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Health Psychology

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The Lasting Legacy of Childhood Adversity for Disease Risk in Later Life

AQ: au

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Objective: There has been an increased interest in the role of the childhood social environment in the etiology of adult diseases in recent years. The present study examines whether the experience of adversity during childhood increases risk for disease in later life independent of later life socioeconomic, behavioral, and psychosocial factors. ***Method:*** The study involved a nationally representative sample of 6,912 persons aged 50 years and older who were participating in the first wave of the Irish Longitudinal Study on Ageing. Childhood adversity was indexed using a 4-item measure that captured challenging and potentially noxious childhood environmental exposures including, socioeconomic disadvantage, substance abuse among parents, physical abuse, and sexual abuse. A doctor diagnosis of disease across 9 chronic disease types represented the primary outcome variables. ***Results:*** The experience of adversity during childhood was associated with increased risk of disease in midlife and older ages across a large number of chronic disease types including cardiovascular disease, lung disease, and emotional, nervous, or psychiatric disorders. Analysis of the dose-response pattern revealed positively graded associations between the number of adverse events experienced during childhood and the occurrence of chronic disease in later life. Cox proportional hazard models revealed that the experience of adversity during childhood was associated with earlier age of onset for any physical disease type or emotional, nervous, or psychiatric disorders. ***Conclusions:*** These findings indicate that childhood may represent a sensitive or critical period in the development of disease and reinforces the necessity of adopting a life-course approach to the study of chronic diseases.

Keywords: adversity, disease, childhood, stress, cohort study, TILDA

Much evidence has accumulated in recent years to support the view that the experience of adversity in early life may compromise longer-term health and wellbeing (Ben-Shlomo & Kuh, 2002; Miller, Chen, & Parker, 2011). Indeed, an increasing body of research finds independent and persisting effects of childhood health (Banks, Oldfield, & Smith, 2011; Goodman, Joyce, & Smith, 2011) and material disadvantage (Blackwell, Hayward, & Crimmins, 2001) for disease risk in later life adjusting for later life factors. Other studies have documented deleterious effects of other types of childhood adversities including family dysfunction, parental illness, and different forms of neglect and abuse for risk of physical diseases and psychopathology in later life (Anda et al., 2009; Benjet, Borges, & Medina-Mora, 2010; Clark, Caldwell, Power, & Stansfeld, 2010; Dong et al., 2004; Wilson et al., 2006). But how does the experience of adversity during childhood increase risk for disease in later life?

One line of reasoning is that childhood adversity is a distal factor exerting its influence through more proximal risk factors such as lower educational attainment leading to lower occupational position and income, which determine material conditions in adulthood (e.g., substandard housing, dietary quality, fuel poverty) and increases the risk of engaging in a variety of health-compromising lifestyle behaviors that are known to be damaging to health. A second set of explanatory models afford greater weight to the role of the psychosocial environment in the etiological pathway from adversity to disease (Repetti, Taylor, & Seeman, 2002; Taylor, Repetti, & Seeman, 1997). Individuals who grow up in risky social environments may develop specific types of coping styles, emotion regulation strategies, and social cognitions that both increase stress exposure and shape the manner in which individuals respond to stress. For example, less responsive and harsher parenting is associated with difficulties in socioemotional adjustment, and children who are more emotionally reactive also tend to be more physiologically reactive (Repetti et al., 2002). Impaired self-regulation may leave children poorly equipped to manage environmental demands contributing to the development of maladaptive coping strategies (e.g., alcohol abuse) or highly reactive emotional states (i.e., anger and hostility) that are associated with increased susceptibility to disease.

A third set of explanatory models focuses on the psychobiological pathways (i.e., neuroendocrine and immunologic) through which early adversity may compromise longer-term health. The neurobiological response to stress induces activation in two neuro-

Cathal McCrory and Cara Dooley, The Irish Longitudinal Study on Ageing (TILDA), Department of Medical Gerontology, Trinity College Dublin; Richard Layte, Department of [illegible], Economic and Social Research Institute, Dublin, Ireland; Rose Anne Kenny, TILDA, Department of Medical Gerontology, Trinity College Dublin.

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endocrine pathways—the sympathetic nervous system and the hypothalamic–pituitary–adrenal axis—that are central to the stress response (Conrad, 2008). Chronic activation of these systems may cause imbalances in the array of biochemical mediators that are involved with initiating, maintaining, and inhibiting the stress response. As a consequence, these physiological systems become chronically dysregulated over time leading to greater "wear and tear" on the body and increased vulnerability to disease (McEwen, 2008). That the experience of adversity in childhood can induce changes in physiological systems that influence disease risk in later life is supported by the results of recent studies that have documented changes in a number of biological parameters in response to early childhood stressors (Miller et al., 2009; Slopen, Kubzansky, McLaughlin, & Koenen, 2013).

