453.4***	614.0***	718.5***	316.9***
	(0.000)	(0.000)	(0.000)	(0.000)
2011.year	1907.0***	895.4***	923.3***	428.7***
	(0.000)	(0.000)	(0.000)	(0.000)
Constant	2909.9*	1314.3	3052.5***	1510.9***
	(0.023)	(0.167)	(0.000)	(0.000)
Observations	1818	1802	1819	1819
rho	0.657	0.567	0.752	0.877

p-values in parentheses

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table E.8: Price CPT Random Effects Excl. Hosp. Part 2

	CPT 45378	CPT 45380	CPT 45385	CPT 52000
ASC	-28.09**	-43.12***	-58.92***	8.170
	(0.001)	(0.000)	(0.000)	(0.633)
Poverty rate	-185.2	-936.9*	-1113.6**	523.9
	(0.510)	(0.015)	(0.007)	(0.422)
White ethnicity	520.3***	593.1***	556.6***	346.0
	(0.000)	(0.000)	(0.001)	(0.155)
65 years and older	152.8	268.4	-739.6	-2555.4**
	(0.783)	(0.718)	(0.342)	(0.006)
Wage Index	368.0***	539.2***	423.5**	-233.8
	(0.000)	(0.000)	(0.002)	(0.236)
2008bn.year	52.05***	78.16***	52.63***	140.7***
	(0.000)	(0.000)	(0.000)	(0.000)
2009.year	111.4***	182.8***	117.4***	237.4***
	(0.000)	(0.000)	(0.000)	(0.000)
2010.year	184.4***	254.9***	195.5***	383.8***
	(0.000)	(0.000)	(0.000)	(0.000)
2011.year	220.0***	324.2***	222.6***	628.8***
	(0.000)	(0.000)	(0.000)	(0.000)
Constant	791.7***	1190.6***	1533.9***	1207.5***
	(0.000)	(0.000)	(0.000)	(0.000)
Observations	1819	1819	1819	1819
rho	0.898	0.889	0.878	0.603

p-values in parentheses

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table E.9: Price CPT Random Effects Excl. Hosp. Part 3

	CPT 62311	CPT 64483	CPT 66984	CPT 69436
ASC	15.07	35.32*	-102.6***	-45.45*
	(0.339)	(0.017)	(0.000)	(0.037)
Poverty rate	-1223.6*	-1037.0*	-490.1	-2078.9*
	(0.038)	(0.050)	(0.507)	(0.012)
White ethnicity	247.0	-97.98	156.8	120.6
	(0.264)	(0.629)	(0.587)	(0.695)
65 years and older	-3045.9***	-3021.6***	-4491.4***	-860.2
	(0.000)	(0.000)	(0.000)	(0.466)
Wage Index	1084.2***	1028.0***	1169.3***	2116.9***
	(0.000)	(0.000)	(0.000)	(0.000)
2008bn.year	46.33	7.793	37.37	134.2***
	(0.092)	(0.724)	(0.183)	(0.001)
2009.year	50.52	37.19	32.53	405.1***
	(0.078)	(0.110)	(0.279)	(0.000)
2010.year	160.0***	11.51	90.81*	515.6***
	(0.000)	(0.679)	(0.015)	(0.000)
2011.year	180.5***	-65.90*	154.0***	628.1***
	(0.000)	(0.016)	(0.000)	(0.000)
Constant	531.3	937.5***	2941.9***	1322.6**
	(0.087)	(0.001)	(0.000)	(0.002)
Observations	1819	1816	1819	1818
rho	0.657	0.757	0.834	0.622

p-values in parentheses

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

E.3 Fixed Effects: Price Regression starting point

Table E.10: Price CPT Fixed Effects Basic Part 1

	CPT 29826	CPT 29880	CPT 29881	CPT 43239
ASC	-18.82	-141.3	-95.56	-23.75
	(0.891)	(0.216)	(0.167)	(0.256)
2008bn.year	440.1***	241.7*	121.4*	91.55***
	(0.000)	(0.011)	(0.034)	(0.000)
2009.year	1023.9***	452.1***	388.7***	219.1***
	(0.000)	(0.000)	(0.000)	(0.000)
2010.year	1112.7***	384.7***	520.7***	293.4***
	(0.000)	(0.000)	(0.000)	(0.000)
2011.year	1662.9***	714.3***	753.5***	410.2***
	(0.000)	(0.000)	(0.000)	(0.000)
Constant	8378.9***	5899.7***	5644.7***	2267.9***
	(0.000)	(0.000)	(0.000)	(0.000)
Observations	1823	1807	1824	1825
rho	0.721	0.658	0.825	0.887

p-values in parentheses

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table E.11: Price CPT Fixed Effects Basic Part 2

	CPT 45378	CPT 45380	CPT 45385	CPT 52000
ASC	-25.57*	-48.73**	-74.66***	-97.28*
	(0.031)	(0.003)	(0.000)	(0.013)
2008bn.year	49.95***	76.81***	50.07***	140.1***
	(0.000)	(0.000)	(0.001)	(0.000)
2009.year	105.8***	171.4***	96.73***	247.8***
	(0.000)	(0.000)	(0.000)	(0.000)
2010.year	147.5***	200.8***	130.7***	382.6***
	(0.000)	(0.000)	(0.000)	(0.000)
2011.year	205.8***	292.9***	175.5***	638.5***
	(0.000)	(0.000)	(0.000)	(0.000)
Constant	1569.4***	2123.4***	2197.8***	1233.1***
	(0.000)	(0.000)	(0.000)	(0.000)
Observations	1825	1826	1825	1824
rho	0.907	0.900	0.893	0.671

p-values in parentheses

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table E.12: Price CPT Fixed Effects Basic Part 3

	CPT 62311	CPT 64483	CPT 66984	CPT 69436
ASC	-5.403	32.65	-53.09	-14.31
	(0.870)	(0.217)	(0.113)	(0.766)
2008bn.year	31.46	-9.517	19.66	114.0**
	(0.248)	(0.663)	(0.478)	(0.004)
2009.year	17.46	1.342	-8.161	358.3***
	(0.528)	(0.952)	(0.772)	(0.000)
2010.year	95.91***	-32.77	24.05	434.4***
	(0.001)	(0.142)	(0.395)	(0.000)
2011.year	115.0***	-126.9***	77.55**	539.1***
	(0.000)	(0.000)	(0.006)	(0.000)
Constant	1276.5***	1331.9***	3440.9***	3016.0***
	(0.000)	(0.000)	(0.000)	(0.000)
Observations	1824	1821	1825	1824
rho	0.725	0.810	0.875	0.714

p-values in parentheses

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

E.4 Comparator analyses

Table E.13: Volume E&M Fixed Effects Part 1

	(1) E&M 99202	(2) E&M 99203	(3) E&M 99204	(4) E&M 99211
TotASClagPop	0.0353	-0.0223	0.0224	0.0195
	(0.120)	(0.429)	(0.157)	(0.249)
agegrp2_mean	0.780	1.412	-0.564	-0.0412
	(0.437)	(0.257)	(0.419)	(0.956)
agegrp3_mean	0.703	-1.088	-2.146*	-0.844
	(0.624)	(0.540)	(0.031)	(0.427)
agegrp4_mean	0.384	1.692	-1.146	0.405
	(0.693)	(0.161)	(0.091)	(0.575)
agegrp5_mean	0.870	1.471	-0.787	0.299
	(0.290)	(0.149)	(0.169)	(0.624)
emprel2_mean	1.340	-0.116	0.333	0.0293
	(0.132)	(0.916)	(0.590)	(0.965)
emprel3_mean	0.409	2.182*	-0.767	0.776
	(0.627)	(0.037)	(0.190)	(0.214)
sex_mean	0.703	-1.413	0.680	0.269
	(0.472)	(0.244)	(0.317)	(0.711)
2008bn.year	0.0136	0.00568	-0.0215	-0.0267
	(0.486)	(0.815)	(0.114)	(0.066)
2009.year	0.00383	-0.00491	-0.0314*	-0.0220
	(0.858)	(0.853)	(0.035)	(0.167)
2010.year	0.0130	0.00838	-0.0151	-0.0289
	(0.569)	(0.767)	(0.339)	(0.087)
2011.year	0.0211	-0.0631	0.00402	-0.0285
	(0.591)	(0.196)	(0.883)	(0.329)
Constant	-1.332	-0.515	0.634	-0.380
	(0.094)	(0.602)	(0.252)	(0.520)
Observations	1815	1815	1815	1815
rho	0.231	0.187	0.228	0.194

p-values in parentheses

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table E.14: Volume E&M Fixed Effects Part 2

