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Title	The health and financial burden of Adverse Childhood Experiences in England and Wales: a combined primary data study of five surveys
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Abstract

Objectives: To estimate the health and financial burden of adverse childhood experiences (ACEs) in England and Wales.

Design: Combined data from five randomly stratified cross-sectional ACE studies. Calculated population attributable fractions (PAFs) for major health risks and causes of ill-health applied to Disability Adjusted Life Years (DALYs) with financial costs estimated using a human capital method.

Setting: Households in England and Wales.

Participants: 15,285 residents aged 18-69.

Outcome measures: PAFs for single and multiple ACE exposure categories for four risk factors (smoking, binge drinking, cannabis use, overweight) and nine causes of ill-health (cancer, type 2 diabetes, heart disease, respiratory disease, stroke, violence victimisation, anxiety, depression, other mental illness). Annual estimated DALYs and financial costs attributable to ACEs.

Results: Cumulative relationships were found between ACEs and risks of all outcomes. For risk factors, PAFs for ACEs were highest for cannabis use (Wales 36.5%, England 33.0%) although ACE-attributable smoking accounted for the highest estimated annual costs (£7.8 billion across England and Wales). For causes of ill-health, PAFs for ACEs were highest for violence (Wales 49.3%, England 43.6%) and mental illness (ranging from 29.2% for anxiety in England to 51.0% for other mental illness in Wales). The greatest ACE-attributable costs were for mental illness (anxiety, depression and other mental illness combined; £11.4 billion across England and Wales) and cancer (£8.3 billion). Across all conditions, total annual ACE-attributable costs were estimated at £45.0 billion (1.6 million DALYs). The majority of costs related to exposures to multiple rather than a single ACE (ranging from 70.4% for overweight to 96.1% for cancer).

Conclusions: ACEs impose a substantial societal burden in England and Wales. Policies and practices that prevent ACEs, build resilience and develop trauma-informed services are needed to reduce burden of disease and avoidable service use and financial costs across health and other sectors.

Article Summary

Strengths and limitations of this study

- Adverse childhood experiences are known to increase individuals' risks of poor health across the life course yet the financial burden they imposes on national economies is largely unmeasured.
- We combined primary data on ACEs and 13 health outcomes from five general population ACE surveys undertaken in England and Wales.
- For each outcome, we generated population attributable fractions for cumulative ACE exposure and applied these to Disability Adjusted Life Years which, in turn, allowed calculation of financial burden of ACEs using a human capital approach.
- ACE data were retrospectively reported and may be affected by recall bias, while general household surveys by their nature are likely to exclude those that have suffered the greatest impact of ACEs (e.g. premature death, incarceration or homelessness)
- Although most major health outcomes were included in the study, data are not yet available on all health outcomes potentially associated with ACEs and financial estimates are likely to be conservative.

Introduction

Evidence linking adverse childhood experiences (ACEs) to the adoption of health-harming behaviours and the development of mental and physical illness has burgeoned in recent years.[1] The term ACEs is used to describe some of the most intense sources of stress that children can suffer whilst growing up, such as being maltreated, witnessing domestic violence or coping with parental substance abuse.[2] Such experiences can have harmful effects on children's developing neurological and physiological systems that can embed vulnerability to poor health and well-being. Thus repeated activation of the stress response system during childhood and a lack of responsive interaction with caring adults can impact on brain structure, neuroendocrine stress regulation, immune functioning and metabolic health, as well as social and emotional development.[3,4] Consistent with such effects, ACEs have been associated with delayed child development (e.g. cognitive and language skills), childhood health and behavioural conditions, the adoption of health-risk behaviours (e.g. substance use), mental illness, and early development of chronic health conditions (e.g. cancer).[1,5-8]

Numerous studies have explored the health impacts and costs of specific ACEs such as child maltreatment.[9-11] However, the ACE framework provides a mechanism for measuring a range of ACE types and the cumulative risks they impose at a population level.[2] Studies using this approach show a dose response relationship between the number of ACEs suffered and poor outcomes across multiple domains, including health, criminal justice, education and employment.[12-15] Studies also show that most individuals who report having suffered any specific ACE type (e.g. physical abuse) report other ACE types (e.g. exposure to domestic violence).[16] Consequently, prevention efforts focused on any individual ACE type are likely to have limited success if the range of other ACEs affecting families are left unaddressed. The rapid proliferation of awareness on the impacts of ACEs on the policy priorities of different sectors is driving multi-agency action to enhance early intervention and develop trauma-informed services.[17,18] However, such policy development requires an understanding of the financial costs of ACEs to society and consequently the potential gains to be made by preventing ACEs for future generations.

Estimates of the financial burden of ACEs are only just starting to emerge. A recent study estimated that the annual costs attributable to ACEs for four risk factors (smoking, harmful alcohol use, illicit drug use and obesity) and six causes of ill-health (anxiety, depression, cancer, type 2 diabetes, cardiovascular disease and stroke) reached $581 billion in Europe

and $748 billion in North America; equivalent to around 3% of each regions' GDP.[12] Here, we combine primary data from five ACE studies undertaken in England and Wales to develop national population attributable fractions (PAFs) for ACEs across an extended range of outcomes. We use these data to estimate the annual cost of the health burden resulting from the life-long impact of ACEs on residents of England and Wales using a human capital model.

Methods

Primary data sources

We combined data from five cross-sectional ACE studies conducted across various geographies in England and Wales between 2012 and 2017.[19-23] Summary information on each study is provided in online supplementary table S1. All studies used stratified random sampling approaches with lower super output area (LSOA; small geographical areas with a mean population of 1,500) as the sampling unit. LSOAs were categorised into deprivation quintiles based on their ranking in the English[24] or Welsh[25] Indexes of Multiple Deprivation (IMD); both of which are composite measures including a range of economic and social indicators. Sample selection was stratified by region (as appropriate, see online supplementary table S1) then deprivation quintile based on the population profile of the relevant study area. Households in sampled areas were identified using the national postcode address file. In four studies, randomly selected households were sent a letter prior to researcher visits that provided information on the study and the opportunity to opt out. In one study,[22] researchers randomly selected households in sampled LSOAs and provided study information materials at the door. Interviews were undertaken face-to-face at participants' homes by professional market research companies using computer assisted personal interviewing. Informed consent was obtained from all participants. Sensitive questions, including those on ACEs, were self-completed. Participation was voluntary and anonymous and only one resident participated per selected household (inclusion criteria: within age range, resident in the LSOA, cognitively able to participate in a face-to-face interview). Across the five samples, weighted average compliance was 55.7% (see online supplementary table S1) with a total sample size of 15,658. For this study, data were restricted to individuals aged 18-69 with complete demographic and ACE data, resulting in a final sample of 15,285.

All questionnaires used the Centers for Disease Control and Prevention short ACE tool[26] to collect data on nine ACEs occurring before the age of 18: physical abuse; sexual abuse; verbal abuse; parental separation; exposure to domestic violence; and household member alcohol abuse; drug abuse; mental illness; and incarceration. For the purpose of analysis, positive responses to ACE questions were summed and participants were allocated to an ACE count category: 0 ACEs, 1 ACE, 2-3 ACEs, ≥4 ACEs. Questions used to determine ACEs and the thirteen health outcomes analysed in this study are shown in online supplementary table S2. All studies provided data on current smoking, lifetime cannabis use and violence victimisation in the past 12 months; four provided data on current binge drinking, overweight, and lifetime diagnosis of cancer, type 2 diabetes, heart disease, stroke and respiratory disease; and one provided data on lifetime treatment for depression, anxiety and other mental illness (see online supplementary table S3). Demographic variables included gender, age, ethnicity (self-assigned using UK census categories) and deprivation quintile.

Calculating PAFs

Statistical analysis was undertaken in SPSS v23 with data editing and calculations undertaken in Excel. Binomial generalized linear modelling was used to calculate risk ratios (RRs) and 95% confidence intervals (CIs) associated with ACE count level for each health outcome, controlling for study location, gender, ethnicity (white or non-white) and deprivation quintile of residence. Binomial regression did not converge in a model for smoking and consequently for this outcome we calculated hazard ratios using cox regression with a constant in the time variable.[27] In line with cost estimates for global regions,[12] we calculated PAFs for each ACE count level according to:

$$PAF_{ACE\alpha} = \frac{P_{ACE\alpha} \times (RR_{ACE\alpha} - 1)}{(P_{ACE0}) + (P_{ACE1} \times RR_{ACE1}) + (P_{ACE2\text{-}3} \times RR_{ACE2\text{-}3}) + (P_{ACE4+} \times RR_{ACE4+})}$$

where $_{\alpha}$ is the category of ACE count for the PAF in question, RR_{ACE} is the pooled RR associated with each ACE count and P_{ACE} is the proportion of the sample exposed to each ACE count. Separate PAFs were generated for England and Wales using regional ACE prevalence levels.

Calculating ACE-attributable costs

Consistent with previous studies,[11,12,28] we used a human capital approach to calculate ACE-attributable costs associated with each health outcome. The human capital approach is a commonly used method in economic evaluations to calculate the cost of lost productivity to society as a result of separation of an individual from the labour force due to premature death or morbidity.[29] Health outcomes were matched to risk factor and cause categories in the 2017 Global Burden of Disease Study[30] (GBD; see online supplementary table S4). For each matched category, disability adjusted life years (DALY) estimates were extracted for England and Wales for age categories 15-49 years, 50-69 years and 70+ years. Previous cost estimates using a human capital approach have assumed one DALY is equal to a regions' GDP per capita and calculated costs based on DALYs*GDP per capita.[11,12,28] GDP is not calculated separately for England and Wales, thus we used the related measure of regional Gross Value Added (GVA; equivalent to GDP plus subsidies less taxes on products) with GVA per capita (balanced, current basic 2017 prices) being £28,096 for England and £19,899 for Wales.[31] PAFs were applied to the total cost (by UK region) for each risk factor and cause to estimate the economic value of DALYs lost by ACE level. The equivalent value of DALYs lost as a proportion of total GVA was also calculated. To estimate the total costs attributed to ACEs across all health outcomes studied, we excluded DALYs for risk factors that related to included causes of ill health (e.g. those for alcohol use attributed to cancer). Sensitivity analyses were run limiting DALYs to those for 15-69 year olds; using the upper and lower bounds (uncertainty intervals) for DALYs (extracted from the GBD); and by generating PAFs using the upper and lower confidence intervals for RRs.

Patient and Public Involvement

There was no patient involvement in this study. Public participants in all five contributing studies were provided with an information sheet with the contact details of the relevant research team if they wanted to request copies of study publications (reports and open access journal papers). All study findings are publicly available.

