

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (<u>http://bmjopen.bmj.com</u>).

If you have any questions on BMJ Open's open peer review process please email <u>info.bmjopen@bmj.com</u>

BMJ Open

CHILDHOOD DEATHS, DEPRIVATION, AND MODIFIABLE FACTORS: FINDINGS FROM THE NATIONAL CHILD MORTALITY DATABASE

Journal:	BMJ Open
Manuscript ID	bmjopen-2022-066214
Article Type:	Original research
Date Submitted by the Author:	01-Jul-2022
Complete List of Authors:	Odd, David; Cardiff University, Division of Population Medicine; University of Bristol, National Child Mortality Database Stoianova, Sylvia; University of Bristol, National Child Mortality Database Williams, Tom; University of Bristol, National Child Mortality Database Odd, Dawn; University of the West of England, School of Health and Social Wellbeing Kurinczuk, Jennifer; University of Oxford, National Perinatal Epidemiology Unit Wolfe, Ingrid; King's College London, Department of Women's and Children's Health Luyt, Karen; University of Bristol, National Child Mortality Database
Keywords:	EPIDEMIOLOGY, PAEDIATRICS, PUBLIC HEALTH





I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our <u>licence</u>.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which <u>Creative Commons</u> licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

review only

CHILDHOOD DEATHS, DEPRIVATION, AND MODIFIABLE FACTORS: FINDINGS FROM THE NATIONAL CHILD MORTALITY DATABASE

David Odd MD^{1,2}, Sylvia Stoianova MSc², Tom Williams BSc², Dawn Odd³, Jennifer J Kurinczuk⁴, Ingrid Wolfe PhD⁵, Karen Luyt PhD^{2*}

- 1. School of Medicine, Division of Population Medicine, Cardiff University, UK
- 2. National Child Mortality Database, Bristol Medical School, University of Bristol, St Michael's Hospital, Southwell Street, Bristol, UK
- 3. School of Health and Social Wellbeing, University of the West of England, Blackberry Hill, Bristol, UK
- 4. National Perinatal Epidemiology Unit, Nuffield Department of Population Health, University of Oxford, UK

5. School of Life Course Sciences, Department of Women and Children's Health, King's College London, London, UK

Reziewony

- * Corresponding author
- Dr Karen Luyt
- Email: Karen.Luyt@bristol.ac.uk
- Telephone: +441173425439

Key Words:

deprivation, inequalities, pandemic, mortality, death, child, infant

Word Count: 3478

ABSTRACT

Objectives: The aim of this analysis is to identify and report the patterns of social deprivation in relation to childhood mortality; and identify potential points where public health, social and education interventions or health policy may be best targeted.

Design: Decile of deprivation and underlying population distribution was derived using Office for National Statistics (ONS) data. The risk of death was then derived using a Poisson regression model, calculating the increasing risk of death for each increasing deprivation decile.

Setting: England

Participants: 2688 childhood deaths in England reviewed between the April 2019 and March 2020.

Main Outcome Measures: The relationship between deprivation and risk of death; for deaths with, and without modifiable factors.

Results: There was evidence of increasing mortality risk with increase in deprivation decile (RR 1.08 (1.07 to 1.10)), with the gradient of risk stronger in children who died with modifiable factors than those without (RR 1.12 (1.09 to 1.15)) vs (RR 1.07 (1.05 to 1.08)). Deprivation sub-domains of Employment, Adult Education, Barriers to Housing and Services, and Indoor Living Environments appeared to be the most important predictors of child mortality

Conclusions: There is a clear gradient of increasing child mortality across England as measures of deprivation increase; with a striking finding that this varied little by area, age or other demographic factor. Over a fifth of all child deaths may be avoided if the most deprived half of the population had the same mortality as the least deprived. Children dying in more deprived areas may have a greater proportion of avoidable deaths. Adult employment and education, and improvements to housing, may be the most efficient place to target resources to reduce these inequalities.

BACKGROUND

The death of every child is a devastating loss that profoundly affects bereaved parents as well as siblings, grandparents, extended family members, friends and professionals. The evidence relating to social deprivation and death is strongest for infant mortality however the effects appear measurable across the life course.[1] A systematic review examining the relationship between social factors and early childhood health and developmental outcomes provides strong evidence that factors such as neighbourhood deprivation, lower parental income, unemployment and educational attainment, lower occupational social class, heavy physical occupational demands, lack of housing tenure, and material deprivation in the household are all independently associated with a wide range of adverse health outcomes.[2]

We know that early child development plays a major role in affecting future life chances and health throughout the life course[3] with adverse exposures having greater impacts on younger children[4]. While initiatives have been proposed to reduce the impact of deprivation on health[5]; babies, children, and young people remain the most vulnerable in society. Currently England has one of the highest infant mortality rates in Europe[6,7] and while much of the variation may be due to socioeconomic factors[8], it is clear that since infant mortality among the most deprived groups continues to rise[9], effective policies and other interventions are either lacking or have not been successfully implemented. While the COVID pandemic continues to impact delivery of social and healthcare programs across the world, the longer term impact on economies and social and healthcare budgets is likely to be substantial, and social inequalities even in developed nations, may worsen.

The National Child Mortality Database (NCMD) Programme was established in 2018 to collate and analyse data about all children in England who die before their 18th birthday, with statutory death notifications required within 48 hours[10]. The data are collated from the 58 Child Death Overview Panels (CDOPs) in England who carry out detailed analysis of the circumstances of death and identify the modifiable contributory factors relevant to the death as part of the child death review (CDR) process with the aim of identifying common themes to guide learning and inform actions to reduce future child deaths.[11] The CDR process is statutory, with the Children Act 2004 mandating the review and analysis of all child deaths so the circumstances of death that relate to the welfare of children locally and nationally, or to public health and safety, are identified and understood, and preventive actions established. This work is based on the NCMD Programme's first thematic report[12].