	(1) E&M 99212	(2) E&M 99213	(3) E&M 99214
TotASClagPop	-0.0151	-0.0624	0.0402
	(0.741)	(0.401)	(0.515)
agegrp2_mean	-0.783	-5.620	2.007
	(0.698)	(0.087)	(0.461)
agegrp3_mean	0.401	-1.511	0.426
	(0.889)	(0.747)	(0.913)
agegrp4_mean	-2.936	-2.217	4.060
	(0.133)	(0.487)	(0.125)
agegrp5_mean	-0.431	-2.052	1.102
	(0.794)	(0.446)	(0.622)
emprel2_mean	-0.739	0.645	-2.145
	(0.679)	(0.825)	(0.374)
emprel3_mean	0.230	-3.343	0.872
	(0.892)	(0.225)	(0.703)
sex_mean	-0.788	2.955	-4.107
	(0.688)	(0.355)	(0.122)
2008bn.year	-0.0151	0.0150	0.0716
	(0.701)	(0.814)	(0.177)
2009.year	-0.0224	0.0984	0.0643
	(0.603)	(0.161)	(0.269)
2010.year	-0.00640	0.0814	0.0173
	(0.889)	(0.274)	(0.780)
2011.year	-0.0962	0.228	0.0205
	(0.223)	(0.076)	(0.848)
Constant	1.480	2.499	1.035
	(0.354)	(0.337)	(0.632)
Observations	1815	1815	1815
rho	0.178	0.199	0.189

p-values in parentheses

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table E.15: Volume E&M Fixed Effects Part 3

	(1) E&M 99215	(2) E&M 99243	(3) E&M 99244
TotASClagPop	0.0264	-0.00466	-0.0139
	(0.179)	(0.800)	(0.482)
agegrp2_mean	0.893	0.699	0.517
	(0.303)	(0.389)	(0.554)
agegrp3_mean	0.359	0.381	-0.398
	(0.771)	(0.742)	(0.749)
agegrp4_mean	0.124	-0.960	1.228
	(0.882)	(0.223)	(0.148)
agegrp5_mean	-0.692	0.811	-0.222
	(0.330)	(0.223)	(0.756)
emprel2_mean	0.973	-0.318	0.802
	(0.205)	(0.659)	(0.300)
emprel3_mean	-0.182	0.0123	-0.146
	(0.802)	(0.986)	(0.842)
sex_mean	1.188	0.687	0.751
	(0.159)	(0.384)	(0.377)
2008bn.year	-0.0180	-0.0227	-0.00405
	(0.286)	(0.150)	(0.812)
2009.year	-0.00570	-0.0104	-0.0323
	(0.758)	(0.549)	(0.083)
2010.year	-0.0148	-0.0257	-0.0195
	(0.450)	(0.162)	(0.324)
2011.year	-0.0254	-0.0394	-0.00740
	(0.454)	(0.215)	(0.829)
Constant	-0.934	-0.384	-0.690
	(0.174)	(0.550)	(0.319)
Observations	1815	1815	1815
rho	0.203	0.185	0.193

p-values in parentheses

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table E.16: Price E&M Fixed Effects Excl. Hosp. Part 1

	E&M 99202	E&M 99203	E&M 99204	E&M 99211
ASC	0.459	-0.353	-0.704	0.101
	(0.120)	(0.355)	(0.255)	(0.716)
Poverty rate	10.38	0.468	1.283	11.57
	(0.205)	(0.965)	(0.940)	(0.135)
White ethnicity	-4.809	5.855	-12.25	6.913*
	(0.152)	(0.177)	(0.081)	(0.029)
65 years and older	90.33**	106.1**	253.3***	-9.558
	(0.001)	(0.004)	(0.000)	(0.719)
Wage Index	11.70***	4.503	9.206	-1.665
	(0.000)	(0.253)	(0.149)	(0.562)
2008bn.year	0.125	0.460	3.282***	-0.379
	(0.621)	(0.159)	(0.000)	(0.112)
2009.year	0.967***	1.829***	6.966***	-0.697*
	(0.001)	(0.000)	(0.000)	(0.010)
2010.year	2.531***	4.791***	13.03***	-0.562
	(0.000)	(0.000)	(0.000)	(0.123)
2011.year	4.805***	6.814***	18.41***	-0.729*
	(0.000)	(0.000)	(0.000)	(0.047)
Constant	55.74***	89.15***	128.3***	23.26***
	(0.000)	(0.000)	(0.000)	(0.000)
Observations	1819	1819	1819	1819
rho	0.959	0.961	0.960	0.811

p-values in parentheses

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table E.17: Price E&M Fixed Effects Excl. Hosp. Part 2

	E&M 99212	E&M 99213	E&M 99214
ASC	-0.0398	-0.162	-0.292
	(0.822)	(0.542)	(0.443)
Poverty rate	5.736	-2.772	0.111
	(0.241)	(0.708)	(0.992)
White ethnicity	-4.341*	-9.318**	6.305
	(0.030)	(0.002)	(0.146)
65 years and older	25.01	134.1***	181.9***
	(0.138)	(0.000)	(0.000)
Wage Index	2.604	5.839*	0.973
	(0.152)	(0.034)	(0.805)
2008bn.year	0.398**	3.383***	3.998***
	(0.008)	(0.000)	(0.000)
2009.year	1.135***	5.942***	7.520***
	(0.000)	(0.000)	(0.000)
2010.year	1.816***	8.776***	11.95***
	(0.000)	(0.000)	(0.000)
2011.year	3.074***	11.88***	15.35***
	(0.000)	(0.000)	(0.000)
Constant	43.36***	51.10***	70.68***
	(0.000)	(0.000)	(0.000)
Observations	1819	1819	1819
rho	0.959	0.964	0.967

p-values in parentheses

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table E.18: Price E&M Fixed Effects Excl. Hosp. Part 3

	E&M 99215	E&M 99243	E&M 99244
ASC	-0.0632	1.101	-0.0173
	(0.913)	(0.085)	(0.986)
Poverty rate	8.099	-0.330	11.01
	(0.614)	(0.985)	(0.690)
White ethnicity	15.30*	-18.88**	-11.28
	(0.020)	(0.009)	(0.319)
65 years and older	227.6***	304.8***	336.2***
	(0.000)	(0.000)	(0.000)
Wage Index	-3.877	10.10	13.71
	(0.516)	(0.126)	(0.182)
2008bn.year	3.143***	1.918***	6.078***
	(0.000)	(0.000)	(0.000)
2009.year	7.584***	4.909***	12.67***
	(0.000)	(0.000)	(0.000)
2010.year	12.48***	8.265***	20.54***
	(0.000)	(0.000)	(0.000)
2011.year	15.52***	10.19***	23.71***
	(0.000)	(0.000)	(0.000)
Constant	104.2***	115.1***	161.8***
	(0.000)	(0.000)	(0.000)
Observations	1819	1819	1819
rho	0.959	0.962	0.954

p-values in parentheses

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table E.19: Volume DRG Fixed Effects Part 1