Results

Demographics and ACE count levels of the individual and combined study samples are shown in online supplementary table S5. Across the combined samples, over half (54.9%) of participants were female and 85.7% were of white ethnicity. ACE prevalence levels (used to generate PAFs) were 53.1% 0 ACEs, 19.0% 1 ACE, 15.2% 2-3 ACEs and 12.6% ≥4 ACEs in

Welsh samples, and 56.2% 0 ACEs, 20.1% 1 ACE, 15.4% 2-3 ACEs and 8.4% ≥4 ACEs in English samples.

RRs for each ACE count level and each health outcome are presented in table 1 (unadjusted proportions are provided in online supplementary table S6). All outcomes showed a graded relationship with ACEs, with RRs increasing as ACE count increased. Risks of binge drinking, smoking, cannabis use, being a victim of violence and mental illness outcomes were increased in individuals with any level of ACEs. Risks of being overweight, type 2 diabetes, heart disease and respiratory disease were increased in individuals with ≥2 ACEs, and risks of cancer and stroke in those with ≥4 ACEs only.

Total PAFs for ACEs were slightly higher in Wales than in England for all outcomes due to higher ACE prevalence levels (table 2). Across the four risk factors, cannabis use had the highest PAFs due to ACEs (36.5% Wales, 33.0% England). However, smoking carried the highest ACE-attributable costs given higher numbers of DALYs for this risk factor. ACE-attributable costs due to smoking were £7.3 billion in England and £465.0 million in Wales. Being overweight had the lowest PAFs due to ACEs (2.3% Wales, 2.0% England), although ACE-attributable costs still reached £692.9 million in England and £33.1 million in Wales. Across causes of ill-health, violence and mental illness had the highest PAFs due to ACEs while cancer and type 2 diabetes had the lowest. ACEs were attributed to 49.3% of recent violence victimisation in Wales and 43.6% in England, with associated costs of £16.7 million and £357.2 million respectively. Up to a third of depression and anxiety, and half of other mental illnesses, were attributed to ACEs with associated costs across the three mental health outcomes being £473.6 million in Wales and almost £11 billion in England. Despite having low PAFs, high DALYs for cancer meant that this cause carried the greatest ACE-attributable costs across all individual outcomes measured; reaching £491.2 million in Wales and £7.9 billion in England.

Figure 1 shows the proportion of ACE-attributable costs for each outcome that were accounted for by 1, 2-3 and ≥4 ACEs. For cancer, the 1 ACE category accounted for only 3.9% of ACE-attributable financial costs while the ≥4 ACEs category accounted for 78.5%. For other outcomes, the 1 ACE category accounted for between 9.5% (violence) and 29.6% (overweight) of costs and the ≥4 ACEs for between 26.1% (overweight) and 52.5% (stroke).

To calculate a total ACE-attributable cost across all risk factors and causes of ill-health, we excluded DALYs from the four risk factors that related to included causes (e.g. those for smoking related to cancer). Total ACE-attributable costs across all included outcomes and both geographies were £45.0 billion (£2.3 billion for Wales and £42.7 billion for England; table 3). These costs are equivalent to 3.7% of total annual GVA in Wales and 2.7% in England (2.8% across the combined geographies). In sensitivity analysis (see methods) combined estimated ACE-attributable costs for England and Wales ranged from £17.2 billion (equivalent to 1.1% of GVA) to £72.0 billion (4.4% of GVA; table 3).

Discussion

In this study of 15,285 adults in England and Wales, we found a dose-response relationship between ACEs and all outcomes measured. Violence, mental illness and cannabis use had the highest PAFs due to ACEs, while mental illness, cancer and smoking carried the highest ACE-attributable costs. Across all outcomes studied, the total estimated annual ACE-attributable costs across England and Wales were £45.0 billion, equivalent to more than £1,800 per household per annum.[32] The majority of these costs related to multiple ACE categories.

Comparison with other studies

There are no previous studies estimating the costs of ACEs in England and Wales. However, regionally the annual costs of ACEs have been estimated to be equivalent to 2.7% of GDP in Europe and 3.6% of GDP in North America; comparable to our estimate of 2.8% of GVA in England and Wales.[12] Other studies have measured the costs of specific ACEs, particularly violence against children. Such costs have been estimated to be equivalent to between 1.2% and 3.5% of sub-regional GDP in East Asia and the Pacific;[11] to 4.3% of GDP in South Africa;[33] and to 0.8% of GDP for physical abuse, 0.5% for emotional abuse and 0.4% for sexual abuse in China.[34] In the UK, the lifetime cost per victim of non-fatal child maltreatment by a primary caregiver has conservatively been estimated at £90,000.[35] However, this estimate excluded costs for several outcomes considered in our study, including those for cancer, type 2 diabetes and heart disease, due to no association being found between these conditions and the study's single measure of child maltreatment. We found no associations between such conditions and the single ACE category, yet strong associations with multiple ACEs. Thus 96.1% of the ACE-attributable costs of cancer, 88.4%

of those for heart disease and 76.3% of those for type 2 diabetes were accounted for by suffering more than one type of ACE.

Strengths and weaknesses of the study

We used an established human capital methodology[11,12,28] and based our approach on that used to estimate the financial burden of ACEs across Europe and North America.[12] This previous study generated PAFs through meta-analyses of risk estimates in published literature and acknowledged the lack of consistency in study methodologies as a limitation. Key strengths of the current study are the use of primary data and consistency in study methodologies, with all studies using representative household samples and the same set of questions to measure ACEs. However not all outcomes were measured in all studies, and mental illness was only measured in Wales.[23] Further, generalisability of findings beyond England and Wales would depend on potential differences in the prevalence of ACEs and their relationships with key outcomes in other countries. Further, outcome measures could not be matched directly to GBD categories (see online supplementary table S4). Like previous ACE studies, the retrospective, self-reported nature of questions makes findings subject to recall issues and any reluctance to report historical experiences. Our samples were restricted to adults aged 18-69 years, yet some conditions such as stroke occur predominantly in older age groups; thus sensitivity analyses were undertaken limiting DALYs to the 15-69 year age group. While samples were broadly demographically representative of study populations, compliance across studies was 55.7% and some population groups who may be at increased exposure to ACEs (e.g. those incarcerated[36] or homeless[37]) will have been underrepresented. Finally, our estimates of the costs of ACEs should be considered conservative. Whilst our approach included many key risks for, and causes of, ill-health associated with ACEs it did not account for other associated outcomes (e.g. risky sexual behaviour, suicide, crime), nor for the burden of child deaths related to ACEs. A study of child death reviews in an English locality found evidence of at least one ACE in the records of 63% of children that died over a four-year period, and of at least four ACEs in 20% of cases.[38] The lifetime cost of a child maltreatment death in the UK has been estimated at almost £1 million.[35]

Meaning of the study

Nearly half of all adults in England and Wales experienced some form of ACE as a child and around one in 10 experienced ≥4 ACEs (see online supplementary table S5). This equates to approximately 20 million adults with any ACE and four million with ≥4 ACEs. Our results

quantify the substantive proportion of common health-harming behaviours and long-term health conditions that are associated with ACEs, and consequently that could be avoided in future generations through offering better quality childhoods. Currently however, an estimated 2.3 million children in England live in families with substantial complex needs and only a third of these children are receiving established support from statutory services.[39] An imperative to increase expenditure on safe and nurturing childhoods is emphasised by findings that around a third of mental illness could be avoided if ACEs were either prevented or their impacts moderated through early intervention. Mental illness carries one of the highest costs to health systems in England and Wales[40] and also creates substantial pressure on educational, social and criminal justice systems. For the latter in particular, strong relationships found here between ACEs and violence are an additional concern with many types of police recorded violence increasing in England and Wales.[41] Across all measured outcomes, we identify potentially avoidable costs from ACEs equivalent to more than a quarter of the UK's annual government healthcare expenditure.[42] The potential to avoid such costs is unrealised whilst the majority of health expenditure focuses on adults who have already developed pathologies. Evidence-based mechanisms to prevent ACEs and build resilience to their long-term harms are available, offering return on investments in years rather than decades through benefits on child development, health and education.[43-46] The benefits of such interventions reach across sectors, and a whole of government approach could more immediately resource interventions capable of diminishing a current annual ACE burden of £45 billion.

Unanswered questions and future research

As with most ACE studies our data were collected retrospectively and consequently provide no information on the current levels of ACEs experienced by children in England and Wales. Options to measure ACE prevalence now form part of the international Health Behaviour in School-aged children survey (HSBC)[47] but have not yet been used in the English or Welsh survey iterations. Nor are such data routinely being collected through other major school-based surveys in the UK. While estimates of current exposure to some ACEs are available,[39] routine measurement of ACEs in children is required to better understand their extent and socio-demographic and geographic distribution, as well as the impact of interventions to address them. Further, our findings identified that, despite having the lowest prevalence, the majority of costs generated by ACEs fall on those experiencing ≥4 ACEs (table 2). There is an urgent need to better understand the cumulative impact of ACEs on health outcomes

across the life course, integrating epidemiology with fields including epigenetics, immunology and neurology. Equally, there is a critical need for knowledge on how services can become more trauma-informed, what impact trauma-informed service delivery can have, and how services for children and families affected by child maltreatment, substance abuse, domestic violence or incarceration, for instance, can be better integrated to provide a cohesive offer. Finally, as well as the core ACE categories included here, measurements of other childhood adversities such as neglect, parental bereavement, bullying and exposure to community level violence are increasingly being incorporated into the list of potential ACEs. Public services that recognise the impacts of childhood adversity on lifelong health but neglect to implement preventative measures may yet feature in future lists.

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Author Contributions

MAB and KH designed the study. MAB developed the statistical modelling and KH and KF conducted data analyses. KH wrote the manuscript with contributions from MAB, KF and RK. All authors reviewed the study findings and read and approved the final version before submission. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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Competing interests

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Ethics approval

Ethical approval for the 2017 Welsh national sample was obtained from Bangor University's Healthcare and Medical Sciences Ethics Committee with ethical approval for all other studies obtained through Liverpool John Moores University Research Ethics Panel. Additional approval for both Welsh surveys was provided by Public Health Wales Research and Development Office.

Data sharing

The datasets analysed in the current study are available from the corresponding author on reasonable request.

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Figure 1: Proportion of ACE-attributable costs for each risk factor and cause of ill health attributed to 1, 2-3 and ≥4 ACE categories

ACE, adverse childhood experience.