Despite the burgeoning literature that finds links between early adversity and disease in later life, a number of fundamental questions remains unanswered. First, does the accumulation of adverse exposures during childhood increase risk of disease in a graded manner? Although a series of papers from the Adverse Childhood Experiences Study has documented graded relationships between adversity in early life and chronic disease in later life (Anda et al., 2009; Dong et al., 2004; Felitti et al., 1998), these studies do not routinely control for later life socioeconomic or lifestyle related factors, so the possibility remains that the association arises simply because childhood adversity serves as a particularly robust marker of lifetime socioeconomic status (SES). Moreover, few studies control for the experience of stressful life events during adulthood. Doing so is important to rule out the idea that stress in early life simply predicts continuing exposure to episodic life events that are damaging to health (i.e., accumulation hypothesis; Ben-Shlomo & Kuh, 2002).

A related issue is whether cumulative adversity is associated with earlier age of disease onset. This is an important theoretical and empirical issue. If exposure to stress causes greater wear and tear on physiological systems, and childhood represents a critical/sensitive period of vulnerability (Miller et al., 2011), then one might expect that greater exposure to stress in early life will be associated with earlier age of disease onset and comorbidity of disease types. Unfortunately this issue has not been subjected to the type of systematic investigation such an important question warrants, possibly because very few prospective studies have cohort members in the age range where chronic diseases of ageing are highly prevalent (Haas, 2007).

Finally, this study also examines the relationship between the experience of early adversity and a wide array of disease types. Evans & Kim (2010) contend that most of the data on multiple risk exposure relates to cognitive and socioemotional outcomes rather than physical health, so the present study will help fill this deficit. Doing so is important in order to establish whether the experience of stress acts on general or specific mechanisms. McEwen has speculated that the limbic system (particularly the hippocampus and amygdala) and the cardiovascular system may be particularly vulnerable to the effects of stress (McEwen, 2004; McEwen & Gianaros, 2010). If the stress pathway is implicated, it follows therefore that the experience of adversity in early life will be more strongly associated with psychiatric disorders and diseases of the cardiovascular system compared with other disease types.

This study uses retrospective cross-sectional data from the first wave of The Irish Longitudinal Study on Ageing (TILDA) to explore whether the experience of adversity in early life (disadvantaged socioeconomic circumstances, parental substance abuse, physical abuse, and sexual abuse) is associated with increased risk of disease in later life controlling for a range of potentially confounding factors. Following from the discussion above it is hypothesized that (a) the experience of adversity in early life will increase risk for disease in later life independent of later life factors, (b) the risk of disease in later life will increase in a graded manner with the number of stressors to which children were exposed during childhood independent of later life factors, and (c) that the experience of adversity in early life will be associated with earlier age of disease onset and comorbidity of disease types.

Materials and Method

Sample

The sample was generated using a three-stage selection process and the Irish Geodirectory (a database of private residential addresses) as the sampling frame. Subdivisions of district electoral divisions, prestratified by socioeconomic status, age and geographical location served as the primary sampling units. The second stage involved the selection of a random sample of 40 addresses from within each of 640 primary sampling units, resulting in an initial sample of 25,600 addresses. The third stage involved the attempted recruitment of all members of the household at these addresses aged 50 years and over (and their spouse/partner of any age). The response rate was defined as the proportion of households including an eligible participant from whom an interview was successfully obtained. A response rate of 62% was achieved at the household level resulting in a final sample of 8,175 respondents aged 50 years or over. As part of the household component of the survey, respondents completed a computer-assisted personal interview administered by a trained interviewer. Respondents also completed a postal self-completion questionnaire (SCQ), which contained further questions on sensitive topics. A total of 6,912 respondents (84.6%) returned a completed SCQ. Comparisons of the characteristics of TILDA respondents with data available from the 2011 Quarterly National Household Survey revealed that those individuals with lower levels of educational attainment are underrepresented in TILDA, and there are minor differences in response rate among particular age and gender groups. AQ: 1

To account for sampling design (stratification and clustering), inverse probability weights were constructed (based on education, age, gender, and geographical location) using the Quarterly National Household Survey. A separate weight was used in the present analysis to take account of differential nonresponse at the unit level (i.e., nonresponse to the SCQ). The derived estimates are therefore nationally representative of the Irish population aged 50 years and over. A more detailed description of TILDA survey methodology, weighting, and sample design is available elsewhere (Whelan & Savva, 2013). Ethical approval for the study was granted by the Trinity College Dublin Research Ethics Committee.

Outcome Variables: Disease Measures and Age at Diagnosis

Respondents to the TILDA survey were asked, "Has a doctor *ever* told you that you have any of the following conditions?" and

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AQ: 2 were presented with the following list: (a) cardiovascular disease types (angina, heart attack, heart failure, stroke, TIA, heart murmur and "other types of heart trouble"), (b) asthma, (c) lung disease, (d) osteoporosis, (e) cancer, (f) arthritis, (g) diabetes, (h) ulcers (stomach and varicose). Respondents were also asked whether they had *ever* been diagnosed with any (i) emotional, nervous, or psychiatric disorders, which included depression, anxious disorders, mood disorders, and psychoses. Respondents reporting two or more disease types were characterized as having comorbidity. Validation studies have shown that self-reports of disease obtained using questionnaire methods have good concordance with administrative medical records (Okura, Urban, Mahoney, Jacobsen, & Rodehefer, 2004), particularly for chronic diseases that have clear diagnostic criteria that are easily communicated to the patient (Haapanen, Miilunpalo, Pasanen, Oja, & Vuori, 1997).