	DRG 313	DRG 392	DRG 470	DRG 579
TotASClagPop	0.0000664*	-0.0000571	0.0000913*	-0.0000139**
	(0.021)	(0.099)	(0.024)	(0.002)
agegrp2_mean	-0.00206	0.00224	-0.00212	-0.000116
	(0.105)	(0.140)	(0.232)	(0.481)
agegrp3_mean	-0.00218	-0.00445*	-0.000841	0.000520*
	(0.229)	(0.041)	(0.741)	(0.022)
agegrp4_mean	-0.00218	0.00523***	0.000820	0.0000871
	(0.076)	(0.000)	(0.634)	(0.598)
agegrp5_mean	-0.00116	0.000894	0.0135***	0.000189
	(0.267)	(0.477)	(0.000)	(0.194)
emprel2_mean	0.000499	0.00357**	-0.00264	0.0000594
	(0.661)	(0.009)	(0.096)	(0.711)
emprel3_mean	-0.000402	0.000276	0.00551***	0.0000530
	(0.708)	(0.831)	(0.000)	(0.698)
sex_mean	0.00178	0.00359*	-0.000339	0.0000131
	(0.155)	(0.016)	(0.846)	(0.938)
2008bn.year	-0.000157***	-0.000153***	0.0000293	0.00000359
	(0.000)	(0.000)	(0.399)	(0.222)
2009.year	-0.000257***	-0.000205***	0.000186***	-0.000000307
	(0.000)	(0.000)	(0.000)	(0.930)
2010.year	-0.000393***	-0.000188***	0.000251***	-0.00000359
	(0.000)	(0.000)	(0.000)	(0.330)
2011.year	-0.000537***	-0.000271***	0.000130	-0.000000685
	(0.000)	(0.000)	(0.062)	(0.914)
Constant	0.00140	-0.00187	-0.00111	-0.0000819
	(0.164)	(0.124)	(0.432)	(0.524)
Observations	1791	1820	1824	891
rho	0.712	0.685	0.589	0.861

p-values in parentheses

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table E.20: Volume DRG Fixed Effects Part 2

	DRG 580	DRG 581	DRG 582	DRG 583
TotASClagPop	-0.0000105	-0.0000143	0.00000350	-0.0000277***
	(0.166)	(0.088)	(0.428)	(0.000)
agegrp2_mean	0.000373	0.000507	0.000319	-0.000312
	(0.257)	(0.160)	(0.053)	(0.181)
agegrp3_mean	0.0000952	-0.000193	-0.0000597	-0.000760*
	(0.838)	(0.708)	(0.789)	(0.024)
agegrp4_mean	0.000110	-0.000226	-0.0000605	0.000326
	(0.727)	(0.535)	(0.717)	(0.153)
agegrp5_mean	0.000483	0.000284	0.000261	0.0000768
	(0.067)	(0.345)	(0.063)	(0.701)
emprel2_mean	-0.000262	0.000587	-0.00000903	-0.0000934
	(0.370)	(0.093)	(0.958)	(0.681)
emprel3_mean	0.000338	-0.0000308	0.0000392	0.000592**
	(0.212)	(0.920)	(0.786)	(0.003)
sex_mean	-0.000323	0.000242	-0.0000451	-0.000193
	(0.316)	(0.501)	(0.792)	(0.411)
2008bn.year	0.000000659	-0.00000245	-0.00000342	-0.0000195***
	(0.915)	(0.720)	(0.253)	(0.000)
2009.year	-0.0000435***	-0.0000356***	-0.00000503	-0.0000112*
	(0.000)	(0.000)	(0.132)	(0.019)
2010.year	-0.0000563***	-0.0000346***	-0.0000130***	-0.0000228***
	(0.000)	(0.000)	(0.000)	(0.000)
2011.year	-0.0000752***	-0.0000608***	-0.0000177**	-0.0000351***
	(0.000)	(0.000)	(0.008)	(0.000)
Constant	0.000109	-0.000104	-0.0000257	0.000195
	(0.663)	(0.714)	(0.835)	(0.270)
Observations	1564	1562	985	1231
rho	0.584	0.861	0.796	0.814

p-values in parentheses

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table E.21: Volume DRG Fixed Effects Part 3

	DRG 584	DRG 585	DRG 743	DRG 765
TotASClagPop	-0.00000552	0.00000819	-0.0000310	-0.0000621*
	(0.263)	(0.179)	(0.444)	(0.026)
agegrp2_mean	-0.000336*	0.000317	0.00376*	0.00350**
	(0.026)	(0.175)	(0.035)	(0.004)
agegrp3_mean	-0.000238	-0.000424	0.000728	-0.00163
	(0.209)	(0.191)	(0.776)	(0.353)
agegrp4_mean	0.0000212	-0.000367	0.000522	0.000735
	(0.891)	(0.100)	(0.763)	(0.537)
agegrp5_mean	-0.000411**	0.000198	0.00250	-0.000929
	(0.001)	(0.291)	(0.089)	(0.356)
emprel2_mean	0.000456**	-0.0000763	-0.00281	-0.00221*
	(0.002)	(0.756)	(0.077)	(0.043)
emprel3_mean	-0.0000264	0.000446*	0.00572***	0.00194
	(0.846)	(0.030)	(0.000)	(0.059)
sex_mean	0.000485**	-0.000171	0.00447*	0.00468***
	(0.002)	(0.437)	(0.011)	(0.000)
2008bn.year	0.00000113	-0.0000149***	-0.000127***	0.000121***
	(0.643)	(0.000)	(0.000)	(0.000)
2009.year	0.00000756**	-0.0000133**	-0.000218***	0.000153***
	(0.009)	(0.004)	(0.000)	(0.000)
2010.year	0.00000362	-0.0000168***	-0.000470***	0.000161***
	(0.260)	(0.001)	(0.000)	(0.000)
2011.year	0.0000129*	-0.0000417***	-0.000962***	0.000111*
	(0.033)	(0.000)	(0.000)	(0.021)
Constant	-0.000139	0.0000571	-0.00269	-0.00170
	(0.164)	(0.732)	(0.059)	(0.082)
Observations	466	933	1823	1820
rho	0.907	0.759	0.733	0.547

p-values in parentheses

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table E.22: Volume DRG Fixed Effects Part 4

	DRG 766	DRG 775	DRG 794	DRG 885
TotASClagPop	-0.0000366	0.0000675	0.00000382	-0.0000588
	(0.307)	(0.290)	(0.159)	(0.213)
agegrp2_mean	0.00659***	0.0249***	-0.0000235	-0.00142
	(0.000)	(0.000)	(0.845)	(0.493)
agegrp3_mean	0.00477*	-0.00297	-0.000163	-0.00887**
	(0.035)	(0.460)	(0.339)	(0.003)
agegrp4_mean	-0.000914	-0.0153***	0.0000895	0.00140
	(0.552)	(0.000)	(0.440)	(0.489)
agegrp5_mean	-0.00217	-0.00363	-0.0000480	-0.000813
	(0.095)	(0.117)	(0.624)	(0.634)
emprel2_mean	-0.000205	-0.00121	-0.0000256	-0.000904
	(0.884)	(0.629)	(0.812)	(0.626)
emprel3_mean	-0.00104	0.00365	-0.0000221	0.00555**
	(0.435)	(0.124)	(0.826)	(0.002)
sex_mean	0.00407**	0.0253***	0.0000439	0.00142
	(0.009)	(0.000)	(0.707)	(0.484)
2008bn.year	-0.0000482	-0.000181***	0.00000824***	0.0000559
	(0.119)	(0.001)	(0.000)	(0.169)
2009.year	-0.0000553	-0.000360***	0.000000141	0.000117**
	(0.102)	(0.000)	(0.956)	(0.009)
2010.year	-0.000144***	-0.000326***	-0.000000122	0.000115*
	(0.000)	(0.000)	(0.964)	(0.015)
2011.year	-0.000205***	-0.000813***	-0.00000324	0.000141
	(0.001)	(0.000)	(0.489)	(0.083)
Constant	-0.000932	-0.00913***	0.0000125	0.00131
	(0.461)	(0.000)	(0.895)	(0.431)
Observations	1822	1824	1818	1821
rho	0.582	0.714	0.322	0.631

p-values in parentheses

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

E.5 Other Results

E&M code	Description
99202	New Patient office visit level 2
99203	New Patient office visit level 3
99204	New Patient office visit level 4
99211	Established patient office visit level 1
99212	Established patient office visit level 2
99213	Established patient office visit level 3
99214	Established patient office visit level 4
99215	Established patient office visit level 5
99243	Consultation for new or established patient, level 3
99244	Consultation for new or established patient, level 4