Aims

The aim of this analysis is to identify and report the patterns of social deprivation, and modifiable factors in relation to childhood mortality, and identify potential intervention points and high risk groups where public health, social and education, or health policy may be best targeted.

METHODS

Three external sources of data were linked to the child death review data using the smallest geographical level of the deprivation index (the Lower Super Output Area (LSOA)). This allowed further estimation of the population estimates of age and sex[13], its rural (Rural town and fringe, Rural village) or urban (Urban city and town, Urban major conurbation) status[14] and its location in England (East Midlands, East of England, London, North East, North West, South East, South West, West Midlands, Yorkshire and the Humber)[15]

Exploratory Variables

For the primary exploratory analysis variables of interest were:

2 3

4

5 6

7

8 9 10

11 12

13

14

15 16

17

18 19

20

21 22

23

24 25

26

27 28

29

30

31 32 33

34 35

36

37 38

39

40 41

45

47

49

51

53

55 56

57 58

59

60

BMJ Open

- Age of death (age as a continuous measure) then coded for analysis and presentation as <1 year, 1-4 years, 5-9 years, 10-14 years and 15-17 years).
- Sex (male, female, or missing (including "indeterminate", "not known", "N/A", "NULL" etc)).
- Area of residence: Urban vs Rural[15] •
- Region of England. •
- Ethnicity was coded as White, Asian or British Asian, Black or British Black, Mixed or Other. •

Specific Detailed Data from Child Death Review Process

The CDOP is responsible for identifying any modifiable factors in relation to the child's death. Modifiable factors are those which may have contributed to the death of the child and which might, by means of a locally or nationally achievable intervention, be modified to reduce the risk of future deaths. Factors identified by the CDOP were further classified as:

- Characteristics of the child (e.g. loss of key relationships, risk taking behaviour, comorbidity, prematurity, congenital anomaly, learning disability, eating disorder, suicidal ideation or previous suicide attempt)
- Social Environment (e.g. abuse, parenting, consanguinity, financial pressures/hardship) •
- Physical Environment (e.g. animal attack, homicide, vehicle related deaths, safety within the home, unsafe • infant sleeping practices, and public equipment)
- Service Provision (e.g. gaps in service provision, failure to follow guidelines, poor communication, staffing issues and bed occupancy)

Category of death was allocated by the CDOP while reviewing the case and was categorised as; Acute Medical and Surgical, Congenital Anomalies, Chronic Medical, Deliberately inflicted injury, Infection, Malignancy, Perinatal, Sudden Unexplained Death in Childhood (SUDIC), Suicide or deliberate self-inflicted harm or Trauma.

Analysis

Initially the characteristics of all child deaths reviewed between April 2019 and March 2020 were derived, stratified by the available covariates (listed above). Next we derived the proportion of deaths in each deprivation decile. Evidence of any trend in proportions by increasing deprivation decile were tested using a nonparametric test for trend across ordered groups[16]. This was then repeated for each category of death.

Second, to assess any association between deprivation and the risk of death, the population distribution was derived 42 using ONS data for each LSOA producing a dataset with the predicted numbers of children of each age, sex, 43 rural/urban status and region. The risk of death was then derived using a Poisson regression model, calculating the 44 increasing risk of death for each increasing deprivation decile, with the model then adjusted for the other known 46 underlying population characteristics or possible confounders (sex, age, rural/urban area and region). Lastly both the 48 unadjusted and adjusted model were repeated for each reported category of death and tested (using the likelihood ratio test) to assess if the association between deprivation measures and overall mortality was modified by sex, age 50 category, region or rural/urban status. Finally for overall mortality a separate model was derived for those children in 52 the lowest five vs the highest five deciles of deprivation, and used to estimate the population attributable risk fraction for those children living the in the most deprived five deciles. 54

Next, to interrogate the possible causes we initially derived the number, proportion and evidence of trend[16] of modifiable factors identified at the CDOP review across each deprivation decile. We then calculated the increasing risk of death for each increasing deprivation decile separately for those deaths with, or without, modifiable factors identified. The analyses were repeated, stratified by the sub-categories of modifiable factors, and by the category of death.

Role of Funding Source

NHS England provided additional funding to the NCMD to enable rapid set up of the real-time surveillance system and staff time to support its function.

Patient and public involvement

Parent and public involvement is at the heart of the NCMD programme. We are indebted to Charlotte Bevan (Sands -Stillbirth and Neonatal Death Charity), Therese McAlorum (Child Bereavement UK) and Jenny Ward (Lullaby Trust), who represent bereaved families on the NCMD programme steering group.

RESULTS

A total of 2688 childhood deaths were reviewed by CDOPs between April 2019 and March 2020 and linked to deprivation measures (Table 1).