Table 1: Risk ratios for risk factors and causes of ill health at each ACE count level

	1 ACE			2-3 ACEs			≥4 ACEs		
	RR	95%CIs	P	RR	95%CIs	P	RR	95%CIs	P
Risk factors									
Binge drinking	1.338	1.170-1.529	<0.001	1.443	1.251-1.664	<0.001	2.280	1.993-2.609	<0.001
Smoking	1.186	1.090-1.291	<0.001	1.446	1.327-1.575	<0.001	2.076	1.902-2.267	<0.001
Cannabis use	1.644	1.500-1.801	<0.001	2.173	1.990-2.372	<0.001	3.176	2.935-3.436	<0.001
Overweight	1.031	0.986-1.078	0.181	1.061	1.011-1.114	0.016	1.064	1.002-1.130	0.043
Causes of ill health									
Depression	1.561	1.305-1.866	<0.001	2.144	1.826-2.517	<0.001	2.782	2.390-3.239	<0.001
Anxiety	1.440	1.178-1.760	<0.001	2.152	1.807-2.564	<0.001	2.755	2.322-3.268	<0.001
Other mental illness	1.724	1.033-2.878	0.037	3.329	2.159-5.133	<0.001	5.354	3.531-8.117	<0.001
Victim of violence	1.370	1.097-1.711	0.005	2.942	2.440-3.548	<0.001	5.780	4.883-6.841	<0.001
Cancer	1.023	0.811-1.290	0.850	1.133	0.879-1.461	0.334	2.063	1.578-2.698	<0.001
Type 2 diabetes	1.169	0.968-1.411	0.105	1.244	1.014-1.527	0.037	1.830	1.438-2.328	<0.001
Heart disease	1.094	0.831-1.441	0.522	1.419	1.078-1.868	0.013	1.923	1.368-2.704	<0.001
Stroke	1.277	0.826-1.974	0.271	1.534	0.975-2.413	0.064	2.772	1.708-4.497	<0.001
Respiratory disease	1.248	0.945-1.646	0.118	1.855	1.422-2.420	<0.001	2.676	1.979-3.617	<0.001

Analysis uses generalized linear modelling controlling for study location, age, gender, ethnicity and deprivation quintile.
Reference category = 0 ACEs. ACE, adverse childhood experience; RR, risk ratio; CI, confidence interval.

Table 2: Population attributable fractions and DALYs and costs attributable to ACEs

		Population attributable fraction				Total DALYs (age 15+)	DALYs attributable to ACEs				Total estimated cost (£ million)*	Attributable costs by ACE count (£ million)			
		1 ACE	2-3 ACEs	≥4 ACEs	All ACEs		1 ACE	2-3 ACEs	≥4 ACEs	All ACEs		1 ACE	2-3 ACEs	≥4 ACEs	All ACEs
Binge drinking	Wales	0.049	0.052	0.125	0.227	38114	1887	1991	4770	8647	758.4	37.5	39.6	94.9	172.1
	England	0.055	0.055	0.086	0.196	606086	33041	33225	52379	118645	17028.6	928.3	933.5	1471.7	3333.4
Smoking	Wales	0.028	0.055	0.110	0.193	121011	3444	6641	13281	23366	2408.0	68.5	132.1	264.3	465.0
	England	0.031	0.057	0.075	0.164	1590656	49649	91218	120073	260940	44691.1	1394.9	2562.9	3373.6	7331.4
Cannabis use	Wales	0.077	0.113	0.175	0.365	22518	1744	2555	3930	8230	448.1	34.7	50.8	78.2	163.8
	England	0.087	0.121	0.122	0.330	331956	28752	40128	40624	109504	9326.6	807.8	1127.4	1141.4	3076.6
Overweight	Wales	0.006	0.009	0.008	0.023	73423	422	663	581	1665	1461.0	8.4	13.2	11.6	33.1
	England	0.006	0.009	0.005	0.020	1203925	7339	10988	6334	24661	33825.5	206.2	308.7	178.0	692.9
Depression	Wales	0.071	0.116	0.150	0.336	16161	1141	1872	2417	5430	321.6	22.7	37.2	48.1	108.1
	England	0.078	0.122	0.104	0.305	294592	23062	36042	30637	89741	8276.9	647.9	1012.6	860.8	2521.4
Anxiety	Wales	0.056	0.119	0.150	0.325	12434	700	1476	1863	4038	247.4	13.9	29.4	37.1	80.3
	England	0.062	0.125	0.104	0.292	203872	12732	25580	21252	59564	5728.0	357.7	718.7	597.1	1673.5
Other mental illness	Wales	0.067	0.174	0.269	0.510	28076	1887	4880	7564	14331	558.7	37.5	97.1	150.5	285.2
	England	0.078	0.192	0.196	0.465	517544	40247	99187	101185	240619	14540.9	1130.8	2786.8	2842.9	6760.4
Violence	Wales	0.036	0.150	0.307	0.493	1703	61	256	522	839	33.9	1.2	5.1	10.4	16.7
	England	0.042	0.168	0.226	0.436	29134	1221	4906	6587	12714	818.6	34.3	137.8	185.1	357.2
Cancer	Wales	0.004	0.018	0.116	0.137	179919	667	3153	20863	24683	3580.2	13.3	62.7	415.2	491.2
	England	0.004	0.018	0.080	0.103	2725146	11129	50104	218214	279447	76565.7	312.7	1407.7	6130.9	7851.3
Type 2 diabetes	Wales	0.027	0.032	0.089	0.148	23306	635	739	2082	3456	463.8	12.6	14.7	41.4	68.8
	England	0.030	0.033	0.061	0.124	356871	10595	11740	21781	44115	10026.6	297.7	329.8	611.9	1239.5
Heart disease	Wales	0.015	0.053	0.097	0.166	112947	1682	6023	10997	18703	2247.5	33.5	119.9	218.8	372.2
	England	0.016	0.056	0.067	0.139	1616873	26326	89796	107904	224025	45427.7	739.6	2522.9	3031.7	6294.2
Stroke	Wales	0.039	0.060	0.165	0.264	39189	1515	2350	6464	10330	779.8	30.2	46.8	128.6	205.5
	England	0.043	0.064	0.116	0.223	546308	23608	34882	63148	121638	15349.1	663.3	980.0	1774.2	3417.6
Respiratory disease	Wales	0.034	0.094	0.152	0.280	50697	1713	4758	7730	14201	1008.8	34.1	94.7	153.8	282.6
	England	0.038	0.099	0.106	0.243	784621	29493	78057	83469	191018	22044.7	828.6	2193.1	2345.1	5366.9

ACE, Adverse childhood experience; DALY, Disability adjusted life year. *Calculated as 1 DALY = GVA per capita (£19,899 Wales, £28,096 England; Balanced, current basic prices, 2017).

Table 3: Total ACE-attributable DALYs and costs and sensitivity analyses

	ACE-attributable DALYs (thousands)			ACE-attributable costs (£ billion)			Equivalent % of GVA		
	England	Wales	England & Wales	England	Wales	England & Wales	England	Wales	England & Wales
Best estimate	1521.4	114.8	1636.2	42.7	2.3	45.0	2.7%	3.7%	2.8%
Limited to DALYs for 15-69 year olds	972.2	69.9	1042.1	27.3	1.4	28.7	1.7%	2.2%	1.8%
PAFs generated using lower CIs for RRs	576.5	49.3	625.9	16.2	1.0	17.2	1.0%	1.6%	1.1%
PAFs generated using upper CIs for RRs	2438.9	177.1	2616.0	68.5	3.5	72.0	4.4%	5.7%	4.4%
Lower bound (uncertainty interval) for DALYs	1348.5	100.7	1449.2	37.9	2.0	39.9	2.4%	3.2%	2.5%
Upper bound (uncertainty interval) for DALYs	1717.9	131.1	1849.0	48.3	2.6	50.9	3.1%	4.2%	3.1%

ACE, Adverse childhood experience; DALY, Disability adjusted life year; GVA, gross value added; PAF, population attributable fraction; CI, confidence interval; RR, risk ratio.

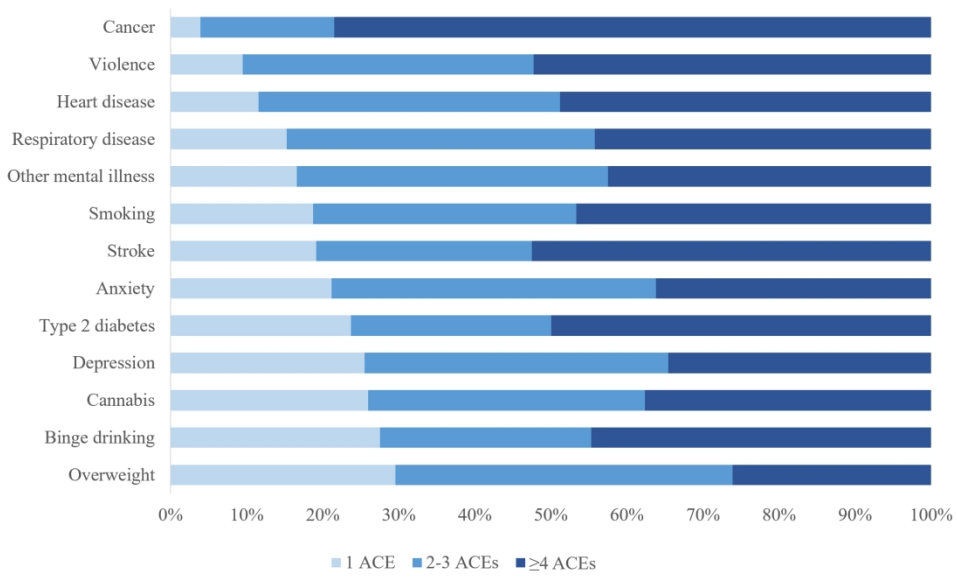

Figure 1: Proportion of ACE-attributable costs for each risk factor and cause of ill health attributed to 1, 2-3 and ≥4 ACE categories

ACE, adverse childhood experience.

Supplementary table 1 Study information

Country	Study location	Stratification for sampling[a]	Recruitment	Dates	Age range (years)	Total sample[e] (n)	Compliance	Deprivation measure	Reference
England	Blackburn with Darwen (North West England)	Blackburn with Darwen Local Authority[b]	Study information letter sent to randomly selected households; households not opting out upon receipt of letter visited by researchers	2012 (Aug-Sep)	18-70[d]	1500	70.4%	IMD 2010	1
England	National sample	English Administrative Regions (n=10)[c]		2013 (Apr-Jul)	18-69	4010	53.5%	IMD 2010	2
England	Luton, Hertfordshire Northamptonshire (South East England)	Luton, Hertfordshire Northamptonshire (n=3)		2015 (Jun-Sep)	18-69	5623	55.8%	IMD 2011	3
Wales	National sample	Welsh Health Regions (n=7)		2017 (Mar-Jun)	18-69	2497	58.5%	WIMD 2014	4
Wales	National sample	Welsh Health Regions (n=7)	Households in sampled areas randomly selected by researchers	2015 (Feb-May)	18-69	2028	49.1%	WIMD 2014	5

[a]Lower Super Output Area level stratification by deprivation quintile. [b]No sub-regional stratification was undertaken in Blackburn with Darwen due to the relatively small size of the sample area. [c]London was split into Inner and Outer London for regional sampling. [d]Individuals aged 70 years were excluded from the sample for consistency. [e]Individuals not completing all questions on variables of interest were excluded. IMD, Index of Multiple Deprivation; WIMD, Welsh Index of Multiple Deprivation.