Table E.23: E&M comparator codes

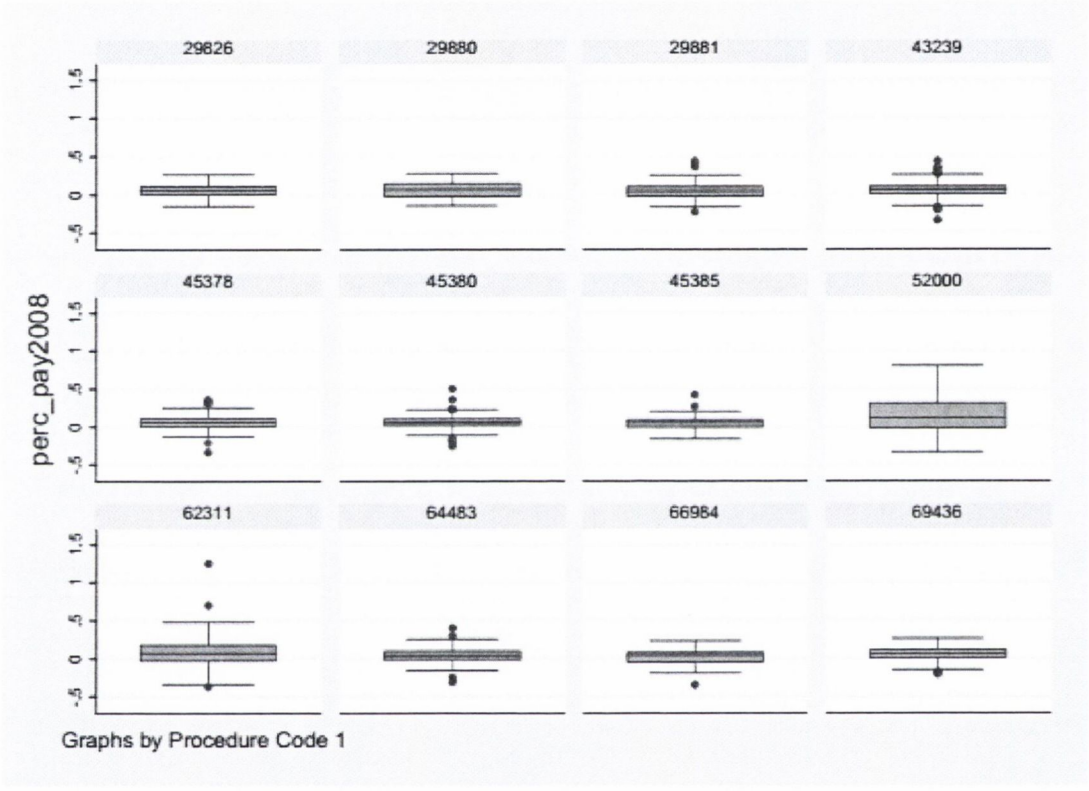

Figure E.1: Percentage price increase from 2007 - 2008 for each CPT

Example 1:			
Facility/ Professional	**CPT**	**revcode**	**description**
P	45380	-	Colonoscopy, flexible, proximal to splenic flexure; diagnostic, with or without collection of specimen(s) by brushing or washing, with or without colon decompression (separate procedure) with biopsy, single or multiple
P	43250	-	Upper gastrointestinal endoscopy including esophagus, stomach, and either the duodenum and/or jejunum as appropriate; diagnostic, with or without collection of specimen(s) by brushing or washing (separate procedure) with removal of tumor(s), polyp(s), or other lesion(s) by hot biopsy forceps or bipolar cautery
P	43239	-	Upper gastrointestinal endoscopy including esophagus, stomach, and either the duodenum and/or jejunum as appropriate; diagnostic, with or without collection of specimen(s) by brushing or washing (separate procedure) with biopsy, single or multiple
F	-	-	-
Example 2:			
Facility/ Professional	**CPT**	**Revenue code**	**description**
P	88305	-	Level 4 Surgical Pathology, gross and microscopic examination
P	45385	-	Colonoscopy, flexible, proximal to splenic flexure; diagnostic, with or without collection of specimen(s) by brushing or washing, with or without colon decompression (separate procedure) with removal of tumor(s), polyp(s), or other lesion(s) by snare technique
F	-	312	Laboratory pathological-histology
F	-	750	Gastro-intestinal services-general classification
F	-	250	Pharmacy-general classification
F	-	258	Pharmacy-IV solutions
F	-	272	Medical/surgical supplies-sterile supply

Table E.24: Further examples of codes occurring during a single "patient day" of care

DRG code	Description
313	Chest pain
392	Esophagitis, gastroent. & miscellaneous digestive disorders without MCC
470	Major joint replacement or reattachment of lower extremity without MCC
579	Other skin, subcutaneous tissue, and breast procedure with MCC
580	Breast cancer: other skin, subcutaneous tissue, and breast procedure with CC
581	Breast cancer: other skin, subcutaneous tissue, and breast procedure without CC / MCC
582	Mastectomy for malignancy with CC / MCC
583	Mastectomy for malignancy without CC / MCC
584	Breast biopsy, local excision, and other breast procedures with CC / MCC
585	Breast biopsy, local excision, and other breast procedures without CC / MCC
743	Uterine and Adnexa Procedures for Non-malignancy without CC/MCC
765	Cesarean section with CC / MCC
766	Cesarean section without CC / MCC
775	Vaginal delivery without complicating diagnoses
794	Neonate with other significant problems
885	Psychoses