Table 1. Characteristics of the populations of child deaths reviewed by CDOPs in England during 2019/2020

Table 1. Characteristics of the po		
Measure	N	Child deaths reviewed 2019/20
All Deaths	2688	-
Age of Death	2688	
<1 year		1675 (62.3%)
1-4 Years		322 (12.0%)
5-9 Years		211 (7.9%)
10-14 Years		227 (8.4%)
15-17 Years		253 (9.4%)
Sex	2670	
Male		1505 (56.4%)
Female		1165 (43.6%)
Area of residence	2688	
Rural		328 (12.2%)
Urban		2360 (87.8%)
Ethnicity	2390	6
White		1554 (65.0%)
Asian or British Asian		427 (17.9%)
Black or British Black		188 (7.9%)
Mixed		136 (5.7%)
Other		85 (3.6%)
Region of residence	2688	
East Midlands		214 (8.0%)
East of England		211 (8.2%)
London		473 (17.6%)
North East		109 (4.1%)
North West		362 (13.5%)
South East		336 (12.5%)
South West		232 (8.6%)
West Midlands		400 (12.9%)
Yorkshire and the Humber		341 (12.7%)

BMJ Open

The most common age at death was less than 1 year (62.3%) and more boys than girls died (56.5 vs 43.6%

respectively). The majority lived in areas defined as urban (87.8%) and most were of a white ethnic background

(65.0%). Deaths were more common in children in the most deprived deciles (Table 2) (p=0.003).

Measure		D	eprivation Deci	le		Median (IQR)	P _{trend}
	1/2 N (%) (Least Deprived)	3/4 N (%)	5/6 N (%)	7/8 N (%)	9/10 N (%) (Most Deprived)		
All Deaths	293 (10.9%)	383 (14.2%)	476 (17.7%)	644 (24.0%)	892 (33.2%)	7 (4-9)	0.00
Category of Death							
Acute Medical and Surgical	22 (12.9%)	30 (17.5%)	28 (16.4%)	46 (27.0%)	45 (26.3%)	7 (4-9)	0.01
Congenital Anomalies	60 (9.0%)	71 (10.7%)	117 (17.6%)	147 (22.1%)	270 (40.6%)	7 (5-9)	0.00
Chronic Medical	15 (11.2%)	16 (11.9%)	30 (22.4%)	31 (23.1%)	42 (31.3%)	7 (5-9)	0.00
Deliberately inflicted injury	8 (13.1%)	8 (13.1%)	8 (13.1%)	16 (26.2%)	21 (34.4%)	8 (4-9)	0.02
Infection	23 (13.4%)	15 (8.7%)	25 (14.5%)	54 (31.4%)	55 (32.0%)	7 (5-9)	0.02
Malignancy	38 (18.1%)	41 (19.5%)	42 (20.0%)	36 (17.1%)	53 (25.2%)	5 (3-8)	0.32
Perinatal	74 (8.8%)	128 (15.1%)	152 (18.0%)	223 (26.4%)	268 (31.7%)	7 (4-9)	0.00
SUDIC	17 (8.0%)	30 (14.2%)	44 (20.8%)	48 (22.6%)	73 (34.4%)	7 (4-9)	0.00
Suicide or deliberate self-inflicted harm	19 (18.6%)	20 (19.6%)	17 (16.7%)	18 (17.7%)	28 (27.5%)	6 (3-9)	0.29
Trauma	17 (14.7%)	24 (20.7%)	13 (11.2%)	25 (21.6%)	37 (31.9%)	7 (3-9)	0.03

Table 2. Deaths by deprivation decile, stratified by the category of death and patient characteristics of child

When looking at the categories of death, deaths due to acute medical or surgical disease (p=0.017), congenital anomalies (p=0.003), chronic medical (p=0.006), deliberate inflicted injury (p=0.025), infection (p=0.021), perinatal (p=0.006), SUDIC (p=0.003) and trauma (p=0.038) appeared to be associated with increasing deprivation. There was little evidence of an association between increasing deprivation and deaths from malignancy (p=0.326) or suicide or deliberate self-inflicted harm (p=0.296).

When estimating the relative risk of death using an unadjusted Poisson model, there was an increasing risk of all cause mortality as measures of deprivation increased (RR 1.11 (95% CI 1.09-1.12), p<0.001); but also for death categorised as acute medical or surgical (p=0.030), congenital anomalies (p<0.001), chronic medical (p=0.004), deliberately inflicted injury (p=0.009), infection (p<0.001), perinatal (p<0.001), and SUDIC (p<0.001) (Table 3). After adjusting for age, sex, region and rural status, the association with all cause mortality (RR 1.08 (95% CI 1.07-1.10), p < 0.001) and for congenital anomalies (p < 0.001), chronic medical (p = 0.007), deliberately inflicted injury (p = 0.040), infection (p<0.001), perinatal (p<0.001), and SUDIC (p<0.001) remained. However, in the adjusted analysis, the association between death in the acute medical or surgical category with increasing measures of deprivation weakened slightly (p=0.052).

There was little evidence to suggest an association with malignancy (p=0.868), suicide or deliberate self-inflicted harm (p=0.831) or trauma (p=0.075) in the unadjusted (p=0.868, p=0.831 and p=0.075 respectively) or in the adjusted analyses (p=0.979, p=0.475 and p=0.174 respectively) (Table 3).