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Supplementary Table 2 ACE and health outcome questions used

ACE questions. All ACE questions were preceded by the statement "While you were growing up, before the age of 18..."		
ACE	**Question**	**Qualifying responses**
Physical abuse	How often did a parent or adult in your home ever hit, beat, kick, or physically hurt you in any way? This does not include gentle smacking for punishment?	Once; more than once
Verbal abuse	How often did a parent or adult in your home ever swear at you, insult you, or put you down?	More than once
Sexual abuse	How often did anyone at least 5 years older than you (including adults) ever touch you sexually? How often did anyone at least 5 years older than you (including adults) try to make you touch them sexually? How often did anyone at least 5 years older than you (including adults) force you to have any type of sexual intercourse (oral, anal, or vaginal)?	Once or more than once to any of the questions
Parental separation	Were your parents ever separated or divorced?	Yes
Domestic violence	How often did your parents or adults in your home ever slap, hit, kick, punch, or beat each other up?	Once; more than once
Mental illness	Did you live with anyone who was depressed, mentally ill, or suicidal?	Yes
Alcohol abuse	Did you live with anyone who was a problem drinker or alcoholic?	Yes
Drug abuse	Did you live with anyone who used illegal street drugs or who abused prescription medications?	Yes
Incarceration	Did you live with anyone who served time or was sentenced to serve time in a prison or young offenders' institution?	Yes
Health outcome	**Question**	**Qualifying responses**
Binge drinking	How often do you have 6 or more standard drinks on one occasion?	Weekly; daily/almost daily
Smoking	In terms of smoking tobacco, which of the following best describes you?	I smoke daily; I smoke occasionally but not daily
Cannabis use	How often, if ever, have you taken…. Cannabis?	Used but not in the last 12 months; Used in the past 12 months
Overweight	What is your height? (in feet/inches or metres/centimetres) What is your weight? (in stone/pound, kilograms or pounds) Answers used to calculate BMI	BMI 25.0 or higher
Depression	Are you currently or have you ever been treated for… depression?	Yes, currently; Yes, in the past
Anxiety	Are you currently or have you ever been treated for… anxiety?	Yes, currently; Yes, in the past
Other mental illness	Are you currently or have you ever been treated for… another mental illness?	No, never; Yes, currently; Yes, in the past
Victim of violence	How many times have you been physically hit in the past 12 months? Or (in Wales, 2017): In the past 12 months, have you been physically hit by someone else?	Once; 2 or 3 times; More than 3 times Yes
Cancer	Has a doctor or nurse ever told you that you have… Cancer?	Yes
Type 2 diabetes	Has a doctor or nurse ever told you that you have… Type 2 diabetes?	Yes
Heart disease	Has a doctor or nurse ever told you that you have… Coronary Heart Disease or heart attack?	Yes
Stroke	Has a doctor or nurse ever told you that you have… Stroke?	Yes
Respiratory disease	Has a doctor or nurse ever told you that you have… Respiratory disease such as Chronic bronchitis/ Emphysema/ Chronic Obstructive Pulmonary Disease?	Yes

ACE, adverse childhood experience; BMI, body mass index.

Supplementary Table 3 Outcomes measured across studies

	All	England (national)	England (South East)	England (North West)	Wales 2015 (national)	Wales 2017 (national)
Total sample (n)	15285	3885	5454	1421	2028	2497
Binge drinking	n=12769					
Missing (n)	19	2	4	11	2	-
Yes (%)	9.9	11.3	6.6	12.6	14.1	-
Smoking	n=15281					
Missing (n)	4	0	0	4	0	0
Yes (%)	26.3	26.9	23.1	37.1	27.9	25.3
Cannabis use	n=15241					
Missing (n)	44	7	28	5	3	1
Yes (%)	18.1	19.5	14.6	18.1	25.0	17.6
Overweight	n=11527					
Missing (n)	1261	424	481	16	340	-
Yes (%)	49.8	50.9	49.0	45.7	53.2	-
Depression	n=2496					
Missing (n)	1	-	-	-	-	1
Yes (%)	29.2	-	-	-	-	29.2
Anxiety	n=2493					
Missing (n)	4	-	-	-	-	4
Yes (%)	25.0	-	-	-	-	25.0
Other mental illness	n=2491					
Missing (n)	6	-	-	-	-	6
Yes (%)	6.0	-	-	-	-	6.0
Victim of violence	n=15267					
Missing (n)	18	2	10	2	4	0
Yes (%)	5.1	5.3	3.7	6.3	9.1	4.1
Cancer	n=12765					
Missing (n)	23	4	12	7	0	-
Yes (%)	3.7	4.4	2.9	3.2	4.8	-
Type 2 Diabetes	n=12769					
Missing (n)	19	3	12	4	0	-
Yes (%)	5.1	4.8	4.7	7.3	5.3	-
Heart disease	n=12773					
Missing (n)	15	1	12	2	0	-
Yes (%)	2.7	3.2	2.3	4.2	1.5	-
Stroke	n=12773					
Missing (n)	19	1	13	5	0	-
Yes (%)	1.1	1.1	1.0	1.8	0.8	-
Respiratory disease	n=12766					
Missing (n)	22	0	15	7	0	-
Yes (%)	2.8	3.5	1.9	5.2	2.1	-

- outcome not measured in survey.

Supplementary Table 4: Study outcome and matched Global Burden of Disease (GBD) category

Outcome	GBD category matched (ID)
Risk factors	
Binge drinking	Alcohol use (102)
Smoking	Smoking (99)
Cannabis use	Drug use (103)
Overweight	High body-mass index (108)
Causes of ill health	
Depression	Major depressive disorder (586)
Anxiety	Anxiety disorders (571)
Other mental illness	Mental disorders (558), excluding major depressive disorder (586) and anxiety disorders (571)
Victim of violence	Interpersonal violence (724)
Cancer	Neoplasms (410)
Type 2 diabetes	Diabetes mellitus type 2 (976)
Heart disease	Cardiovascular diseases (491), excluding stroke (494)
Stroke	Stroke (494)
Respiratory disease	Chronic respiratory diseases (508), excluding asthma (515)

ID, identification.

Supplementary Table 5 Sample demographics and ACE count prevalence

	All	England (national)	England (South East)	England (North West)	Wales 2015 (national)	Wales 2017 (national)
Total sample (n)	15285	3885	5454	1421	2028	2497
Gender (%)						
Male	45.1	45.0	44.7	39.9	49.8	45.3
Female	54.9	55.0	55.3	60.1	50.2	54.7
Age group (%)						
18-29	21.9	21.0	20.6	24.6	30.4	17.9
30-39	19.9	19.9	22.5	21.5	14.2	18.4
40-49	20.3	20.5	20.6	22.2	17.8	20.1
50-59	17.7	18.0	17.0	14.6	17.5	20.6
60-69	20.2	20.7	19.3	17.0	20.2	23.1
Ethnicity (%)						
White	85.7	86.3	80.6	71.3	95.4	96.4
Other	14.3	13.7	19.4	28.7	4.6	3.6
Deprivation quintile (%)						
(least deprived) 1	21.7	20.1	28.5	5.5	21.7	18.7
2	19.1	19.5	20.2	10.2	19.4	20.9
3	19.9	19.7	20.8	8.1	19.4	25.1
4	19.2	19.9	20.0	14.5	18.7	19.3
(most deprived) 5	20.1	20.7	10.5	61.7	20.7	15.9
ACE count (%)						
0	55.3	53.6	58.4	54.4	54.4	52.1
1	19.7	22.7	18.2	20.0	19.0	18.9
2-3	15.3	15.4	15.3	15.8	13.0	17.1
≥4	9.6	8.3	8.1	9.8	13.6	11.9

ACE, Adverse childhood experience.

Supplementary Table 6 Unadjusted proportion reporting each outcome by ACE count category

	n	ACE count			
		0 ACEs	1 ACE	2-3 ACEs	≥4 ACEs
Binge drinking	12769	7.1	11.2	12.0	19.9
Smoking	15281	20.3	26.3	32.9	50.6
Cannabis use	15241	10.6	19.9	26.2	43.9
Overweight	11527	49.3	49.8	51.1	50.6
Depression	2496	18.4	29.4	41.3	59.1
Anxiety	2493	16.0	24.2	36.5	49.8
Other mental illness	2491	2.8	4.9	9.9	16.4
Violence	15267	2.5	3.8	8.3	18.2
Cancer	12765	3.5	3.5	3.7	5.1
Type 2 diabetes	12769	5.0	5.0	5.3	5.6
Heart disease	12773	2.5	2.5	3.2	3.1
Stroke	12769	0.9	1.1	1.3	1.8
Respiratory disease	12766	2.2	2.7	4.0	4.7

ACE, adverse childhood experience.

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4-6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4, Table S1
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5, Table S2
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5, Tables S2 & S3
Bias	9	Describe any efforts to address potential sources of bias	6
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5, 6, Table S2
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5,6
		(*b*) Describe any methods used to examine subgroups and interactions	5,6
		(*c*) Explain how missing data were addressed	Table S3
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	5
		(*e*) Describe any sensitivity analyses	6
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	4, Table S1
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table S5
		(b) Indicate number of participants with missing data for each variable of interest	Table S3
Outcome data	15*	Report numbers of outcome events or summary measures	Table S3

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	5, Table S6, Table 1
		(*b*) Report category boundaries when continuous variables were categorized	NA
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	7, Table 2
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	8, Table 3
Discussion			
Key results	18	Summarise key results with reference to study objectives	8
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	9
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	8-10
Generalisability	21	Discuss the generalisability (external validity) of the study results	9
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	12

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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The health and financial burden of Adverse Childhood Experiences in England and Wales: a combined primary data study of five surveys

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Abstract

Objectives: To estimate the health and financial burden of adverse childhood experiences (ACEs) in England and Wales.

Design: Combined data from five randomly stratified cross-sectional ACE studies. Population attributable fractions (PAFs) calculated for major health risks and causes of ill-health and applied to disability adjusted life years (DALYs) with financial costs estimated using a modified human capital method.

Setting: Households in England and Wales.

Participants: 15,285 residents aged 18-69.