Table E.25: DRG comparator codes

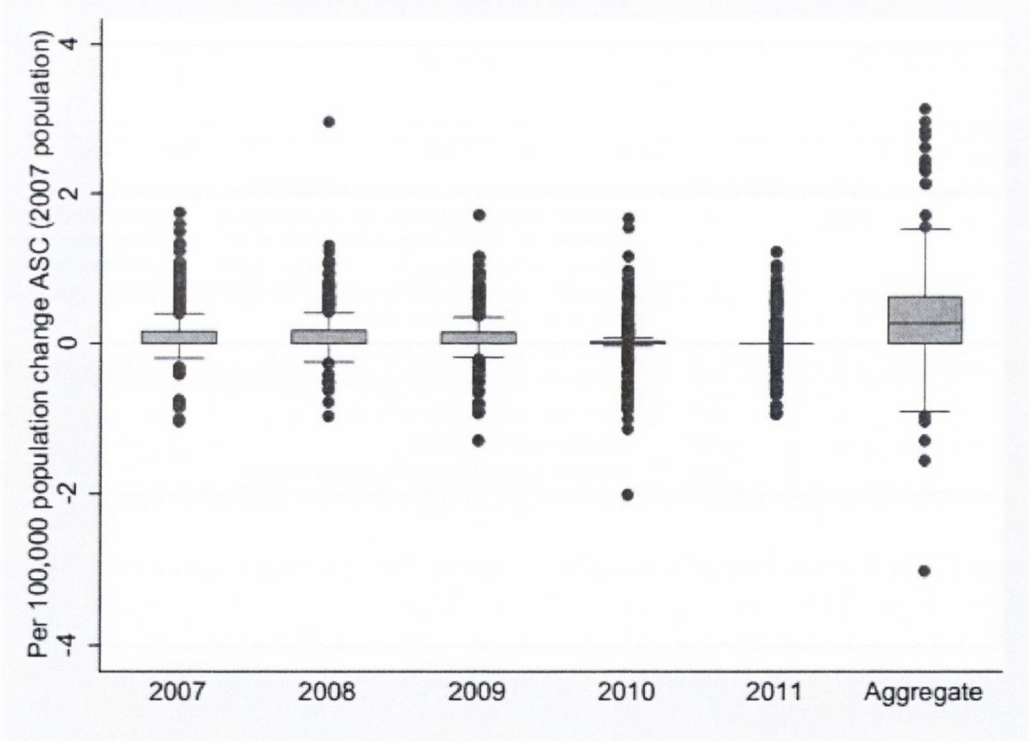

Figure E.2: Net change in ASC number per 100,000 population

	2007			2008		2009		2010		2011	
CPT	Total Spend	Prop. spend	Order	Prop. spend	Order	Prop. spend	Order	Prop. spend	Order	Prop. spend	Order
45378	287,585,184	12.7	1	12.0	1	11.4	1	10.4	1	9.4	1
45380	187,662,160	8.3	2	8.7	3	8.9	3	8.6	3	8.9	3
43239	186,078,896	8.2	3	8.7	2	9.2	2	8.9	2	9.0	2
45385	134,362,752	5.9	4	5.8	4	5.6	4	5.5	4	5.7	4
29881	113,365,488	5.0	5	4.9	5	4.8	5	4.7	5	4.8	5
66984	109,681,184	4.8	6	4.7	6	4.7	6	4.4	6	4.6	6
50590	72,097,832	3.2	7	3.4	7	3.2	7	3.2	7	3.3	7
20610	62,163,968	2.7	8	2.7	8	2.7	8	2.8	8	2.8	8
69436	54,036,332	2.4	9	2.4	9	2.3	11	2.3	11	2.3	11
62311	53,324,688	2.4	10	2.2	12	2.1	13	2.0	13	2.0	13
29826	52,469,236	2.3	11	2.4	11	2.5	10	2.5	10	2.4	10
64483	51,500,732	2.3	12	2.4	10	2.5	9	2.6	9	2.6	9
29888	48,583,776	2.1	13	2.1	13	2.1	12	2.2	12	2.2	12
45384	43,187,532	1.9	14	1.7	14	1.4	18	1.2	19	1.1	20
29880	37,401,180	1.6	15	1.7	15	1.6	15	1.6	15	1.6	15
77003	36,219,700	1.6	16	1.6	16	1.6	16	1.4	17	0.9	25
49505	35,575,804	1.6	17	1.5	17	1.5	17	1.5	16	1.5	16
29877	30,978,030	1.4	18	1.3	19	1.2	19	1.0	23	0.9	28
29827	30,411,104	1.3	19	1.5	18	1.7	14	1.8	14	1.8	14
64721	29,942,614	1.3	20	1.3	20	1.2	20	1.2	18	1.3	17
52000	29,106,444	1.3	21	1.2	21	1.2	21	1.1	21	1.1	19
43235	27,544,562	1.2	22	1.1	22	1.1	23	1.1	22	1.1	21
28296	26,143,610	1.2	23	1.1	23	1.1	22	1.0	25	0.9	24
31255	24,654,068	1.1	24	1.0	25	1.0	25	0.9	28	0.9	29
62310	23,251,696	1.0	25	1.0	24	1.0	24	1.0	24	1.1	23
17311	21,981,586	1.0	26	0.9	27	0.9	27	0.9	27	0.9	27
20680	21,273,308	0.9	27	1.0	26	1.0	26	1.0	26	1.1	22
30140	19,626,038	0.9	28	0.9	28	0.9	28	0.9	29	0.9	26
28285	18,601,302	0.8	29	0.8	29	0.8	29	0.7	33	0.7	35
19120	17,330,264	0.8	30	0.7	30	0.6	34	0.6	37	0.5	39

Table E.26: Top 30 CPTs ranked by total spend

	2007			2008		2009		2010		2011	
CPT	Volume	Prop. Volume	Order	Prop. Volume	Order	Prop. Volume	Order	Prop. Volume	Order	Prop. Volume	Order
20610	612055	17.6	1	17.8	1	18.3	1	17.9	1	19.0	1
45378	358936	10.3	2	9.7	2	9.1	3	8.2	2	7.4	3
77003	304062	8.7	3	9.1	3	9.6	2	8.0	3	5.9	5
43239	276057	7.9	4	8.4	4	8.4	4	8.0	4	8.1	2
45380	221898	6.4	5	6.7	5	6.7	5	6.5	5	6.7	4
45385	143892	4.1	6	4.1	6	3.9	6	3.8	6	3.9	6
62311	117915	3.4	7	3.1	7	3.0	8	2.8	8	3.0	8
52000	93340	2.7	8	2.6	9	2.5	9	2.4	9	2.4	9
64483	88346	2.5	9	2.7	8	3.0	7	3.0	7	3.0	7
66984	61725	1.8	10	1.7	10	1.7	10	1.7	10	1.7	10
29881	60171	1.7	11	1.7	11	1.6	11	1.5	11	1.5	12
45384	53481	1.5	12	1.4	14	1.1	17	1.0	19	0.9	23
69436	52346	1.5	13	1.4	12	1.3	15	1.3	15	1.3	16
11042	51981	1.5	14	1.4	13	1.4	14	1.3	16	1.7	11
43235	50360	1.4	15	1.3	16	1.2	16	1.1	18	1.1	18
62310	46604	1.3	16	1.3	15	1.4	12	1.4	14	1.4	14
64484	39222	1.1	17	1.3	17	1.4	13	1.4	13	1.4	15
76872	35912	1.0	18	1.0	18	1.0	18	0.9	21	1.0	20
55700	33448	1.0	19	0.9	20	0.8	21	0.8	23	0.8	24
29826	30406	0.9	20	0.9	19	0.9	19	0.9	20	0.9	22
29877	27966	0.8	21	0.8	22	0.7	22	0.6	29	0.5	36
17311	27743	0.8	22	0.9	21	0.9	20	0.9	22	0.9	21
64640	25270	0.7	23	0.7	23	0.6	27	0.4	44	0.3	50
64721	24609	0.7	24	0.6	24	0.6	23	0.6	27	0.6	29
30140	21951	0.6	25	0.6	25	0.6	24	0.6	31	0.6	35
49505	21580	0.6	26	0.6	27	0.5	28	0.5	37	0.5	38
50590	21513	0.6	27	0.6	26	0.6	26	0.6	32	0.6	33
29880	18974	0.5	28	0.5	29	0.5	31	0.5	35	0.5	37
52332	18599	0.5	29	0.6	28	0.6	25	0.6	28	0.6	30
20680	18011	0.5	30	0.5	30	0.5	32	0.5	38	0.5	39