Respondents who indicated that they had received a doctor diagnosis of cardiovascular disease, arthritis, diabetes, cancer, or any emotional, nervous, or psychiatric disorders were asked a further question to ascertain the age at which the illness was first diagnosed. A composite age at "any physical disease" onset variable was derived by calculating the earliest age at which physical disease onset occurred across any of the physical disease types for which information existed regarding age at diagnosis (i.e., cardiovascular disease, arthritis, diabetes, or cancer). In effect, this allows one to derive separate estimates for age at disease onset for (a) each individual physical disease, (b) any physical disease, or (c) any emotional, nervous, or psychiatric disorder.

Limited psychometric information exists regarding the reliability of retrospectively recalled age of onset over long intervals. However, a Swedish study that examined recall of age of onset among asthmatics over a 10-year follow-up period reported strong correspondence when participant-reported age at diagnosis was compared with objective clinic-based records that were obtained at baseline by means of a structured interview with specialized nursing staff. The median difference between the true year of onset as established at the clinical interview, and respondent recall of age at diagnosis at time of follow-up 10 years later was 0 years. They also found that only 12% of the sample deviated by more than 5 years from their true age at diagnosis (as established at the baseline interview) at time of follow-up (Torén, Palmqvist, Lowhagen, Balder, & Tunsater, 2006). A separate study that examined recall of age of onset of depression following diagnosis over a 4-year recall period found that reliability of age of onset of major depression was excellent (Prusoff, Merikangas, & Weissman, 1988).

Predictor Variables: Childhood Adversity Measures

Five dichotomously scored, retrospectively recalled life events occurring before the age of 18 years were used to measure childhood adversity. Three items were adapted from the 22-item lifetime trauma list (Krause, Shaw, & Cairney, 2004) and have been AQ: 3 previously used in the U.S. Health and Retirement Study. Two of the items asked whether the respondent had experienced physical abuse by a parent, or physical abuse by some other person, prior to 18 years of age. The third item asked whether either of the respondent's parents drank or used drugs so often it caused problems in the family (before the respondent was 18 years of age). Two additional items were added to ascertain whether the respondent had experienced sexual abuse by a parent, or sexual abuse by some other person, prior to 18 years of age. Responses to the two physical abuse questions were aggregated to create a binary physical abuse variable (0/1). Similarly, responses to the two sexual abuse questions were aggregated to create a binary sexual abuse variable (0/1).

These major life event measures were supplemented by an additional item that was designed to tap socioeconomic adversity in early life. Respondents were asked to rate the financial circumstances of the household between birth and 14 years of age on a 3-point response scale: pretty well off financially, about average, poor. A binary response was derived by setting those growing up "poor" = 1. Studies have demonstrated reasonable concordance between recall of family socioeconomic position among sibling pairs (Ward, 2011). A composite childhood adversity index was then calculated by summing scores across the four adverse childhood events (range = 0–4). In addition to a dichotomous childhood adversity measure (ever vs. never), a three-level ordered categorical measure was created representing different levels of exposure: none, one, and two or more adverse events during childhood.

Covariates AQ: 4

Sociodemographic variables. Variables representing the respondent's age, gender, and marital status are included in the analysis. As socioeconomic characteristics are among the strongest predictors of adult disease (Matthews & Gallo, 2011), a number of controls for socioeconomic position at interview were also employed. Household social class is represented as a six-level variable: professional/managerial, nonmanual/skilled manual, semiskilled/unskilled, farmers, those who never worked and hence have no social class designation, and those who refused or had insufficient information to make a designation. Household income is represented in quintiles with cut-offs of <€14,000 (Band 1), €14,000 < €24,000 (Band 2), €24,000 < €30,000 (Band 3), €30,000 ≤ €50,000 (Band 4), and >€50,000[1] (Band 5). Finally, Fn1, AQ5 the respondent's highest level of educational attainment is represented as a three-level variable: primary education or less, secondary education, tertiary education.

Lifestyle variables. The respondent's smoking status was measured using a three-level variable: never smoked, past smoker, current smoker. The CAGE alcohol screening test (Ewing, 1984) was used to index problematic drinking. The scale comprises four items and follows a dichotomous yes/no response format. Answering yes to two or more questions indicates a clinically significant profile and constitutes potentially hazardous drinking. The instrument has a sensitivity of 93% and a specificity of 76% for identification of problematic drinking (Bernadt, Taylor, Mumford, Smith, & Murray, 1982). Physical activity was assessed using the 8-item short form of the International Physical Activity Questionnaire (Craig et al., 2003), which measures the amount of time spent walking and engaged in moderate and vigorous physical activity, and the amount of time spent sedentary. This information was used to derive a categorical variable for analysis representing low,

[1] USD equivalents: Lowest quintile = $18,960 or less, 2nd quintile = $18,961–$32,500, 3rd quintile = $32,501–$40,600, 4th quintile = $40,601–$74,500, Highest quintile = $74,501 or more.