Outcome measures: PAFs for single (1 ACE) and multiple (2-3, ≥4 ACEs) ACE exposure categories for four health risks (smoking, alcohol use, drug use, high BMI) and nine causes of ill-health (cancer, type 2 diabetes, heart disease, respiratory disease, stroke, violence, anxiety, depression, other mental illness). Annual estimated DALYs and financial costs attributable to ACEs.

Results: Cumulative relationships were found between ACEs and risks of all outcomes. For health risks, PAFs for ACEs were highest for drug use (Wales 58.8%, England 52.6%) although ACE-attributable smoking had the highest estimated costs (England and Wales, £7.8 billion). For causes of ill-health, PAFs for ACEs were highest for violence (Wales 48.9%, England 43.4%) and mental illness (ranging from 29.1% for anxiety in England to 49.7% for other mental illness in Wales). The greatest ACE-attributable costs were for mental illness (anxiety, depression and other mental illness; England and Wales, £11.2 billion) and cancer (£7.9 billion). Across all outcomes, total annual ACE-attributable costs were estimated at £42.8 billion. The majority of costs related to exposures to multiple rather than a single ACE (ranging from 71.9% for high BMI to 98.3% for cancer).

Conclusions: ACEs impose a substantial societal burden in England and Wales. Policies and practices that prevent ACEs, build resilience and develop trauma-informed services are needed to reduce burden of disease and avoidable service use and financial costs across health and other sectors.

Article Summary

Strengths and limitations of this study

- Adverse childhood experiences (ACEs) are known to increase individuals' risks of poor health across the life course yet the financial burden they impose on national economies is largely unmeasured.
- We combined primary data on ACEs and 13 health outcomes from five general population ACE surveys undertaken in England and Wales.
- For each outcome, we generated population attributable fractions for cumulative ACE exposure and applied these to disability adjusted life years which, in turn, allowed calculation of financial burden of ACEs using a modified human capital approach.
- ACE data were retrospectively reported and may be affected by recall bias, while general household surveys by their nature are likely to exclude those that have suffered the greatest impact of ACEs (e.g. homelessness, incarceration or premature death).
- Although many major health outcomes were included in the study, data are not yet available on all health outcomes potentially associated with ACEs and financial estimates are likely to be conservative.

Introduction

Evidence linking adverse childhood experiences (ACEs) to the adoption of health-risk behaviours and the development of mental and physical illness has burgeoned in recent years.[1] The term ACEs is used to describe some of the most intense sources of stress that children can suffer whilst growing up, such as being maltreated, witnessing domestic violence or coping with parental substance abuse.[2] Such experiences can have harmful effects on children's developing neurological and physiological systems that can embed vulnerability to poor health and well-being. Thus repeated activation of the stress response system during childhood and a lack of responsive interaction with caring adults can impact on brain structure, neuroendocrine stress regulation, immune functioning and metabolic health, as well as social and emotional development.[3,4] Consistent with such effects, ACEs have been associated with delayed child development (e.g. cognitive and language skills), childhood health and behavioural conditions, the adoption of health-risk behaviours (e.g. substance use), mental illness (e.g. depression), and early development of chronic health conditions (e.g. cancer).[1,5-8]

Numerous studies have explored the health impacts and costs of specific ACEs such as child maltreatment.[9-11] However, the ACE framework provides a mechanism for measuring a range of ACE types and the cumulative risks they impose at a population level.[2] Studies using this approach show a dose response relationship between the number of ACEs suffered and poor outcomes across multiple domains, including health, criminal justice, education and employment.[12-15] Studies also show that most individuals who report having suffered any specific ACE type (e.g. physical abuse) also report other ACE types.[16] Consequently, prevention efforts focused on any individual ACE type are likely to have limited success if the range of other ACEs affecting families are left unaddressed. The rapid proliferation of awareness on the impacts of ACEs on the policy priorities of different sectors is driving multi-agency action to enhance early intervention and develop trauma-informed services.[17,18] However, such policy development requires an understanding of the financial costs of ACEs to society and consequently the potential gains to be made by preventing ACEs for future generations.

Estimates of the financial burden of ACEs are only just starting to emerge. A recent study estimated that the annual costs attributable to ACEs for four risk factors (smoking, alcohol use, drug use and obesity) and six causes of ill-health (anxiety, depression, cancer, diabetes,

cardiovascular disease and stroke) reached $581 billion in Europe and $748 billion in North America; equivalent to around 3% of each regions' GDP.[12] Here, we combine primary data from five ACE studies undertaken in England and Wales to develop national population attributable fractions (PAFs) for ACEs across an extended range of outcomes. We use these data to estimate the annual cost of the health burden resulting from the life-long impact of ACEs on residents of England and Wales using a modified human capital model.

Methods

Primary data sources

We combined data from five cross-sectional ACE studies conducted across various geographies in England and Wales between 2012 and 2017.[19-23] Summary information on each study is provided in online supplementary table S1. All studies used stratified random sampling approaches with lower super output area (LSOA; small geographical areas with a mean population of 1,500) as the sampling unit. LSOAs were categorised into deprivation quintiles based on their ranking in the English[24] or Welsh[25] Indexes of Multiple Deprivation (IMD); both of which are composite measures including a range of economic and social indicators. Sample selection was stratified by region (as appropriate, see online supplementary table S1) then deprivation quintile based on the population profile of the relevant study area. Households in sampled areas were identified using the national postcode address file. In four studies, randomly selected households were sent a letter prior to researcher visits that provided information on the study and the opportunity to opt out. In one study,[22] researchers randomly selected households in sampled LSOAs and provided study information materials at the door. Interviews were undertaken face-to-face at participants' homes by professional market research companies using computer assisted personal interviewing. Informed consent was obtained from all participants. Sensitive questions, including those on ACEs, were self-completed. Participation was voluntary and anonymous and only one resident participated per selected household (inclusion criteria: within age range, resident in the LSOA, cognitively able to participate in a face-to-face interview). Across the five samples, weighted average compliance was 55.7% (see online supplementary table S1) with a total sample size of 15,658. For this study, data were restricted to individuals aged 18-69 with complete demographic and ACE data, resulting in a final sample of 15,285.

All questionnaires used the Centers for Disease Control and Prevention short ACE tool[26] to collect data on nine ACEs occurring before the age of 18: physical abuse; sexual abuse; verbal abuse; parental separation; exposure to domestic violence; and household member alcohol abuse; drug abuse; mental illness; and incarceration. For the purpose of analysis, and in line with previous studies,[1,19-23] positive responses to ACE questions were summed and participants were allocated to an ACE count category: 0 ACEs, 1 ACE, 2-3 ACEs, ≥4 ACEs. Questions used to determine ACEs and the thirteen health outcomes analysed in this study are shown in online supplementary table S2. All studies provided data on smoking (current smoker), drug use (ever used heroin or crack cocaine) and violence (victimisation in the past year). Four studies provided data on alcohol use (current, ≥12g per day), high body mass index (BMI, ≥25.0 kg/m^2), and whether respondents had ever been diagnosed with cancer, type 2 diabetes, heart disease (coronary heart disease/heart attack), stroke or respiratory disease. One study provided data on whether respondents had ever been treated for depression, anxiety and other mental illness (see online supplementary table S3). Demographic variables included gender, age, ethnicity (self-assigned using UK census categories) and deprivation quintile.

Calculating PAFs

Statistical analysis was undertaken in SPSS v23 with data editing and calculations undertaken in Excel. Binomial generalized linear modelling was used to calculate risk ratios (RRs) and 95% confidence intervals (CIs) associated with ACE count level for each health outcome, controlling for study sampling region, deprivation quintile of residence, gender, age and ethnicity (white or non-white). In line with cost estimates for global regions,[12] we calculated PAF values at each ACE count level (1 ACE v 0 ACEs; 2-3 ACEs v 0 ACEs; ≥4 ACEs v 0 ACEs) according to:

$$PAF_{ACE\alpha} = \frac{P_{ACE\alpha} \times (RR_{ACE\alpha} - 1)}{(P_{ACE0}) + (P_{ACE1} \times RR_{ACE1}) + (P_{ACE2\text{-}3} \times RR_{ACE2\text{-}3}) + (P_{ACE4+} \times RR_{ACE4+})}$$

where $_\alpha$ is the category of ACE count for the PAF in question, RR_{ACE} is the pooled RR associated with each ACE count and P_{ACE} is the proportion of the sample exposed to each ACE count. Overall PAFs for ACEs were generated by summing the three PAF values.[27] Separate PAFs were generated for England and Wales using regional ACE prevalence levels.

Calculating ACE-attributable costs

Consistent with previous studies,[11,12,28] we used a modified human capital approach to calculate ACE-attributable costs associated with each health outcome. The human capital approach is a commonly used method in economic evaluations to calculate the cost of lost productivity to society as a result of separation of an individual from the labour force due to premature death or morbidity.[29] Health outcomes were matched to risk factor and cause categories in the 2017 Global Burden of Disease Study[30] (GBD; see online supplementary table S4). For each matched category, disability adjusted life years (DALY) estimates were extracted for England and Wales for age categories 15-49 years, 50-69 years and 70+ years. Previous cost estimates using a human capital approach have assumed one DALY is equal to a regions' GDP per capita and calculated costs based on DALYs*GDP per capita.[11,12,28] GDP is not calculated separately for England and Wales, thus we used the related measure of regional Gross Value Added (GVA; equivalent to GDP plus subsidies less taxes on products) with GVA per capita (balanced, current basic 2017 prices) being £28,096 for England and £19,899 for Wales.[31] PAFs were applied to the total cost (by UK region) for each risk factor and cause to estimate the economic value of DALYs by ACE level. The equivalent value of DALYs as a proportion of total GVA was also calculated. To estimate the total costs attributed to ACEs across all health outcomes studied, we excluded DALYs for risk factors that related to included causes of ill-health (e.g. those for alcohol use attributed to cancer). Sensitivity analyses were run limiting DALYs to those for 15-69 year olds; using the upper and lower bounds (uncertainty intervals) for DALYs (extracted from the GBD); and by generating PAFs using the upper and lower confidence intervals for RRs.

Patient and Public Involvement

Patients and the public were not involved in the design or planning of the study.

Results

Demographics and ACE count levels of the individual and combined study samples are shown in online supplementary table S5. Across the combined samples, over half (54.9%) of participants were female and 85.7% were of white ethnicity. ACE prevalence levels (used to generate PAFs) were 53.1% 0 ACEs, 19.0% 1 ACE, 15.2% 2-3 ACEs and 12.6% ≥4 ACEs in Welsh samples, and 56.2% 0 ACEs, 20.1% 1 ACE, 15.4% 2-3 ACEs and 8.4% ≥4 ACEs in English samples.