Table E.27: Top 30 CPTs ranked by total volume

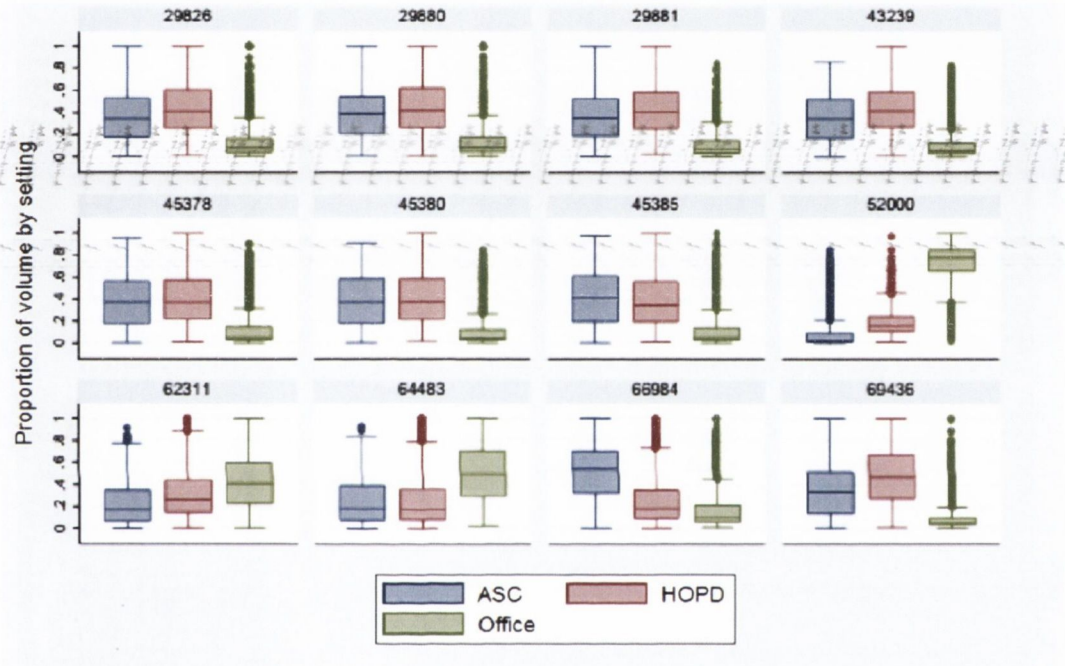

Figure E.3: Proportion of services in each setting (day level)

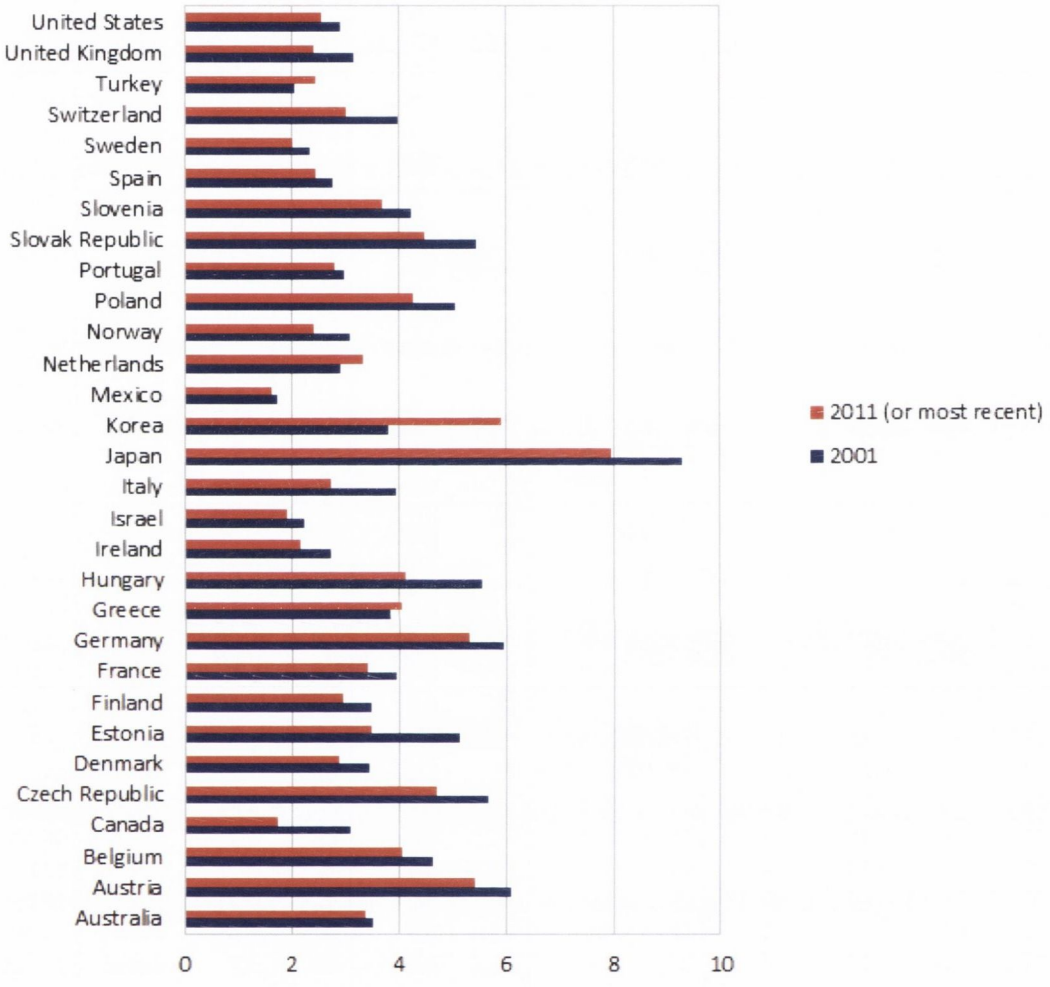

Figure E.4: Acute care beds for OECD countries per 1,000 population

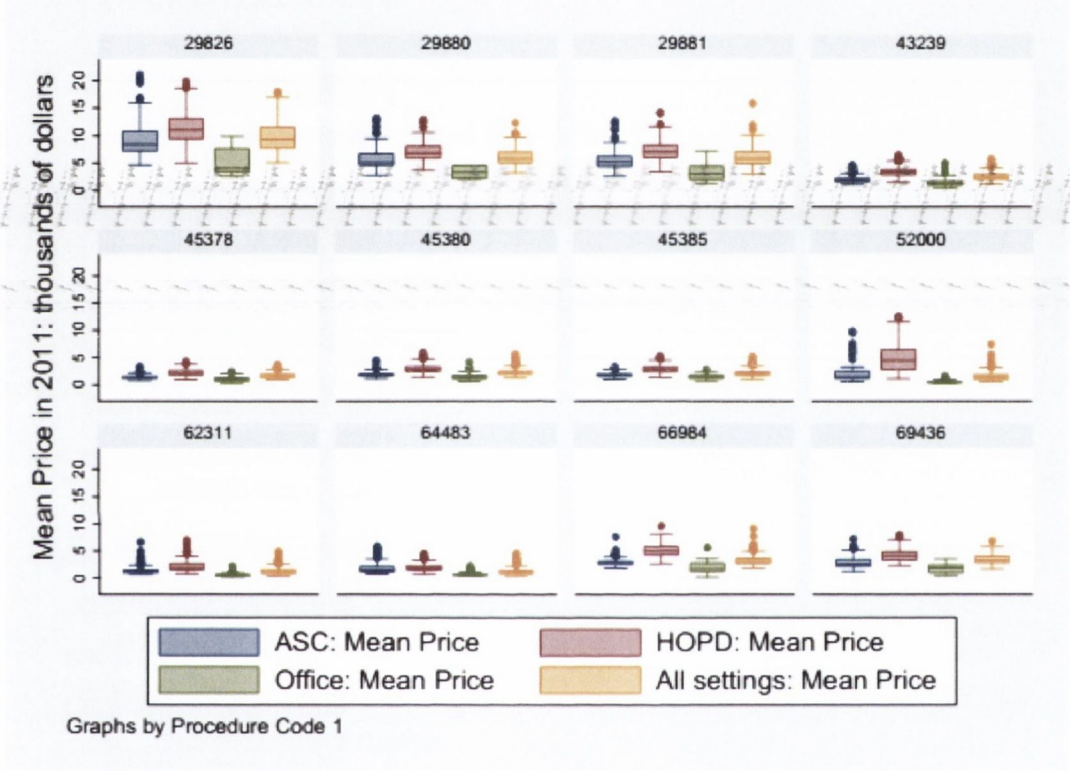

Figure E.5: Mean Price per CPT (specified at the patient/day level)