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medium, and high levels of physical activity using the International Physical Activity Questionnaire protocol (www.ipaq.ki.se).

Adverse Life Events in Adulthood

Three items adapted from the lifetime trauma list (Krause et al., 2004) were used to measure traumatic life events occurring during adult life. Respondents were asked whether they had experienced traumatic life events during their adult life, including (a) whether their spouse/partner/child had ever been addicted to drugs/alcohol, (b) whether their spouse/partner/child had ever experienced a life-threatening illness or accident, and (c) whether they had ever experienced the death of a child. These were measured using binary (yes/no) responses.

Memory

Given that retrospective response biases are a concern for older adult samples, the study employed a control for cognitive functioning by using an episodic memory task. Verbal memory was assessed during the computer-assisted personal interview using a word-learning list and recall task in which participants were asked to recall 10 common aurally presented words after a recall period of approximately 10 mins. Scores ranged from 0 to 10, with higher scores indicating a higher number of correctly recalled words.

Treatment of Missing Cases

Because the child maltreatment items were asked as part of the SCQ, the 6,912 respondents who returned the SCQ form the initial case base for the analysis. A further 197 cases were excluded because they were missing listwise on one or more components of the adversity measure (n = 6,715). The degree of missingness was small (<2%) with respect to most covariates, with the exception of father's education, household income, and the adverse life events occurring in adulthood measures. Dummy variables were created for these variables resulting in a final analytic case base of 6,408 cases.

Results

The analyses were undertaken using STATA 12.0 and release 1–7-4 of the TILDA dataset. More than one fifth (22.3%) of the sample reported that they grew up poor, 8.5% reported alcohol or substance abuse by their parent(s), 6.9% reported that they had experienced physical abuse, and 6.1% reported that they had experienced sexual abuse. Overall, 33.6% of the sample revealed that they had experienced at least one adverse childhood event prior to 18 years of age: 25.8% of the sample experienced one type of adverse childhood event, 5.9% experienced two adverse childhood events, and a further 1.9% experienced three or more adverse childhood events. Because only a small number of respondents reported that they experienced three or more adverse events, they are subsumed within the two-or-more adverse events category. T1 Table 1 describes the baseline characteristics of the sample. Mean T2 age of the sample was 63.9 years and 51.9% were female. Table 2 describes the prevalence of doctor diagnosed disease across each of the disease types under consideration in the present study, and compares prevalence among those who were exposed to adversity during childhood compared with those who ~~did~~ not. Arthritis was the most common disease type (27.5%), followed by cardiovascular disease (16.7%) and ulcers (10.2%). A quarter of the cohort (26.1%) reported comorbidity of disease types. Notably, those who experienced any type of adversity had almost double the risk of emotional, nervous, or psychiatric disorders (11.4%) compared with those who were not exposed (6.6%).

Cohort study designs allow for the direct calculation of relative risks (RRs). RR is considered a more appropriate measure of association compared with the odds ratio (*OR*) because they are easier to interpret (ratio of proportions rather than ratios of odds) and because the *OR* overestimates risk when prevalence approaches 10% (Schmidt & Kohlmann, 2008). Estimates of RR and associated 95% confidence intervals (CIs) for a proportion were derived using survey weighted Poisson regression with Poisson error structure and log link (Zou, 2004). The resulting incident rate ratio is obtained by exponentiating the Poisson regression coefficient and can be interpreted as the relative risk. The p values were adjusted using the false discovery rate (FDR) method (Benjamini & Hochberg, 1995) to reduce the probability of making a Type I error when performing multiple hypothesis testing. FDR methods are considered less conservative than family wise error rate correction methods as they are less concerned with avoiding *any* false positives. In simple terms, FDR increases statistical power while imposing a principled bound on the error rate. Multiple comparison corrections were implemented using the multproc procedure in STATA 12.0. Associations that remain significant after applying the FDR adjustment are denoted in bold typeface.

Table 3 summarizes the multivariable adjusted RR of obtaining T3 a doctor diagnosis of disease across a number of chronic disease types by the experience of adversity during childhood, controlling for the set of covariates shown in Table 1. A fairly consistent pattern of results was evident in the data with the majority of the point estimates tending in the positive direction indicating that the experience of adversity in childhood increases risk for disease in later life independent of later life factors. Growing up poor was associated with significantly increased risk for cardiovascular disease; lung disease; and emotional, nervous, or psychiatric disorders, while childhood sexual abuse was associated with significantly increased risk for five of the nine disease types under investigation. The experience of each type of adverse childhood event also significantly increased risk for comorbidity of disease types. Those who grew up poor were 18% (RR = 1.18, 95% CI [1.07, 1.31]; $p < .001$) more likely to have two or more doctor diagnosed diseases, while the corresponding increase in risk for those who reported parental substance abuse, physical abuse, or sexual abuse was 24%, 49%, and 56%, respectively.