RRs for each ACE count level and each health outcome are presented in table 1 (unadjusted proportions are provided in online supplementary table S6). All outcomes showed a graded relationship with ACEs, with RRs increasing as ACE count increased. Risks of alcohol use, smoking, drug use, violence and mental illness outcomes were increased in individuals with any level of ACEs. Risks of high BMI, heart disease and respiratory disease were increased in individuals with ≥2 ACEs, and risks of type 2 diabetes, cancer and stroke in those with ≥4 ACEs only.

Total PAFs for ACEs were slightly higher in Wales than in England for all outcomes due to higher ACE prevalence levels (table 2). Across the four risk factors, drug use had the highest PAFs due to ACEs (58.8% Wales, 52.6% England). However, smoking carried the highest ACE-attributable costs given higher numbers of DALYs for this risk factor. ACE-attributable costs due to smoking were £7.4 billion in England and £466.5 million in Wales. High BMI had the lowest PAFs due to ACEs (2.4% Wales, 2.2% England), although ACE-attributable costs still reached £729.2 million in England and £35.3 million in Wales. Across causes of ill-health, violence and mental illness had the highest PAFs due to ACEs while cancer and type 2 diabetes had the lowest. ACEs were attributed to 48.9% of recent violence victimisation in Wales and 43.4% in England, with associated costs of £16.6 million and £355.0 million respectively. Up to a third of depression and anxiety, and almost half of other mental illnesses, were attributed to ACEs with associated costs across the three mental health outcomes being £465.3 million in Wales and £10.7 billion in England. Despite having low PAFs, high DALYs for cancer meant that this cause carried the greatest ACE-attributable costs across all individual outcomes measured; reaching £476.4 million in Wales and £7.5 billion in England.

Across all nine causes of ill-health, total ACE-attributable costs were £33.9 billion (£1.7 billion for Wales and £32.1 billion for England). To calculate a total ACE-attributable cost across all risk factors and causes of ill-health, we excluded DALYs from the four risk factors that related to included causes (e.g. those for smoking related to cancer). Total ACE-attributable costs were £42.8 billion (£2.2 billion for Wales and £40.6 billion for England; table 3). These costs are equivalent to 3.5% of total annual GVA in Wales and 2.6% in England (2.6% across the combined geographies). In sensitivity analysis (see methods)

combined estimated ACE-attributable costs for England and Wales ranged from £16.3 billion (equivalent to 1.0% of GVA) to £68.4 billion (4.2% of GVA; table 3).

Figure 1 shows the proportion of ACE-attributable costs for each outcome that were accounted for by 1, 2-3 and ≥4 ACEs. For cancer, the 1 ACE category accounted for only 1.7% of ACE-attributable financial costs while the ≥4 ACEs category accounted for 84.2%. For other outcomes, the proportion of costs accounted for by the 1 ACE category ranged from 9.9% (violence) to 28.1% (high BMI), while the proportion accounted for by ≥4 ACEs ranged from 28.9% (high BMI) to 58.6% (drug use).

Discussion

In this study of 15,285 adults in England and Wales, we found a dose-response relationship between ACEs and all outcomes measured. Violence, mental illness and drug use had the highest PAFs due to ACEs, while mental illness, cancer and smoking carried the highest ACE-attributable costs. Across all outcomes studied, the total estimated annual ACE-attributable costs across England and Wales were £42.8 billion, equivalent to 2.6% of total GVA in England and Wales and representing approximately £1,800 per household per annum.[32] The majority of these costs related to multiple ACE categories.

Comparison with other studies

There are no previous studies estimating the costs of ACEs in England and Wales. However, a study that generated PAFs for ACEs through meta-analyses of risk estimates in published literature estimated the annual costs of ACEs to be equivalent to 2.7% of GDP in Europe and 3.6% of GDP in North America.[12] Other studies have measured the costs of specific ACEs, particularly violence against children using similar human capital approaches. Such costs have been estimated to be equivalent to between 1.2% and 3.5% of sub-regional GDP in East Asia and the Pacific;[11] to 4.3% of GDP in South Africa;[33] and to 0.8% of GDP for physical abuse, 0.5% for emotional abuse and 0.4% for sexual abuse in China.[34] In the UK, the lifetime cost per victim of non-fatal child maltreatment by a primary caregiver has conservatively been estimated at £90,000.[35] However, this estimate excluded costs for several outcomes considered in our study, including those for cancer, type 2 diabetes and heart disease, due to no association being found between these conditions and the study's single measure of child maltreatment. We found no associations between such conditions and the single ACE category, yet strong associations with multiple ACEs. Thus 98.3% of the ACE-

attributable costs of cancer, 87.6% of those for heart disease and 76.3% of those for type 2 diabetes were accounted for by suffering more than one type of ACE.

Strengths and weaknesses of the study

We used an established methodology[11,12,28] and based our approach on that used to estimate the financial burden of ACEs across Europe and North America.[12] An acknowledged limitation of this previous study was the lack of consistency in study methodologies. Key strengths of the current study are the use of primary data and consistency in study methodologies, with all studies using representative household samples and the same set of questions to measure ACEs. However not all outcomes were measured in all studies, and mental illness was only measured in Wales,[23] while some outcome measures could not be matched directly to GBD categories (see online supplementary table S4). Like previous ACE studies, the retrospective, self-reported nature of questions makes findings subject to recall issues and any reluctance to report historical experiences. Further, some population groups who may be at increased exposure to ACEs (e.g. those incarcerated[36] or homeless[37]) will have been underrepresented and we could not account for individuals that had died prematurely through conditions related to ACEs. These biases may have led to reduced relative risks. Conversely, while ACEs made an overall significant contribution to GLMs for all outcomes, for some, RRs were not significant at all ACE levels. Further, our samples were restricted to adults aged 18-69 years, yet some conditions such as stroke occur predominantly in older age groups. Consequently sensitivity analyses were undertaken limiting DALYs to the 15-69 year age group and using lower and upper CIs for RRs. While we excluded DALYs for risk factors linked to included causes of ill-health in calculating our overall cost estimates, it is beyond the ability of this study to calculate the actual burden of ACEs due to multiplicative relationships. However, our estimates of the costs of ACEs are likely to be conservative. Whilst we included many key risks for, and causes of, ill-health associated with ACEs we did not account for other associated outcomes (e.g. risky sexual behaviour, suicide, crime), nor for the burden of child deaths related to ACEs. A study of child death reviews in an English locality found evidence of at least one ACE in the records of 63% of children that died over a four-year period, and of at least four ACEs in 20% of cases.[38] The lifetime cost of a child maltreatment death in the UK has been estimated at almost £1 million.[35]

Meaning of the study

Nearly half of all adults in England and Wales experienced some form of ACE as a child and around one in 10 experienced ≥4 ACEs (see online supplementary table S5). This equates to approximately 20 million adults with any ACE and four million with ≥4 ACEs. Our results quantify the substantive proportion of common health-harming behaviours and long-term health conditions that are associated with ACEs, and consequently that could be avoided in future generations through offering better quality childhoods. Currently however, an estimated 2.3 million children in England live in families with substantial complex needs and only a third of these children are receiving established support from statutory services.[39] An imperative to increase expenditure on safe and nurturing childhoods is emphasised by findings that around a third of mental illness could be avoided if ACEs were either prevented or their impacts moderated through early intervention. Mental illness carries one of the highest costs to health systems in England and Wales[40] and also creates substantial pressure on educational, social and criminal justice systems. For the latter in particular, strong relationships found here between ACEs and violence are an additional concern with many types of police recorded violence increasing in England and Wales.[41] Across all measured outcomes, we identify potentially avoidable costs from ACEs equivalent to more than a quarter of the UK's annual government healthcare expenditure.[42] The potential to avoid such costs is unrealised whilst the majority of health expenditure focuses on adults who have already developed pathologies. Evidence-based mechanisms to prevent ACEs and build resilience to their long-term harms are available, offering return on investments in years rather than decades through benefits on child development, health and education.[43-46] The benefits of such interventions reach across sectors, and a whole of government approach could more immediately resource interventions capable of diminishing a current annual ACE burden of almost £43 billion.

Unanswered questions and future research

As with most ACE studies our data were collected retrospectively and consequently provide no information on the current levels of ACEs experienced by children in England and Wales. Options to measure ACE prevalence now form part of the international Health Behaviour in School-aged children survey (HSBC)[47] but have not yet been used in the English or Welsh survey iterations. Nor are such data routinely being collected through other major school-based surveys in the UK. While estimates of current exposure to some ACEs are available,[39] routine measurement of ACEs in children is required to better understand their extent and socio-demographic and geographic distribution, as well as the impact of interventions to

address them. Further, our findings identified that, despite having the lowest prevalence, the majority of costs generated by ACEs fall on those experiencing ≥4 ACEs (table 2). There is an urgent need to better understand the cumulative impact of ACEs on health outcomes across the life course, integrating epidemiology with fields including epigenetics, immunology and neurology. Equally, there is a critical need for knowledge on how services can become more trauma-informed, what impact trauma-informed service delivery can have, and how services for children and families affected by child maltreatment, substance abuse, domestic violence or incarceration, for instance, can be better integrated to provide a cohesive offer. Finally, as well as the core ACE categories included here, measurements of other childhood adversities such as neglect, parental bereavement, bullying and exposure to community level violence are increasingly being incorporated into the list of potential ACEs. Public services that recognise the impacts of childhood adversity on lifelong health but neglect to implement preventative measures may yet feature in future lists.

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Author Contributions

MAB and KH designed the study. MAB developed the statistical modelling and KH, KF and CS conducted data analyses. KH wrote the manuscript with contributions from MAB, KF and RK. All authors reviewed the study findings and read and approved the final version before submission. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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Competing interests

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest

in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Ethics approval

Ethical approval for the 2017 Welsh national sample was obtained from Bangor University's Healthcare and Medical Sciences Ethics Committee (BU230317) with ethical approval for all other studies obtained through Liverpool John Moores University Research Ethics Panel (12/HEA/016; 13/HEA/052; 14/EHC/008; 14/EHC/0087). Additional approval for both Welsh surveys was provided by Public Health Wales Research and Development Office.

Data sharing

The datasets analysed in the current study are available from the corresponding author on reasonable request.

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Figure 1: Proportion of ACE-attributable costs for each risk factor and cause of ill-health attributed to 1, 2-3 and ≥4 ACE categories

ACE, adverse childhood experience' BMI, body mass index.