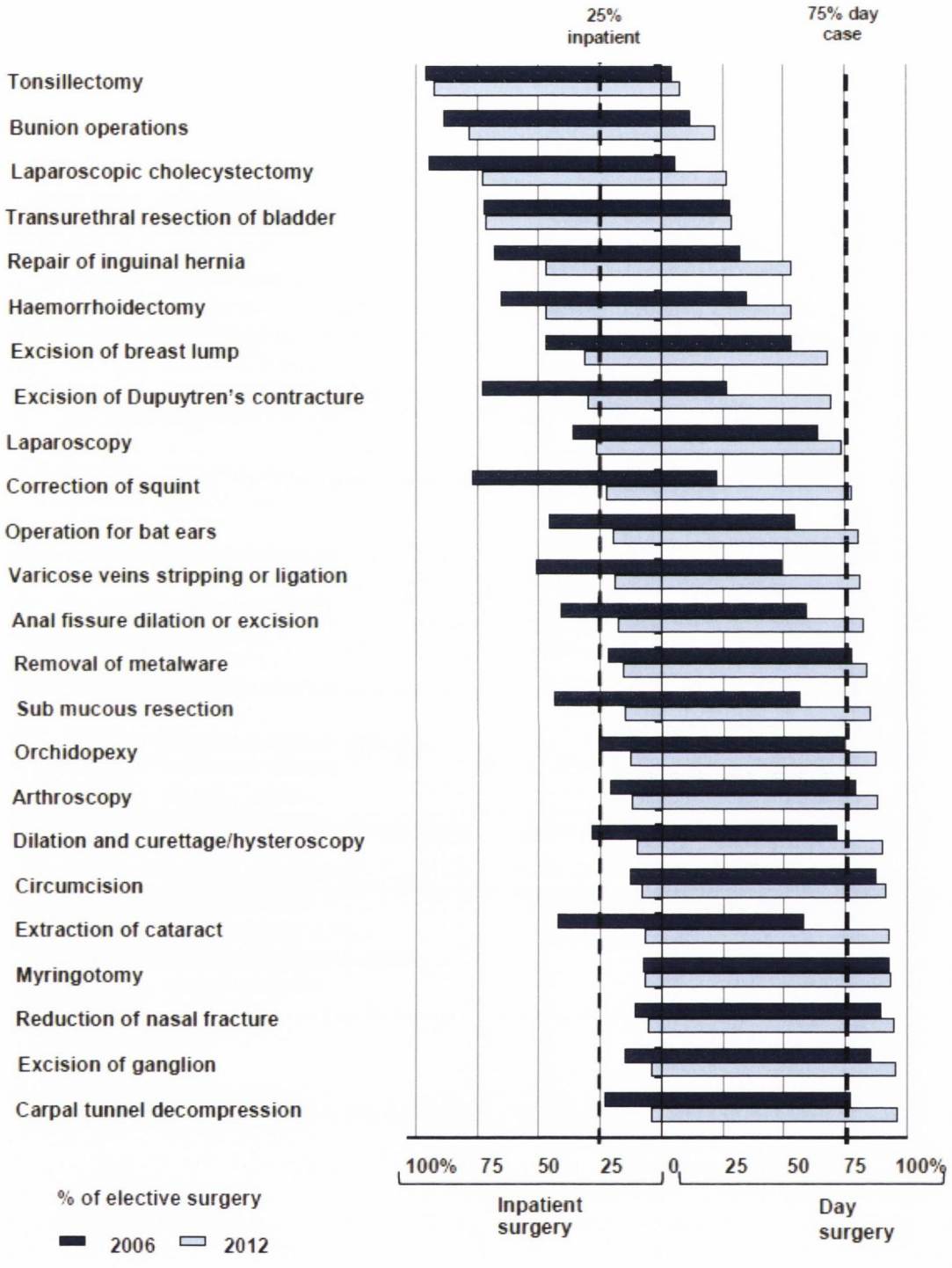

Figure E.6: Day case rate for 24 elective procedures, 2006 and 2012

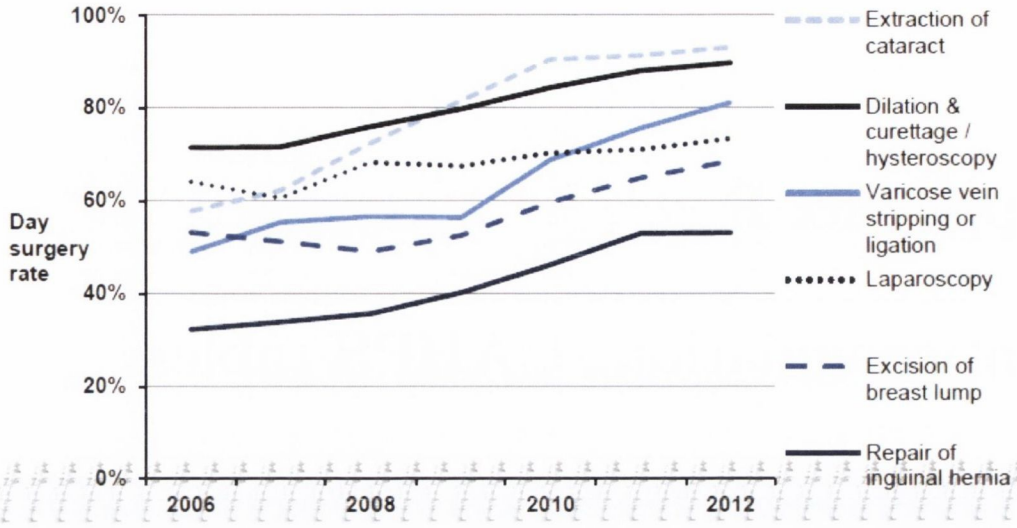

Figure E.7: Trends for six elective procedures, 2006 to 2012

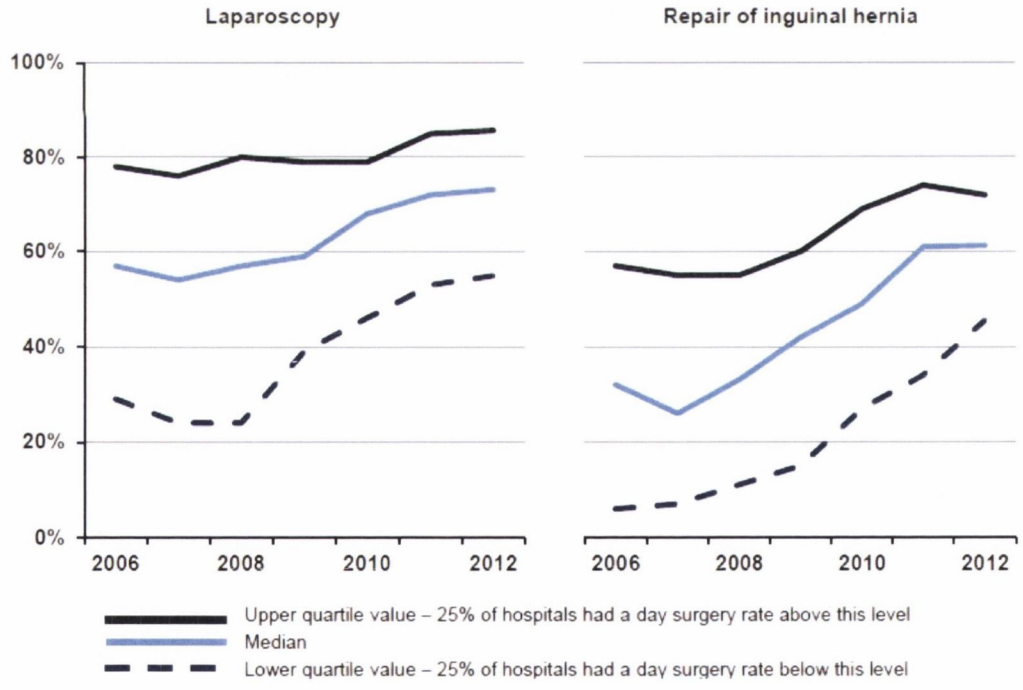

Figure E.8: Distribution of day surgery rates, 2006 to 2012

Appendix F

Anticoagulation: CAHPS tables

Table F.1: CAHPS Mean Scores: Question 1

	Mean CAHPS - Aggregate			
Setting	**A.Fib**	**VTE**	**Other**	**Total**
Pharmacist	3.2	3.2	3.3	3.2
Nurse	3.2	3.1	3.2	3.2
Community	3.4	3.2	3.6	3.4
Total	3.2	3.2	3.2	3.2