When treated as a dichotomous variable (ever vs. never) those who experienced any type of adversity during childhood were found to be at significantly increased risk of cardiovascular disease, lung disease, and any emotional, nervous, or psychiatric disorders (see Table 4). A clear dose–response relationship was T4 evident across the majority of the different disease types examined in the present study and the experience of two or more adverse events during childhood was associated with significantly increased risk of cardiovascular disease, lung disease, asthma, arthritis, ulcers, and any emotional, nervous, or psychiatric disorders in the full multivariable adjusted models.

Cox proportional hazards models (Cox, 1972) were fitted to the data to test the hypothesis that the experience of adversity during

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Table 1
Characteristics of the Sample

Variable	*n*	Weighted % or (Mean)	Sample *n*
Age	6,706	(63.9)	6,706
Gender			
Male	3,063	48.1	6,715
Father's education			
Primary or less	4,595	72.6	6,715
Secondary or equivalent	1,071	13.4	
Third level	519	5.7	
(Missing)	530	8.3	
Marital status			
Married/cohabiting	4,799	68.7	6,715
Never married	605	9.4	
Separated/divorced	417	6.4	
Widowed	894	15.5	
Respondent's education			
Primary or less	1,855	37.6	6,713
Secondary or equivalent	2,746	43.5	
Third level	2,112	18.9	
Household income			
Euros (€)	6,211	(34,615)	6,211
Social class			
Professional/managerial	1,581	17.4	6,715
Nonmanual/skilled manual	1,411	21.2	
Semi/unskilled	809	13.5	
Unknown/refused	653	9.5	
Farmers	419	7.5	
No social class designation	1,842	30.9	
Smoking status			
Never smoked	2,987	43.4	6,715
Past smoker	2,593	38.0	
Current smoker	1,135	18.6	
CAGE alcohol			
Hazardous drinker = yes	797	11.9	6,596
IPAQ			
Low physical activity	2,069	32.8	6,651
Moderate physical activity	2,326	33.8	
High physical activity	2,256	33.4	
Spouse/partner/child addicted to drugs/alcohol			
Yes	495	7.2	6,707
(Missing)	220	3.5	
Spouse/partner/child had a life threatening illness/accident			
Yes	1,476	21.1	6,708
(Missing)	256	4.2	
Experienced death of a child			
Yes	720	11.6	6,705
(Missing)	258	4.0	
Memory			
Word recall	6,606	(5.72)	6,606

Note. IPAQ = International Physical Activity Questionnaire.

childhood is associated with earlier age of disease onset. In these models, doctor diagnosis of disease represented the failure event and age of disease onset represented analysis time. Technically, the hazard ratio (HR) is defined as the probability that an individual who is under observation at time *t* experiences an event at that time (Garson, 2013). An HR of 2.0, for example, implies that at any time, twice as many participants in the exposed group are experiencing an event proportionately compared with the nonexposed group. In the context of the current study, a higher HR for the exposed (i.e., experienced adversity) implies faster progression to the disease endpoint.

T5 Table 5 summarizes the multivariable adjusted HR for disease onset across each of the disease types for which information was collected concerning age of onset, by the number of adverse events experienced during childhood. Once again, the results tended to show graded associations between the amount of adversity experienced during childhood and earlier onset of disease. While the association between the experience of adversity and any individual physical disease was weak, a pooled measure that calculated the earliest age at which physical disease onset occurred across any of the physical disease conditions revealed that those who were exposed to two or more adverse events during childhood progressed more quickly to the physical disease endpoint (RR = 1.27, 95% CI [1.09, 1.49]; $p = .002$). Similarly, experiencing one or more adverse events significantly increased the HR for emotional, nervous, or psychiatric disorders. These relationships are depicted graphically in Figures 1 and 2. F1, 2

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Table 2
Prevalence of Doctor Diagnosed Disease Conditions in Midlife and Older Adulthood

	Adversity = no (n = 4,522)		Adversity = yes (n = 2,193)		All sample (n = 6,715)	
Disease type	n	Weighted %	n	Weighted %	n	Weighted %
Cardiovascular disease	709	15.9	389	18.4	1,098	16.7
Lung disease	151	3.5	119	5.8	270	4.2
Asthma	390	8.8	233	10.6	623	9.4
Arthritis	1,220	27.1	608	28.2	1,828	27.5
Osteoporosis	476	10.1	199	9.0	675	9.7
Ulcers	406	9.5	243	11.5	649	10.2
Diabetes	332	7.7	171	8.3	503	7.9
Cancer	282	6.1	147	6.5	429	6.3
Emotional, nervous, or psychiatric disorder(s)	304	6.6	255	11.4	559	8.2
Comorbidity of disease types	1095	24.5	630	29.3	1,725	26.1