Table 1: Risk ratios for risk factors and causes of ill-health at each ACE count level

	1 ACE			2-3 ACEs			≥4 ACEs		
	RR	95%CIs	P	RR	95%CIs	P	RR	95%CIs	P
Risk factors									
Alcohol use	1.164	1.041-1.301	0.008	1.311	1.165-1.475	<0.001	1.837	1.631-2.069	<0.001
Smoking	1.188	1.091-1.293	<0.001	1.448	1.329-1.578	<0.001	2.079	1.904-2.270	<0.001
Drug use	1.648	1.168-2.327	0.005	3.184	2.342-4.330	<0.001	8.685	6.658-11.328	<0.001
High BMI	1.031	0.986-1.078	0.177	1.062	1.012-1.115	0.015	1.075	1.011-1.142	0.020
Causes of ill-health									
Depression	1.560	1.305-1.865	<0.001	2.137	1.820-2.509	<0.001	2.766	2.374-3.223	<0.001
Anxiety	1.429	1.169-1.747	<0.001	2.151	1.806-2.563	<0.001	2.751	2.316-3.266	<0.001
Other mental illness	1.684	1.008-2.812	0.046	3.216	2.083-4.964	<0.001	5.115	3.356-7.796	<0.001
Violence	1.383	1.107-1.728	0.004	2.955	2.448-3.566	<0.001	5.625	4.745-6.667	<0.001
Cancer	1.009	0.800-1.273	0.937	1.101	0.854-1.419	0.459	2.078	1.588-2.720	<0.001
Type 2 diabetes	1.157	0.958-1.398	0.131	1.223	0.995-1.503	0.056	1.782	1.400-2.268	<0.001
Heart disease	1.102	0.836-1.453	0.492	1.415	1.072-1.868	0.014	1.928	1.366-2.722	<0.001
Stroke	1.238	0.800-1.918	0.338	1.427	0.906-2.250	0.125	2.705	1.660-4.409	<0.001
Respiratory disease	1.224	0.927-1.615	0.155	1.806	1.383-2.358	<0.001	2.612	1.929-3.536	<0.001

Analysis uses generalized linear modelling controlling for study sampling region, deprivation quintile, age, gender and ethnicity.
Reference category = 0 ACEs. ACE, adverse childhood experience; RR, risk ratio; CI, confidence interval.

Table 2: Population attributable fractions and DALYs and costs attributable to ACEs

		Population attributable fraction				Total DALYs (age 15+)	DALYs attributable to ACEs				Total estimated cost (£ million)*	Attributable costs by ACE count (£ million)			
		1 ACE	2-3 ACEs	≥4 ACEs	All ACEs		1 ACE	2-3 ACEs	≥4 ACEs	All ACEs		1 ACE	2-3 ACEs	≥4 ACEs	All ACEs
Alcohol use	Wales	0.026	0.040	0.089	0.156	38114	999	1527	3404	5929	758.4	19.9	30.4	67.7	118.0
	England	0.029	0.042	0.061	0.131	606086	17297	25199	36972	79467	17028.6	486.0	708.0	1038.8	2232.7
Smoking	Wales	0.029	0.055	0.110	0.194	121011	3474	6663	13307	23444	2408.0	69.1	132.6	264.8	466.5
	England	0.031	0.058	0.076	0.165	1590656	50082	91530	120314	261926	44691.1	1407.1	2571.6	3380.3	7359.1
Drug use	Wales	0.051	0.137	0.400	0.588	22518	1140	3090	9011	13241	448.1	22.7	61.5	179.3	263.5
	England	0.062	0.159	0.306	0.526	331956	20459	52832	101413	174704	9326.6	574.8	1484.4	2849.3	4908.5
High BMI	Wales	0.006	0.009	0.009	0.024	73423	422	677	677	1775	1461.0	8.4	13.5	13.5	35.3
	England	0.006	0.009	0.006	0.022	1203925	7346	11219	7388	25954	33825.5	206.4	315.2	207.6	729.2
Depression	Wales	0.071	0.115	0.149	0.335	16161	1142	1865	2401	5407	321.6	22.7	37.1	47.8	107.6
	England	0.078	0.122	0.103	0.303	294592	23073	35890	30416	89379	8276.9	648.3	1008.4	854.6	2511.2
Anxiety	Wales	0.055	0.119	0.150	0.324	12434	684	1477	1861	4023	247.4	13.6	29.4	37.0	80.0
	England	0.061	0.126	0.104	0.291	203872	12452	25606	21239	59297	5728.0	349.9	719.4	596.7	1666.0
Other mental illness	Wales	0.065	0.170	0.262	0.497	28076	1832	4772	7347	13951	558.7	36.5	95.0	146.2	277.6
	England	0.075	0.187	0.189	0.452	517544	38976	96724	98011	233711	14540.9	1095.1	2717.6	2753.7	6566.3
Violence	Wales	0.037	0.152	0.299	0.489	1703	63	260	509	832	33.9	1.3	5.2	10.1	16.6
	England	0.044	0.170	0.220	0.434	29134	1270	4961	6404	12635	818.6	35.7	139.4	179.9	355.0
Cancer	Wales	0.002	0.013	0.118	0.133	179919	279	2397	21263	23939	3580.2	5.6	47.7	423.1	476.4
	England	0.002	0.014	0.082	0.097	2725146	4666	38124	222605	265395	76565.7	131.1	1071.1	6254.3	7456.5
Type 2 diabetes	Wales	0.026	0.029	0.085	0.140	23306	597	681	1982	3260	463.8	11.9	13.5	39.4	64.9
	England	0.028	0.030	0.058	0.116	356871	9939	10802	20707	41448	10026.6	279.2	303.5	581.8	1164.5
Heart disease	Wales	0.016	0.053	0.098	0.167	77275	1243	4077	7556	12877	1537.7	24.7	81.1	150.4	256.2
	England	0.018	0.055	0.067	0.140	1049623	18461	57674	70352	146487	29490.2	518.7	1620.4	1976.6	4115.7
Stroke	Wales	0.034	0.049	0.163	0.246	39189	1336	1926	6372	9634	779.8	26.6	38.3	126.8	191.7
	England	0.038	0.052	0.114	0.204	546308	20801	28579	62218	111597	15349.1	584.4	802.9	1748.1	3135.4
Respiratory disease	Wales	0.031	0.090	0.149	0.270	50697	1570	4550	7545	13664	1008.8	31.2	90.5	150.1	271.9
	England	0.034	0.095	0.104	0.233	784621	27000	74559	81386	182945	22044.7	758.6	2094.8	2286.6	5140.0

ACE, Adverse childhood experience; DALY, Disability adjusted life year. *Calculated as 1 DALY = GVA per capita (£19,899 Wales, £28,096 England; Balanced, current basic prices, 2017).

Table 3: Total ACE-attributable DALYs and costs and sensitivity analyses

	ACE-attributable DALYs (thousands)			ACE-attributable costs (£ billion)			Equivalent % of GVA		
	England	Wales	England & Wales	England	Wales	England & Wales	England	Wales	England & Wales
Best estimate	1444.9	110.0	1554.9	40.6	2.2	42.8	2.6%	3.5%	2.6%
Limited to DALYs for 15-69 year olds	956.4	69.5	1025.8	26.9	1.4	28.3	1.7%	2.2%	1.7%
PAFs generated using lower CIs for RRs	546.7	47.7	594.4	15.4	0.9	16.3	1.0%	1.5%	1.0%
PAFs generated using upper CIs for RRs	2314.3	169.0	2483.2	65.0	3.4	68.4	4.2%	5.4%	4.2%
Lower bound (uncertainty interval) for DALYs	1273.7	96.0	1369.8	35.8	1.9	37.7	2.3%	3.1%	2.3%
Upper bound (uncertainty interval) for DALYs	1638.6	126.0	1764.7	46.0	2.5	48.5	2.9%	4.0%	3.0%

ACE, Adverse childhood experience; DALY, Disability adjusted life year; GVA, gross value added; PAF, population attributable fraction; CI, confidence interval; RR, risk ratio.

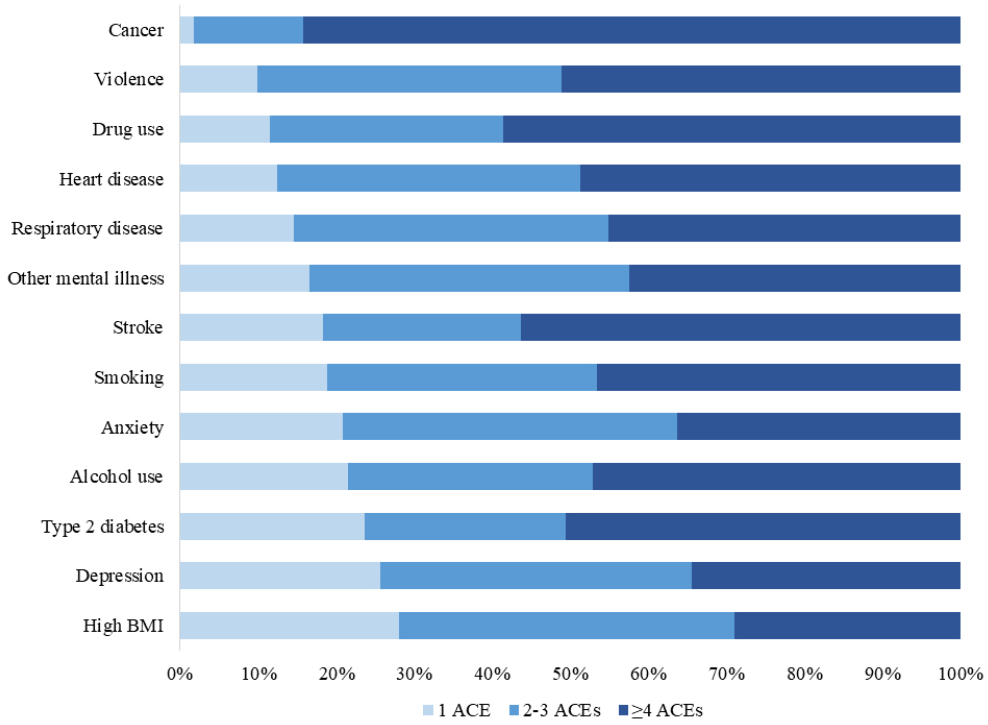

Figure 1: Proportion of ACE-attributable costs for each risk factor and cause of ill-health attributed to 1, 2-3 and ≥4 ACE categories

ACE, adverse childhood experience' BMI, body mass index.