Table F.2: CAHPS Mean Scores: Question 2

	Mean CAHPS Q1			
Setting	**A.Fib**	**VTE**	**Other**	**Total**
Pharmacist	3.5	3.5	3.6	3.5
Nurse	3.4	3.2	3.3	3.4
Community	3.7	3.6	3.4	3.6
Total	3.5	3.4	3.5	3.5

Table F.3: CAHPS Mean Scores: Question 3

	Mean CAHPS Q2			
Setting	**A.Fib**	**VTE**	**Other**	**Total**
Pharmacist	2.5	2.6	2.7	2.6
Nurse	2.6	2.6	2.5	2.6
Community	3.1	2.9	3.5	3.1
Total	2.6	2.6	2.7	2.6

Table F.4: CAHPS Mean Scores: Question 4

	Mean CAHPS Q3			
Setting	**A.Fib**	**VTE**	**Other**	**Total**
Pharmacist	2.4	2.4	2.5	2.4
Nurse	2.2	2.4	2.4	2.3
Community	2.9	2.6	3.4	2.9
Total	2.4	2.4	2.5	2.4

Table F.5: CAHPS Mean Scores: Question 5

	Mean CAHPS Q4			
Setting	**A.Fib**	**VTE**	**Other**	**Total**
Pharmacist	3.8	3.8	3.8	3.8
Nurse	3.9	3.8	3.8	3.8
Community	3.7	3.6	3.6	3.7
Total	3.8	3.8	3.8	3.8

Table F.6: CAHPS Mean Scores: Question 6

	Mean CAHPS Q5			
Setting	**A.Fib**	**VTE**	**Other**	**Total**
Pharmacist	3.8	3.8	3.8	3.8
Nurse	3.8	3.7	3.8	3.8
Community	3.8	3.5	4.0	3.8
Total	3.8	3.8	3.8	3.8

Appendix G

Anticoagulation: DASS tables

Table G.1: DASS Mean Scores: Question 1

	Mean DASS - Aggregate			
Setting	**A.Fib**	**VTE**	**Other**	**Total**
Pharmacist	2.1	2.2	2.2	2.2
Nurse	2.2	2.5	2.4	2.3
Community	2.1	2.7	2.8	2.4
Total	2.1	2.3	2.3	2.2

Table G.2: DASS Mean Scores: Question 2

	Mean DASS - Aggregate (if answered all DASS questions)			
Setting	**A.Fib**	**VTE**	**Other**	**Total**
Pharmacist	2.1	2.2	2.2	2.2
Nurse	2.2	2.5	2.3	2.3
Community	2.1	2.9	2.8	2.5
Total	2.1	2.4	2.3	2.2

Table G.3: DASS Mean Scores: Question 3

	Mean DASS - Benefits			
Setting	**A.Fib**	**VTE**	**Other**	**Total**
Pharmacist	0.8	0.7	0.8	0.8
Nurse	0.8	0.9	0.9	0.9
Community	0.8	0.9	1.0	0.8
Total	0.8	0.8	0.9	0.8

Table G.4: DASS Mean Scores: Question 4

	Mean DASS - Benefits (if answered all DASS questions)			
Setting	**A.Fib**	**VTE**	**Other**	**Total**
Pharmacist	0.8	0.7	0.8	0.8
Nurse	0.9	0.9	0.9	0.9
Community	0.8	1.0	1.0	0.9
Total	0.8	0.8	0.9	0.8

Table G.5: DASS Mean Scores: Question 5

	Mean DASS - Limitations			
Setting	**A.Fib**	**VTE**	**Other**	**Total**
Pharmacist	0.4	0.5	0.5	0.5
Nurse	0.4	0.5	0.5	0.4
Community	0.4	0.6	0.6	0.5
Total	0.4	0.5	0.5	0.5

Table G.6: DASS Mean Scores: Question 6

	Mean DASS - Limitations (if answered all DASS questions)			
Setting	**A.Fib**	**VTE**	**Other**	**Total**
Pharmacist	0.4	0.5	0.5	0.4
Nurse	0.4	0.5	0.5	0.4
Community	0.4	0.6	0.6	0.5
Total	0.4	0.5	0.5	0.4

Table G.7: DASS Mean Scores: Question 7

	Mean DASS - Hassles			
Setting	**A.Fib**	**VTE**	**Other**	**Total**
Pharmacist	0.9	1.0	1.0	1.0
Nurse	0.9	1.1	1.0	1.0
Community	0.9	1.2	1.3	1.0
Total	0.9	1.1	1.0	1.0

Table G.8: DASS Mean Scores: Question 8

	Mean DASS - Hassles (if answered all DASS questions)			
Setting	**A.Fib**	**VTE**	**Other**	**Total**
Pharmacist	0.9	1.1	1.0	1.0
Nurse	0.9	1.1	0.9	1.0
Community	0.9	1.3	1.3	1.1
Total	0.9	1.1	1.0	1.0

Appendix H

Anticoagulation: EQ-5D tables

Table H.1: EQ-5D Mean Scores: Aggregate

	EQ-5D - aggregate			
Setting	**A.Fib**	**VTE**	**Other**	**Total**
Pharmacist	0.8	0.8	0.9	0.8
Nurse	0.9	0.8	0.9	0.9
Community	0.8	0.8	0.9	0.8
Total	0.8	0.8	0.9	0.8

Table H.2: EQ-5D Mean Scores: Score out of 100

	EQ-5D - overall from 100			
Setting	**A.Fib**	**VTE**	**Other**	**Total**
Pharmacist	74.6	80.4	77.6	77.4
Nurse	76.6	79.1	77.9	77.4
Community	78.6	77.0	79.5	78.4
Total	75.9	79.7	77.8	77.5

Table H.3: EQ-5D Mean Scores: Mobility

	EQ-5D - mobility			
Setting	**A.Fib**	**VTE**	**Other**	**Total**
Pharmacist	1.4	1.3	1.3	1.3
Nurse	1.3	1.3	1.2	1.3
Community	1.4	1.4	1.2	1.3
Total	1.3	1.3	1.3	1.3

Table H.4: EQ-5D Mean Scores: Self Care

	EQ-5D - self care			
Setting	**A.Fib**	**VTE**	**Other**	**Total**
Pharmacist	1.1	1.1	1.1	1.1
Nurse	1.0	1.1	1.0	1.0
Community	1.0	1.0	1.0	1.0
Total	1.0	1.1	1.1	1.1

Table H.5: EQ-5D Mean Scores: Usual Activities

	EQ-5D - usual activities			
Setting	**A.Fib**	**VTE**	**Other**	**Total**
Pharmacist	1.3	1.3	1.2	1.3
Nurse	1.3	1.3	1.2	1.3
Community	1.3	1.3	1.2	1.3
Total	1.3	1.3	1.2	1.3

Table H.6: EQ-5D Mean Scores: Pain

	EQ-5D - pain			
Setting	**A.Fib**	**VTE**	**Other**	**Total**
Pharmacist	1.6	1.5	1.3	1.5
Nurse	1.4	1.4	1.4	1.4
Community	1.5	1.4	1.5	1.5
Total	1.5	1.5	1.4	1.5

Table H.7: EQ-5D Mean Scores: Worry

	EQ-5D - worried			
Setting	**A.Fib**	**VTE**	**Other**	**Total**
Pharmacist	1.3	1.4	1.3	1.3
Nurse	1.2	1.4	1.4	1.3
Community	1.3	1.4	1.2	1.3
Total	1.3	1.4	1.3	1.3