Table 3. Relative risk of death for increasing deprivation stratified by category of death, and testing for interactions by characteristics of the child deaths

Measure		Unadju	sted			Adjust	ed"	
	n	RR 95% CI	р		n	RR 95% CI	р	
All Deaths	2688	1.11 (1.09-1.12)	<0.001		2670	1.08 (1.07-1.10)	<0.001	
Acute Medical and Surgical	171	1.06 (1.01-1.12)	0.030		170	1.06 (1.00-1.12)	0.052	
Congenital Anomalies	665	1.17 (1.14-1.21)	<0.001		658	1.13 (1.10-1.17)	<0.001	
Chronic Medical	134	1.09 (1.03-1.16)	0.004		134	1.09 (1.02-1.17)	0.007	
Deliberately inflicted injury	61	1.13 (1.03-1.24)	0.009		61	1.11 (1.00-1.22)	0.040	
Infection	172	1.13 (1.07-1.19)	<0.001		172	1.11 (1.05-1.18)	<0.001	
Malignancy	210	1.00 (0.95-1.04)	0.868		210	1.00 (0.95-1.05)	0.979	
Perinatal	845	1.11 (1.09-1.14)	<0.001		836	1.07 (1.04-1.10)	<0.001	
SUDIC	212	1.13 (1.08-1.19)	<0.001		211	1.10 (1.05-1.16)	<0.001	
Suicide or deliberate self-inflicted harm	102	1.01 (0.94-1.08)	0.831		102	1.03 (0.96-1.10)	0.475	
Trauma and other external factors	116	1.06 (0.99-1.13)	0.075		116	1.05 (0.98-1.12)	0.174	
Interactions		RR 95% CI	р	Pinteraction		RR 95% CI	р	Pinteractio
Sex				0.227				0.1
Female	1165	1.11 (1.09-1.13)	<0.001		1165	1.07 (1.05-1.09)	<0.001	
Male	1505	1.10 (1.08-1.11)	<0.001		1505	1.09 (1.07-1.11)	<0.001	
Age				0.003				<0.0
<1 year	1675	1.11 (1.09-1.13)	<0.001		1659	1.10 (1.08-1.12)	<0.001	
1-4 Years	322	1.10 (1.06-1.14)	<0.001		321	1.09 (1.05-1.13)	<0.001	
5-9 Years	211	1.00 (0.96-1.05)	0.956		210	0.99 (0.95-1.04)	0.785	
10-14 Years	227	1.07 (1.03-1.12)	0.002		227	1.07 (1.02-1.11)	0.006	
15-17 Years	253	1.06 (1.01-1.10)	0.011		253	1.05 (1.01-1.09)	0.028	
Area				0.616				0.4
Urban	2360	1.10 (1.09-1.12)	<0.001		2342	1.08 (1.06-1.10)	<0.001	
Rural	328	1.12 (1.07-1.17)	<0.001		328	1.10 (1.05-1.16)	<0.001	
Region				0.074				0.1
East Midlands	214	1.07 (1.02-1.12)	0.004		214	1.06 (1.01-1.11)	0.023	
East of England	221	1.07 (1.02-1.13)	0.005		220	1.06 (1.01-1.11)	0.030	
London	473	1.06 (1.02-1.10)	0.003		464	1.06 (1.01-1.10)	0.007	
North East	109	1.06 (0.99-1.13)	0.098		109	1.04 (0.97-1.12)	0.233	
North West	362	1.10 (1.06-1.14)	<0.001		360	1.08 (1.04-1.12)	<0.001	
South East	336	1.11 (1.07-1.15)	<0.001		336	1.09 (1.05-1.14)	<0.001	
South West	232	1.10 (1.05-1.16)	<0.001		232	1.09 (1.03-1.14)	0.001	
West Midlands	400	1.16 (1.11-1.20)	<0.001		395	1.14 (1.09-1.19)	<0.001	
Yorkshire and the Humber	3411	1.10 (1.06-1.14)	<0.001		340	1.09 (1.05-1.13)	<0.001	

* Adjusted for age, sex, region and rural/urban area

There was strong evidence that the association between number of deaths and the deprivation index was modified by age (fully adjusted; p<0.001), but not sex (fully adjusted; p=0.196) or rural/urban status (fully adjusted; p=0.463). In the unadjusted model there was some weak evidence that the relationship may be modified by the region of England (p=0.0743), although this weakened in the adjusted model further (p=0.165).

In the final, adjusted, regression model, estimating the risk of death (adjusted for age, sex and rural/urban area), comparing the risk of death in the most deprived five deciles with the least deprived five deciles, gave compatible

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

results to those from the main analysis (RR 1.47 (1.35-1.60), p<0.001), and a population attributable risk fraction of

21.2% (95% Cl 16.7%-25.4%).

The absolute number of deaths where modifiable factors were identified increased as measures of deprivation

increased (Figure 1), with additional strong evidence that the proportion of deaths with modifiable contributory factors identified at the CDOP review increased with increasing measures of deprivation; with 24.2% of deaths in the least deprived, compared with 35.1% of deaths in the most (p_{trend}<0.001) (Table 4).

Table 4. The number of deaths, in each deprivation decile with identified modifiable factors; and the relative risk of death for each increasing deprivation decile with, or without them; split by category of death.