Supplementary table 1 Study information

Country	Study location	Stratification for sampling[a]	Recruitment	Dates	Age range (years)	Total sample[e] (n)	Compliance	Deprivation measure	Reference
England	Blackburn with Darwen (North West England)	Blackburn with Darwen Local Authority[b]	Study information letter sent to randomly selected households; households not opting out upon receipt of letter visited by researchers	2012 (Aug-Sep)	18-70[d]	1500	70.4%	IMD 2010	1
England	National sample	English Administrative Regions (n=10)[c]		2013 (Apr-Jul)	18-69	4010	53.5%	IMD 2010	2
England	Luton, Hertfordshire Northamptonshire (South East England)	Luton, Hertfordshire Northamptonshire (n=3)		2015 (Jun-Sep)	18-69	5623	55.8%	IMD 2011	3
Wales	National sample	Welsh Health Regions (n=7)		2017 (Mar-Jun)	18-69	2497	58.5%	WIMD 2014	4
Wales	National sample	Welsh Health Regions (n=7)	Households in sampled areas randomly selected by researchers	2015 (Feb-May)	18-69	2028	49.1%	WIMD 2014	5

[a]Lower Super Output Area level stratification by deprivation quintile. [b]No sub-regional stratification was undertaken in Blackburn with Darwen due to the relatively small size of the sample area. [c]London was split into Inner and Outer London for regional sampling. [d]Individuals aged 70 years were excluded from the sample for consistency. [e]Individuals not completing all questions on variables of interest were excluded. IMD, Index of Multiple Deprivation; WIMD, Welsh Index of Multiple Deprivation.

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Supplementary Table 2 ACE and health outcome questions used

ACE questions. All ACE questions were preceded by the statement "While you were growing up, before the age of 18..."		
ACE	**Question**	**Qualifying responses**
Physical abuse	How often did a parent or adult in your home ever hit, beat, kick, or physically hurt you in any way? This does not include gentle smacking for punishment?	Once; more than once
Verbal abuse	How often did a parent or adult in your home ever swear at you, insult you, or put you down?	More than once
Sexual abuse	How often did anyone at least 5 years older than you (including adults) ever…. …touch you sexually? …try to make you touch them sexually? …force you to have any type of sexual intercourse (oral, anal, or vaginal)?	Once or more than once to any of the questions
Parental separation	Were your parents ever separated or divorced?	Yes
Domestic violence	How often did your parents or adults in your home ever slap, hit, kick, punch, or beat each other up?	Once; more than once
Mental illness	Did you live with anyone who was depressed, mentally ill, or suicidal?	Yes
Alcohol abuse	Did you live with anyone who was a problem drinker or alcoholic?	Yes
Drug abuse	Did you live with anyone who used illegal street drugs or who abused prescription medications?	Yes
Incarceration	Did you live with anyone who served time or was sentenced to serve time in a prison or young offenders' institution?	Yes
Health outcome	**Question**	**Qualifying responses**
Alcohol use	How often do you have a drink containing alcohol? How many standard drinks containing alcohol do you have on a typical day when you drink? - responses used to estimate daily consumption	Consumption of 12g or more alcohol per day
Smoking	In terms of smoking tobacco, which of the following best describes you?	I smoke daily; I smoke occasionally but not daily
Drug use	How often, if ever, have you used heroin or crack cocaine?	Used but not in the last 12 months; Used in the past 12 months
High BMI	What is your height? (in feet/inches or metres/centimetres) What is your weight? (in stone/pound, kilograms or pounds) - Responses used to calculate BMI	BMI 25.0 or higher
Depression	Are you currently or have you ever been treated for… depression?	Yes, currently; Yes, in the past
Anxiety	Are you currently or have you ever been treated for… anxiety?	Yes, currently; Yes, in the past
Other mental illness	Are you currently or have you ever been treated for… another mental illness?	No, never; Yes, currently; Yes, in the past
Victim of violence	How many times have you been physically hit in the past 12 months? Or (in Wales, 2017): In the past 12 months, have you been physically hit by someone else?	Once; 2 or 3 times; More than 3 times Yes
Cancer	Has a doctor or nurse ever told you that you have… Cancer?	Yes
Type 2 diabetes	Has a doctor or nurse ever told you that you have… Type 2 diabetes?	Yes
Heart disease	Has a doctor or nurse ever told you that you have… Coronary heart disease or heart attack?	Yes
Stroke	Has a doctor or nurse ever told you that you have… Stroke?	Yes
Respiratory disease	Has a doctor or nurse ever told you that you have… Respiratory disease such as Chronic bronchitis/ Emphysema/ Chronic Obstructive Pulmonary Disease?	Yes

ACE, adverse childhood experience; BMI, body mass index.

Supplementary Table 3 Outcomes measured across studies

	All	England (national)	England (South East)	England (North West)	Wales 2015 (national)	Wales 2017 (national)
Total sample (n)	15285	3885	5454	1421	2028	2497
Alcohol use	n=12736					
Missing (n)	52	18	7	23	4	-
Yes (%)	13.6	16.3	10.0	15.3	17.1	-
Smoking	n=15281					
Missing (n)	4	0	0	4	0	0
Yes (%)	26.3	26.9	23.1	37.1	27.9	25.3
Drug use	n=15246					
Missing (n)	39	3	19	14	2	1
Yes (%)	2.4	2.2	2.0	3.1	4.4	1.6
High BMI	n=11527					
Missing (n)	1261	424	481	16	340	-
Yes (%)	49.8	50.9	49.0	45.7	53.2	-
Depression	n=2496					
Missing (n)	1	-	-	-	-	1
Yes (%)	29.2	-	-	-	-	29.2
Anxiety	n=2493					
Missing (n)	4	-	-	-	-	4
Yes (%)	25.0	-	-	-	-	25.0
Other mental illness	n=2491					
Missing (n)	6	-	-	-	-	6
Yes (%)	6.0	-	-	-	-	6.0
Victim of violence	n=15267					
Missing (n)	18	2	10	2	4	0
Yes (%)	5.1	5.3	3.7	6.3	9.1	4.1
Cancer	n=12765					
Missing (n)	23	4	12	7	0	-
Yes (%)	3.7	4.4	2.9	3.2	4.8	-
Type 2 Diabetes	n=12769					
Missing (n)	19	3	12	4	0	-
Yes (%)	5.1	4.8	4.7	7.3	5.3	-
Heart disease	n=12773					
Missing (n)	15	1	12	2	0	-
Yes (%)	2.7	3.2	2.3	4.2	1.5	-
Stroke	n=12773					
Missing (n)	19	1	13	5	0	-
Yes (%)	1.1	1.1	1.0	1.8	0.8	-
Respiratory disease	n=12766					
Missing (n)	22	0	15	7	0	-
Yes (%)	2.8	3.5	1.9	5.2	2.1	-

- outcome not measured in survey. BMI, body mass index

Supplementary Table 4: Study outcome and matched Global Burden of Disease (GBD) category

Outcome	GBD category matched (ID)
Risk factors	
Alcohol use	Alcohol use (102)
Smoking	Smoking (99)
Drug use	Drug use (103)
High BMI	High body-mass index (108)
Causes of ill health	
Depression	Major depressive disorder (586)
Anxiety	Anxiety disorders (571)
Other mental illness	Mental disorders (558), excluding major depressive disorder (586) and anxiety disorders (571)
Violence	Interpersonal violence (724)
Cancer	Neoplasms (410)
Type 2 diabetes	Diabetes mellitus type 2 (976)
Heart disease	Ischaemic heart disease (493), hypertensive heart disease (498)
Stroke	Stroke (494)
Respiratory disease	Chronic respiratory diseases (508), excluding asthma (515)

ID, identification; BMI, body mass index

Supplementary Table 5 Sample demographics and ACE count prevalence

	All	England (national)	England (South East)	England (North West)	Wales 2015 (national)	Wales 2017 (national)
Total sample (n)	15285	3885	5454	1421	2028	2497
Gender (%)						
Male	45.1	45.0	44.7	39.9	49.8	45.3
Female	54.9	55.0	55.3	60.1	50.2	54.7
Age group (%)						
18-29	21.9	21.0	20.6	24.6	30.4	17.9
30-39	19.9	19.9	22.5	21.5	14.2	18.4
40-49	20.3	20.5	20.6	22.2	17.8	20.1
50-59	17.7	18.0	17.0	14.6	17.5	20.6
60-69	20.2	20.7	19.3	17.0	20.2	23.1
Ethnicity (%)						
White	85.7	86.3	80.6	71.3	95.4	96.4
Other	14.3	13.7	19.4	28.7	4.6	3.6
Deprivation quintile (%)						
(least deprived) 1	21.7	20.1	28.5	5.5	21.7	18.7
2	19.1	19.5	20.2	10.2	19.4	20.9
3	19.9	19.7	20.8	8.1	19.4	25.1
4	19.2	19.9	20.0	14.5	18.7	19.3
(most deprived) 5	20.1	20.7	10.5	61.7	20.7	15.9
ACE count (%)						
0	55.3	53.6	58.4	54.4	54.4	52.1
1	19.7	22.7	18.2	20.0	19.0	18.9
2-3	15.3	15.4	15.3	15.8	13.0	17.1
≥4	9.6	8.3	8.1	9.8	13.6	11.9

ACE, Adverse childhood experience.

Supplementary Table 6 Unadjusted proportion reporting each outcome by ACE count category

		ACE count			
	n	0 ACEs	1 ACE	2-3 ACEs	≥4 ACEs
Alcohol use	12736	11.3	14.6	15.9	22.0
Smoking	15281	20.3	26.3	32.9	50.6
Drug use	15246	0.9	1.8	3.4	10.5
High BMI	11527	49.3	49.8	51.1	50.6
Depression	2496	18.4	29.4	41.3	59.1
Anxiety	2493	16.0	24.2	36.5	49.8
Other mental illness	2491	2.8	4.9	9.9	16.4
Violence	15267	2.5	3.8	8.3	18.2
Cancer	12765	3.5	3.5	3.7	5.1
Type 2 diabetes	12769	5.0	5.0	5.3	5.6
Heart disease	12773	2.5	2.5	3.2	3.1
Stroke	12769	0.9	1.1	1.3	1.8
Respiratory disease	12766	2.2	2.7	4.0	4.7

ACE, adverse childhood experience; BMI, body mass index

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4-6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4, Table S1
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5, Table S2
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5, Tables S2 & S3
Bias	9	Describe any efforts to address potential sources of bias	6
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5, 6, Table S2
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5,6
		(*b*) Describe any methods used to examine subgroups and interactions	5,6
		(*c*) Explain how missing data were addressed	Table S3
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	5
		(*e*) Describe any sensitivity analyses	6
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	4, Table S1
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table S5
		(b) Indicate number of participants with missing data for each variable of interest	Table S3
Outcome data	15*	Report numbers of outcome events or summary measures	Table S3

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	5, Table S6, Table 1
		(*b*) Report category boundaries when continuous variables were categorized	NA
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	7, Table 2
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	8, Table 3
Discussion			
Key results	18	Summarise key results with reference to study objectives	8
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	9
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	8-10
Generalisability	21	Discuss the generalisability (external validity) of the study results	9
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	12

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.