Discussion

In this large epidemiologic cohort study of ageing, the experience of adversity during childhood was associated with significantly increased risk for cardiovascular disease, lung disease, asthma, and emotional, nervous, or psychiatric disorders in later life. These associations remained robust to controls for a range of confounding variables. The relationship with adversity was graded such that exposure to a greater number of childhood stressors increased risk for disease in a mostly linear fashion. Although the strongest effects of adversity were observed across diseases that are considered to be closely aligned with the stress response, such as diseases of the cardiovascular system, immune diseases (e.g., asthma, arthritis) and psychiatric disorders; point estimates tending in the positive direction across the majority of disease types suggests that there may be general processes at play. Nevertheless, it should be acknowledged that there was little evidence to suggest that the experience of adversity during childhood increases risk for cancers, osteoporosis, or diabetes. This finding is not entirely unexpected as Felitti et al. (1998) found stronger associations of adversity with ischemic heart disease, stroke and chronic bronchitis than they did with cancers or diabetes.

This study also provides some tentative support for the idea that adversity is associated with earlier age of disease onset. The results of the Cox regression analyses indicated a general trend toward higher failure (i.e., earlier onset) among those who had experienced most adversity during childhood. The experience of adversity in early life was found to be associated with increased risk for earlier onset of any physical disease, and any emotional, nervous, or psychiatric disorder. Taken in conjunction, these findings can be adduced as providing some tentative support for the idea that childhood adversity represents an important link in the pathway between early childhood social environment and risk of chronic disease in older age. This idea is further buttressed by the finding that contemporaneous SES and lifestyle related factors do not explain the association between adversity and disease or that, in many of the multivariate analyses (not shown), childhood adver- AQ: 6

Table 3
Multivariable Adjusted Relative Risk of Doctor Diagnosed Disease in Adulthood by the Experience of Different Types of Adversity During Childhood (n = 6,408)

	Grew up poor		Substance abuse in family		Childhood physical abuse		Childhood sexual abuse	
Disease type	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI
Cardiovascular disease	**1.19**	[1.04, 1.37]*	1.07	[0.86, 1.34]	1.22	[0.98, 1.52]	1.23	[0.98, 1.56]
Lung disease	**1.51**	[1.14, 2.00]**	**1.65**	[1.13, 2.41]**	1.00	[0.63, 1.60]	**1.69**	[1.11, 2.57]*
Asthma	1.16	[0.95, 1.42]	1.14	[0.87, 1.49]	**1.48**	[1.14, 1.93]**	**1.39**	[1.05, 1.83]*
Arthritis	1.10	[0.99, 1.22]	0.98	[0.84, 1.16]	**1.23**	[1.05, 1.43]**	**1.24**	[1.06, 1.46]**
Osteoporosis	1.01	[0.82, 1.23]	1.12	[0.85, 1.48]	1.02	[0.72, 1.43]	1.02	[0.76, 1.38]
Ulcers	0.91	[0.74, 1.11]	1.33	[1.03, 1.70]*	**1.54**	[1.20, 1.98]***	**1.60**	[1.23, 2.06]***
Diabetes	1.15	[0.92, 1.43]	0.85	[0.59, 1.23]	1.14	[0.82, 1.60]	1.15	[0.79, 1.69]
Cancer	1.13	[0.88, 1.45]	0.99	[0.68, 1.44]	1.17	[0.79, 1.74]	1.37	[0.93, 2.02]
Emotional, nervous, or psychiatric disorder	**1.28**	[1.04, 1.57]*	**1.65**	[1.31, 2.07]***	**1.91**	[1.51, 2.41]***	**2.06**	[1.65, 2.59]***
Comorbidity	**1.18**	[1.07, 1.31]***	**1.24**	[1.07, 1.44]**	**1.49**	[1.30, 1.71]***	**1.56**	[1.36, 1.79]***

Note. RR = relative risk. Adjusted for gender, age, marital status, father's education, current social class, education, current income, smoking, hazardous drinking, physical activity, adverse life events (adulthood), and delayed word recall. Bold typeface indicates associations that remain significant after applying the false discovery rate (FDR) correction.
* Significant at the .05 level. ** Significant at the .01 level. *** Significant at the .001 level. Corrected overall critical p value = .023 using the FDR correction.