Category of Death		Percer	ntage of de		Relative risk of death for increasing deprivation decile*				
	All deciles		Split by	Deprivatio	on Decile				
		1/2 N (%) (Least Deprived)	3/4 N (%)	5/6 N (%)	7/8 N (%)	9/10 N (%) (Most Deprived)	P _{trend}	Death without Modifiable Factors	Deaths with Modifiable Factors
All Deaths	842 (31.3%)	71 (24.2%)	114 (29.8%)	125 (26.3%)	219 (34.0%)	313 (35.1%)	<0.001	1.07 (1.05- 1.08)	1.12 (1.09- 1.15)
Split by type of Modifiable Factors									
Characteristics of the child	70 (2.6%)	9 (3.1%)	14 (3.7%)	6 (1.3%)	15 (2.3%)	26 (2.9%)	0.797	1.08 (1.07- 1.10)	1.10 (1.01- 1.21)
Physical Environment	185 (6.9%)	18 (6.1%)	30 (7.8%)	29 (6.1%)	41 (6.4%)	67 (7.5%)	0.764	1.08 (1.07- 1.10)	1.08 (1.02- 1.14)
Service Provision	243 (7.9%)	26 (8.9%)	43 (11.2%)	47 (9.9%)	57 (8.9%)	70 (7.9%)	0.131	1.08 (1.07- 1.10)	1.07 (1.02- 1.12)
Social Environment	416 (15.5%)	29 (9.9%)	46 (12.0%)	51 (10.7%)	106 (16.5%)	184 (20.6%)	<0.001	1.07 (1.05- 1.09)	1.15 (1.11- 1.20)
Split by Category of Death									
Acute Medical and Surgical	42 (24.6%)	5 (22.7%)	8 (26.7%)	7 (25.0%)	9 (20.0%)	13 (29.0%)	0.815	1.05 (0.98- 1.12)	1.10 (0.98- 1.24)
Congenital Anomalies	99 (14.9%)	5 (8.3%)	6 (8.5%)	11 (9.4%)	27 (18.4%)	50 (18.5%)	0.001	1.11 (1.07- 1.15)	1.27 (1.16- 1.40)
Chronic Medical	21 (15.7%)	1 (6.7%)	2 (12.5%)	6 (20.0%)	4 (12.9%)	8 (19.1%)	0.597	1.09 (1.01- 1.17)	1.14 (0.96- 1.35)
Deliberately inflicted injury	43 (70.5%)	4 (50.0%)	7 (87.5%)	6 (75.0%)	12 (75.0%)	14 (66.7%)	0.911	1.08 (0.90- 1.29)	1.12 (0.99- 1.26)
Infection	61 (35.5%)	6 (26.1%)	1 (6.7%)	13 (52.0%)	20 (37.0%)	21 (38.2%)	0.126	1.07 (1.00- 1.15)	1.20 (1.07- 1.33)
Malignancy	11 (5.2%)	0 (0.0%)	1 (2.4%0	5 (11.9%)	2 (5.6%)	3 (5.7%)	0.181	0.99 (0.94- 1.05)	1.15 (0.91- 1.46)
Perinatal	270 (32.0%)	18 (24.3%)	39 (30.5%)	34 (22.4%)	83 (37.2%)	96 (35.8%)	0.015	1.06 (1.03- 1.10)	1.09 (1.04- 1.14)
SUDIC	157 (75.1%)	9 (52.9%)	23 (76.7%)	28 (63.6%)	38 (79.2%)	59 (80.8%)	0.045	1.02 (0.92-	1.14 (1.07- 1.21)
Suicide	59 (57.8%)	12 (63.2%)	9 (45.0%)	8 (47.1%0	9 (50.00%)	21 (75.0%)	0.317	1.01 (0.90- 1.12)	1.04 (0.95- 1.14)
Trauma	79 (68.1%)	11 (64.7%)	18 (75.0%)	7 (53.9%)	15 (60.0%)	28 (75.7%)	0.743	1.00 (0.89-	1.07 (0.99- 1.17)

* Adjusted for age, sex, region and rural/urban area

Children who died with modifiable factors showed a stronger gradient with increasing deprivation (RR 1.12 (1.09-1.15)) compared to those who died without (RR 1.07 (1.05-1.08)). Individually, only those modifiable factors relating to social environment appeared to show this gradient (p<0.001), with less evidence (but small numbers) for those factors around the child, services, or their physical environment. When stratifying by the category of death there was evidence that modifiable factors were more commonly identified in deaths in areas or greater deprivation for congenital anomalies (p=0.001), perinatal (p=0.045) and SUDIC (p=0.045) deaths; with corresponding greater relative risks with deprivation compared to deaths without modifiable factors identified (e.g. Relative risk of death from a congenital abnormality with increasing deprivation was 1.11 (1.07-1.15) for deaths without modifiable factors, and 1.27 (1.16-1.40) for those with).

When analysing the associations between the risk of childhood death and the deprivation sub-domains (Appendix 1), many of the components of the IMD appeared to be closely correlated, with Income and Employment the highest correlation of 0.939 (Appendix 2). The sub-domains selected by the adaptive model, as the strongest associations with childhood deaths (and each categories of death), are shown in Table 5.



					Category of	of Dooth					
			1		Category	Death	1				
IMD Sub-decile	All Deaths	Acute Medical and Surgical	Congenital Anomalies	Chronic Medical	Deliberately inflicted injury	Infection	Malignancy	Perinatal	SUDIC	Suicide or deliberate self- harm	Trauma
Income											
Employment	1.04 (1.01-1.07)							1.04 (1.01-1.07)		1.12 (1.02-1.23)	
Child Education						1.11 (1.05-1.18)					
Adult Education	1.03 (1.00-1.05)		1.12 (1.08-1.16)								
Health		1.07 (1.01-1.14)		1.13 (1.05-1.21)							
Crime	0.97 (0.95-0.99)		0.95 (0.91-0.99)							0.90 (0.82-0.99)	
Geographic Barriers											
Wider Barriers	1.06 (1.03-1.08)		1.07 (1.02-1.12)					1.06 (1.02-1.11)			
Outdoor Living Environment			1.04 (1.01-1.07)								
Indoor Living Environment	1.03 (1.01-1.05)		1.05 (1.01-1.09)								

* Adjusted for age, sex, region and rural/urban area

Red boxes show measures where increase in deprivation measures are associated with high risks of death Green boxes show measures where increase in deprivation measures are associated with lower risks of death

Measures of deprivation in the domains of Employment, Adult Education, Wider barriers and Indoor Living Environments were identified as most correlated with all cause mortality. Crime also appeared correlated, but in the opposite direction to the others (i.e. increasing measures of deprivation was associated with lower mortality). There was no clear association of any sub-domain and death by malignancy or deliberately inflicted injury; while in contrast the model for perinatal deaths (the single most common category of death) identified measures of Employment and Wider Barriers as possible predictors. Due to the unexpected association between measures of Crime and reductions in risk of death in the adaptive models, a post-hoc analysis was performed to assess the association between this measure and overall mortality. In this model (without the other sub-domain measures of deprivation), increases in measures of deprivation related to crime were associated with increased child mortality (RR 1.06 (1.03-1.09), p<0.001).