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Table 4
Multivariable Adjusted Relative Risk of Doctor Diagnosed Disease in Adulthood by the Number of Adverse Events Experienced During Childhood (n = 6,408)

Disease type	Experienced any type of adversity during childhood		One adverse childhood event		Two or more adverse childhood events	
	RR	95% CI	RR	95% CI	RR	95% CI
Cardiovascular disease	**1.17**	[1.03, 1.32]*	1.11	[0.97, 1.27]	**1.38**	[1.12, 1.71]**
Lung disease	**1.51**	[1.17, 1.96]**	1.36	[1.02, 1.82]*	**2.05**	[1.40, 3.01]***
Asthma	1.18	[0.99, 1.40]	1.10	[0.90, 1.33]	**1.45**	[1.12, 1.88]**
Arthritis	1.10	[1.01, 1.21]*	1.08	[0.97, 1.19]	**1.22**	[1.04, 1.42]*
Osteoporosis	1.03	[0.87, 1.23]	1.04	[0.86, 1.25]	1.02	[0.75, 1.40]
Ulcers	1.11	[0.94, 1.31]	1.02	[0.85, 1.23]	**1.43**	[1.12, 1.83]**
Diabetes	1.03	[0.84, 1.26]	0.99	[0.80, 1.23]	1.17	[0.84, 1.63]
Cancer	1.13	[0.91, 1.41]	1.10	[0.86, 1.40]	1.25	[0.86, 1.83]
Emotional, nervous, or psychiatric disorder	**1.56**	[1.30, 1.86]***	**1.28**	[1.04, 1.57]*	**2.31**	[1.83, 2.92]***
Comorbidity	**1.23**	[1.13, 1.35]***	**1.13**	[1.02, 1.25]*	**1.62**	[1.42, 1.85]***

Note. RR = relative risk. Reference category for the binary and categorical dependent variable did not experience adversity during childhood. Adjusted for gender, age, marital status, father's education, current social class, education, current income, smoking, hazardous drinking, physical activity, adverse life events (adulthood), and delayed word recall. Bold typeface indicates associations that remain significant after applying the FDR correction.
* Significant at the .05 level. ** Significant at the .01 level. *** Significant at the .001 level. Corrected overall critical *p* value = .022.

sity was as strong a predictor of disease as some of the contemporaneous markers of SES. While a few small scale studies have provided some interesting leads regarding intermediary phenotypes in the pathway from adversity to disease (Miller et al., 2009; Ward et al., 2009), additional epidemiological studies, ideally employing biomarkers of autonomic and immune activation, are required to further disambiguate the cross-sectional relationships that have been observed in this study.

AQ: 7

Limitations

The essential criticism of this study and one that pertains to the majority of studies in this field is that the measures of childhood adversity were obtained retrospectively and hence may be subject to recall biases. In mitigation, some investigators have claimed that retrospective recall of childhood adversity is reliable, particularly where the information is highly salient (Delaney & Smith, 2012; Hardt & Rutter, 2004). A second limitation is that the number of adversities reported was used as a proxy for the chronicity of childhood stressful exposures. In essence, this means that each adversity is given equal weight in the analysis even though the different types of adversity might differ both in terms of their salience and their sequalae (Benjet et al., 2010). It would be expected that the severity and duration of the exposure would be an important moderator of the impact of the stressor.

A third limitation is that the items that were used to define the childhood adversity measure do not reflect the full range of adversities that could have been measured. Likewise, it should be acknowledged that the measures of stressful life events in adulthood represent only a small sample of the universe of items that could have been included. Furthermore, the results of the survival analysis are predicated on the basis that respondents can accurately recall the age at which they were first diagnosed, so the results should be considered exploratory in this regard. It should be acknowledged that relying on retrospective self-reports of both the exposure (i.e., adverse events) and the outcome (i.e., age at onset) is far from ideal, and that future work would benefit from attempting to link prospectively acquired information relating to the exposure of interest to objective information concerning diagnosis

Table 5
Multivariable Adjusted Hazard Rates of Time to Disease Onset Resulting From Cox Proportional Regression Models by the Number of Adverse Events Experienced During Childhood

Disease type	One adverse childhood event		Two or more adverse childhood events		*n*
	HR	95% CI	HR	95% CI	
Cardiovascular disease	1.12	[0.94, 1.33]	1.30	[0.95, 1.77]	6,183
Arthritis	1.10	[0.97, 1.24]	1.27	[1.05, 1.53]*	6,362
Diabetes	0.98	[0.78, 1.24]	1.17	[0.82, 1.68]	6,407
Cancer	1.09	[0.85, 1.40]	1.26	[0.86, 1.85]	6,408
Any physical disease	1.10	[0.99, 1.21]	**1.27**	[1.09, 1.49]**	6,256
Any emotional, nervous, or psychiatric disorder	1.31	[1.04, 1.65]*	**2.63**	[2.02, 3.41]***	6,392

Note. HR = hazard rate. Reference category for the categorical dependent variable did not experience adversity during childhood. Adjusted for gender, age, marital status, father's education, current social class, education, current income, smoking, hazardous drinking, physical activity, adverse life events (adulthood), and delayed word recall. Bold typeface indicates associations that remain significant after applying the FDR correction.
* Significant at the .05 level. ** Significant at the .01 level. *** Significant at the .001 level. Corrected overall critical *p* value = .008.

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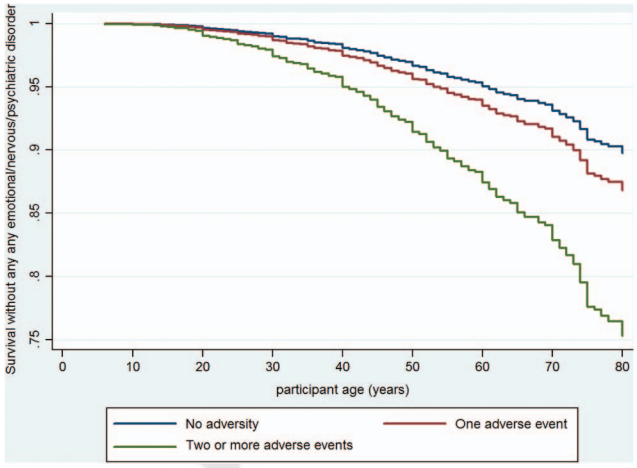
and age at onset contained in other administrative databases (e.g., hospital or general-practitioner-based clinical registries). This was not possible in the present study because there is currently no administrative system in Ireland for collating and centralizing this information.

Finally, it could also be argued that the measures of socioeconomic position at interview do not adjust adequately for lifetime socioeconomic position, health behaviors and material circumstances (e.g., suboptimal household environmental conditions, poor diet, occupational exposures). If so, it is possible that the observed association between childhood adversity and later disease simply reflects the correlation of early life adversity with adult socioeconomic position. Therefore, one cannot exclude the possibility that increased risk of disease among those who were exposed to adversity during childhood represents residual confounding. Nonetheless, the finding that the effects of childhood adversities are cumulative and exist independently of father's educational background and other later life socioeconomic factors suggests that a psychobiological interpretation may have some traction.

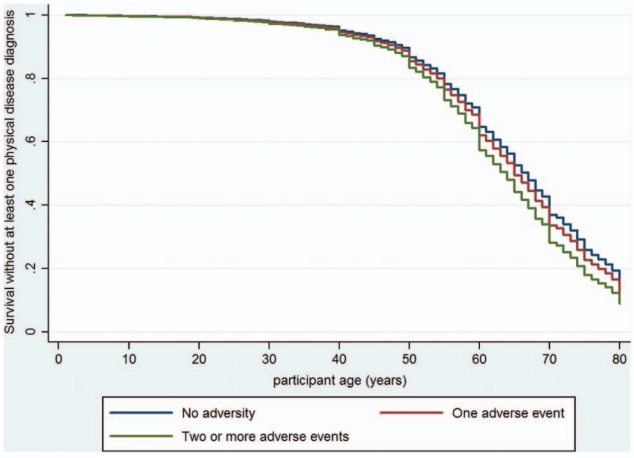
Strengths

This study also has a number of strengths, in addition to utilizing data for a nationally representative sample of the older population. First, the study benefits from employing a multidimensional measure of adversity with each component of the measure indexing different influences on health. Material disadvantage during childhood reflects a number of different influences of income including the quality of nutrition, household environmental conditions, economic resources, and intergenerational reproduction of inequalities. Alcohol or drug dependency of a parent may be indicative of a dysfunctional and less emotionally supportive family social climate; while childhood sexual and physical abuse, and the negative emotional states they elicit, represent noxious life events that may compromise emotion regulation and the development of social competencies. Second, while many studies examining the relationship between adversity and disease tend to be disease specific, or focus on only a small number of diseases, this study was able to examine the effect of adversity across multiple disease types, which, it was argued, is an important step in trying to characterize the mechanism underlying different pathologies. Finally, by using a cumulative adversity measure this study examined whether the effects of early adverse exposures on diseases were sensitive to dose.



ONLINE COLOR

Figure 2. Survival function for psychiatric disorder free survival resulting from Cox proportional hazards regression by the number of adverse events experienced during childhood. Adjusted for gender, age, marital status, father's education, current social class, education, current income, smoking, hazardous drinking, physical activity, adverse life events (adulthood), and delayed word recall. The color version of this figure appears in the online article only.



ONLINE COLOR

Figure 1. Survival function for physical disease free survival resulting from Cox proportional hazards regression by the number of adverse events experienced during childhood. Adjusted for gender, age, marital status, father's education, current social class, education, current income, smoking, hazardous drinking, physical activity, adverse life events (adulthood), and delayed word recall. The color version of this figure appears in the online article only.

Conclusions

The finding that an adverse exposure occurring early in life can increase risk of disease in later life independent of later socioeconomic and lifestyle factors is a remarkable finding; particularly as there is a sizable corpus of research that shows that childhood social circumstances may operate as an independent risk factor for disadvantaged social position in later life (Case, Fertig, & Paxson, 2005), and increases the likelihood of engaging in lifestyle related behaviors that are known to be damaging to health (Felitti et al., 1998). These findings indicate that childhood may represent a sensitive or critical period in the development of disease and reinforces the necessity of adopting a life-course approach to chronic disease epidemiology.

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