Repeating the main analysis but using the IDACI as the measure of deprivation also gave similar results to the main analysis (unadjusted RR 1.10 (1.09-1.12), p<0.001)); fully adjusted RR 1.08 (1.06-1.09), p<0.001).

DISCUSSION

Over a fifth of all child deaths may be avoided if the most deprived half of the population had the same mortality as the least deprived, alongside pervasive evidence of a clear gradient of increasing childhood mortality across England as measures of deprivation increase; with a striking finding that this varied little by area, age or other demographic factors. While we acknowledge this gradient is not new[17], the magnitude of the associations is sobering and this study adds detail around the social

BMJ Open

patterning of potentially modifiable factors. The proportion of modifiable factors increased with increasing deprivation; and this appeared to be restricted to social factors such as financial difficulties, homelessness or poor maternal nutrition. In this detailed analysis an association was seen in most of the categories of death (including the largest category, perinatal); with only causation of death by malignancies, suicide or deliberate self-inflicted harm, and trauma not having clear evidence of an association.

Chance and statistical power are always potential limitations in any statistical analysis, although results in this work were relatively precise. As death notifications are a statutory requirement, the NCMD data is likely to have captured the vast majority of deaths, although some may not have been reported. In addition, postcode data may not have been the child's only residence; so other influences, unmeasured in this work, may have also impacted on their outcome. However this seems unlikely to have introduced significant bias, and the population nature of the index is more likely to reduce any direct effect of inequalities than introduce a false association. It is important to note that measures of deprivation are derived from neighbourhood measures, and even if directly relevant to the child, assumptions of causality are complex. In contrast, the relative increase in reported modifiable factors, as the index of deprivation increases does suggest that some of the excess mortality estimated here maybe avoidable. This work is novel, with the ability to report and review an individual/record level cohort of childhood mortality, alongside the detailed information obtained at the multi-agency review of every death.

The population attributable risk (of 20%) identifed here is crude, but a worrying estimate of the impact of deprivation in child mortality in England; and would equate to over 700 excess deaths a year in England. It highlights the importance of future work to identify the causal pathways involved and to develop interventions that effectively address the causes and improve survival. While some areas appear relatively unrelated to deprivation (e.g. malignancy) most of these represent relatively uncommon categories of death. Perinatal events, which was the most prevalent, were strongly associated with deprivation and modifiable factors.

We did identify some levels of variation of this association across some measures available to us, but overall the increasing risk with deprivation and child mortality was seen across the whole of England, in all age groups, and communities. Children under 1 living in areas of greater deprivation did appear to have the highest risk of death and this needs further analysis and exploration of potential causal mechanisms but may be due to different disease processes affecting children at different ages, or the differential impact of deprivation at critical periods of the children's lives. This finding is consistent with the findings from the national perinatal mortality surveillance data, which reported that women living in the most deprived areas are at an 80% higher risk of stillbirth and neonatal death compared to women living in the least deprived areas[18]. Given that death caused by perinatal events also represents the biggest number of childhood deaths in England[19], these findings provide further evidence for the importance of prioritising interventions around pregnancy and the start of life when parents are

Page 12 of 22

especially open to support, and targeting families at higher risk[1]. The Marmot review and subsequent reviews recommend that equity be placed at the heart of national decisions about education policy and funding[1]. This study provides further evidence for continued investment in current policies such as the National Healthy Child Programme which are based in the concept of proportionate universalism and designed to address health inequalities for children aged 0-19[20].

Like the wider association with all deaths, the mechanisms are likely to be highly complex, and a combination of the intergenerational impact of poverty on family health and lifestyle choices such as maternal diet and family nutrition[21], parental smoking[22], as well as the environmental impacts of deprivation, such as housing quality, road traffic pollution, and access to health and social care services which create intersectional disadvantage. Further evaluation of community level interventions is needed, for example there is evidence that programmes such as Sure Start reduced the likelihood of hospitalisation among children of primary school age with greater impact on children living in the most deprived areas[23].

Reviewing the components which make up the deprivation index, it should be noted that many of the measures remain very inter-dependent (e.g. income and education) and interpretation should be cautious. Despite universal healthcare, employment was a key association for several of the cause of death categories, and access to care is likely to be an important mediating factor that is amenable to change[24]. A strong association between child mortality and income inequality has been reported amongst the wealthier OECD countries[25] and the UK has among the highest levels of income inequality in Europe.[26] The highest reported measure of income inequality in the UK over the last decade was in the period April 2019 to March 2020[27] and impacts from the COVID pandemic are likely to have worsened this trend. It is notable that Employment, Adult Education, Wider barriers and Indoor Living Environments appear important predictors of child mortality suggesting that adult employment and education opportunities, and access and improvements to housing, may be the most efficient place to target resources in order to reduce these inequalities. This triangulates with gualitative work which identified the lack of cleanliness, unsuitable accommodation (e.g. overcrowding or damp/mould) and financial issues being commonly reported modifiable factors after a child dies.[12] Some component of reverse causality is possible, with households moving to more deprived areas due to family impact of childhood ill health and disability; although children with chronic health conditions may find accessing services or housing/financial support more difficult than others.[12] One other interesting finding was that death by malignancy did not appear strongly associated with any measure of deprivation, and is a childhood condition where outcomes after diagnosis have improved dramatically in recent decades. This supports the view that delivery of healthcare (at least for this condition) does not appear heavily influenced by social inequality. It may be the case that for some of the other categories of death, for example, preterm birth, much of the impact of deprivation relates to the risks of developing the disease/condition in the first place rather than the healthcare delivery afterwards. However further work, looking at differential impact of outcomes after similar clinical presentation may help clarify this. The unexpected association, in the multivariable model, was

BMJ Open

 that of an inverse relationship (compared to the other data) with measures of crime. While it should be noted that before adjusting for other, correlated, measures of deprivation, increasing measures of crime remained associated with increased risk of childhood death; the finding is interesting, and some component measured in the crime metric provides additional and novel information in this area. Currently the child death review data collection form contains a free text area where social deprivation related factors are noted if considered relevant by the CDOP review panel. The form does not include specific and prompting questions for possible factors relating to social deprivation, and improvements in collecting these data in a standardised format would assist in more detailed analysis of future deaths. Any future analyses should explore the information collected about the circumstances of death and modifiable factors in greater detail while analyses following on from this will also need to interpret the results in the context of the economic and social impact of the COVID-19 pandemic.

Conclusion

There is evidence of a clear gradient of increasing child mortality across England as measures of deprivation increase; with a striking finding that this varied little by area, age or other demographic factor. Over a fifth of all child deaths may be avoided if the most deprived half of the population had the same mortality as the least deprived. Children dying in more deprived areas may have a greater proportion of avoidable deaths, while adult employment and education opportunities, and access and improvements to housing, may be the most efficient place to target resources in order to reduce these inequalities.

Acknowledgements

We thank all Child Death Overview Panels (CDOPs) who submitted data for the purposes of this report and all child death review professionals for submitting data and providing additional information when requested.

Parent and public involvement is at the heart of the NCMD programme. We are indebted to Charlotte Bevan (Sands - Stillbirth and Neonatal Death Charity), Therese McAlorum (Child Bereavement UK) and Jenny Ward (Lullaby Trust), who represent bereaved families on the NCMD programme steering group.

We thank the NCMD team for technical and administrative support.

Competing Interests

David O: I have no conflicts of interest.

SS: I have no conflicts of interest.

TW: I have no conflicts of interest.

Dawn O: I have no conflicts of interest.

JK: I have no conflicts of interest.

IW: I have no conflicts of interest.

KL: I have no conflicts of interest.

Ethics approval and consent to participate

The NCMD legal basis to collect confidential and personal level data under the Common Law Duty of Confidentiality has been established through the Children Act 2004 Sections M - N, Working Together to Safeguard Children 2018 (<u>https://consult.education.gov.uk/child-protection-safeguarding-and-family-law/working-together-to-safeguard-children-revisions-</u>

<u>t/supporting_documents/Working%20Together%20to%20Safeguard%20Children.pdf</u>) and associated Child Death Review Statutory & Operational

Guidance <u>https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_d</u> ata/file/859302/child-death-review-statutory-and-operational-guidance-england.pdf).

The NCMD legal basis to collect personal data under the General Data Protection Regulation (GDPR) without consent is defined by GDPR Article 6 (e) Public task and 9 (h) Health or social care (with a basis in law).

Funding

The National Child Mortality Database (NCMD) Programme is commissioned by the Healthcare Quality Improvement Partnership (HQIP) as part of the National Clinical Audit and Patient Outcomes Programme (NCAPOP). HQIP is led by a consortium of the Academy of Medical Royal Colleges, the Royal College of Nursing, and National Voices. Its aim is to promote quality improvement in patient outcomes. HQIP holds the contract to commission, manage and develop the National Clinical Audit and Patient Outcomes Programme (NCAPOP), comprising around 40 projects covering care provided to people with a wide range of medical, surgical and mental health conditions. NCAPOP is funded by

 NHS England, the Welsh Government and, with some individual projects, other devolved administrations and crown dependencies <u>www.hqip.org.uk/national-programmes.</u> NHS England provided additional funding to the NCMD to enable rapid set up of the real-time surveillance system and staff time to support its function but had no input into the data analysis or interpretation.

Availability of data

Aggregate data may be available on request to the corresponding author, and subject to approval by HQIP.

Authors Contributions

David O: I declare that I participated in the study concept and design, contributed to acquisition, analysis and interpretation of data, drafting and review of the manuscript and that I have seen and approved the final version.

SS: I declare that I participated in the study design, contributed to data acquisition, linkage, analysis and interpretation of analysis, drafting and review of the manuscript; and that I have seen and approved the final version.

TW: I declare that I participated in the study design, contributed to data acquisition, linkage, analysis and interpretation of data analyses, reviewing the manuscript; and that I have seen and approved the final version.

Dawn O: I declare that I contributed to study design, interpretation of data analysis, reviewing the manuscript; and that I have seen and approved the final version.

JK: I declare that I contributed to study design, interpretation of data analysis, reviewing the manuscript; and that I have seen and approved the final version.

IW: I declare that I contributed to study design, interpretation of data analysis, reviewing the manuscript; and that I have seen and approved the final version.

KL: I declare that I obtained funding for this work, participated in the study concept and design, contributed to data acquisition and interpretation of data, drafting and reviewing the manuscript; and that I have seen and approved the final version.

REFERENCES

- 1 Marmot M. Fair society, healthy lives: the Marmot review. Strategic Review of Health Inequalities in England Post 2010. 2010.
- Pillas D, Marmot M, Naicker K, *et al.* Social inequalities in early childhood health and development: a European-wide systematic review. *Pediatric research* 2014;**76**:418–24. doi:10.1038/pr.2014.122
- 3 Marmot M, Friel S, Bell R, *et al.* Closing the gap in a generation: health equity through action on the social determinants of health. *Lancet (London, England)* 2008;**372**:1661–9. doi:10.1016/S0140-6736(08)61690-6
- Bundy DAP, de Silva N, Horton S, *et al.* Investment in child and adolescent health and development: key messages from Disease Control Priorities, 3rd Edition. *Lancet (London, England)* 2018;**391**:687–99. doi:10.1016/S0140-6736(17)32417-0
- 5 The NHS long term plan. 2019.
- 6 MacDorman MF, Matthews TJ, Mohangoo AD, *et al.* International comparisons of infant mortality and related factors: United States and Europe, 2010. *National vital statistics reports : from the Centers for Disease Control and Prevention, National Center for Health Statistics, National Vital Statistics System* 2014;**63**:1–6.
- Lozano R, Fullman N, Mumford JE, *et al.* Measuring universal health coverage based on an index of effective coverage of health services in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *The Lancet* 2020;**396**:1250–84. doi:10.1016/S0140-6736(20)30750-9
- Zylbersztejn A, Gilbert R, Hjern A, *et al.* Child mortality in England compared with Sweden: a birth cohort study. *Lancet (London, England)* 2018;**391**:2008–18. doi:10.1016/S0140-6736(18)30670-6
- 9 Taylor-Robinson D, Lai ETC, Wickham S, *et al.* Assessing the impact of rising child poverty on the unprecedented rise in infant mortality in England, 2000-2017: time trend analysis. *BMJ open* 2019;**9**:e029424. doi:10.1136/bmjopen-2019-029424
- 10 National Child Mortality Database. https://www.ncmd.info/] (accessed 24 May 2020).
- 11 Child Death Review: Statutory and Operational Guidance (England). London: 2018.
- 12 Odd D, Stoianova S, Sleap V, *et al.* Child Mortality and Social Deprivation. 2021. https://www.ncmd.info/2021/05/13/dep-report-2021/
- 13 Lower layer Super Output Area population estimates (supporting information). 2020.
- Rural Urban Classification (2011) of Lower Layer Super Output Areas in England and Wales.2018.
- 15 Population estimates for the UK, England and Wales, Scotland and Northern Ireland: mid-2019. Office for National Statistics (UK).

2		
3 4 5		2020.https://www.ons.gov.uk/peoplepopulationandcommunity/populationandmigration/po pulationestimates/bulletins/annualmidyearpopulationestimates/mid2019estimates
6 7 8	16	Cuzick J. A Wilcoxon-type test for trend. <i>Statistics in medicine</i> 1985; 4 :87–90. doi:10.1002/sim.4780040112
9 10 11 12	17	Taylor-Robinson D, Lai ETC, Wickham S, <i>et al.</i> Assessing the impact of rising child poverty on the unprecedented rise in infant mortality in England, 2000-2017: time trend analysis. <i>BMJ open</i> 2019; 9 :e029424–e029424. doi:10.1136/bmjopen-2019-029424
13 14	18	UK Perinatal Deaths for Births from January to December 2018. 2020.
15 16 17	19	Williams T, Sleap V, Stoianova S, <i>et al.</i> NCMD second annual report. National Child Mortliaty Database (UK). 2021.
18 19 20 21 22 23	20	Healthy child programme 0 to 19: health visitor and school nurse commissioning. 2021. https://www.gov.uk/government/publications/healthy-child-programme-0-to-19-health- visitor-and-school-nurse-commissioning#full-publication-update-history (accessed 2 Mar 2022).
24	21	Growing Up in the UK. 2013.
25 26	22	PHE Strategy 2020-25. 2019.
27 28 29	23	Cattan S, Conti G, Farquharson C, <i>et al.</i> The Health Effects of Sure Start. Institute for Fiscal Studies. 2019.
30 31 32 33 34	24	Dixon-Woods M, Cavers D, Agarwal S, <i>et al.</i> Conducting a critical interpretive synthesis of the literature on access to healthcare by vulnerable groups. <i>BMC medical research methodology</i> 2006; 6 :35. doi:10.1186/1471-2288-6-35
35 36 37	25	Collison D, Dey C, Hannah G, <i>et al.</i> Income inequality and child mortality in wealthy nations. Journal of public health (Oxford, England) 2007; 29 :114–7. doi:10.1093/pubmed/fdm009
38 39	26	Francis-Devine B. Income inequality in the UK. 2020.
40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58	27	Household income inequality, UK: financial year ending 2020. Office of National Statistics (UK). 2021. https://www.ons.gov.uk/peoplepopulationandcommunity/personalandhouseholdfinances/in comeandwealth/bulletins/householdincomeinequalityfinancial/financialyearending2020
59		

Figure 1. Number of deaths with modifiable factors identified at review, split by measure of local deprivation

for peer teriew only

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

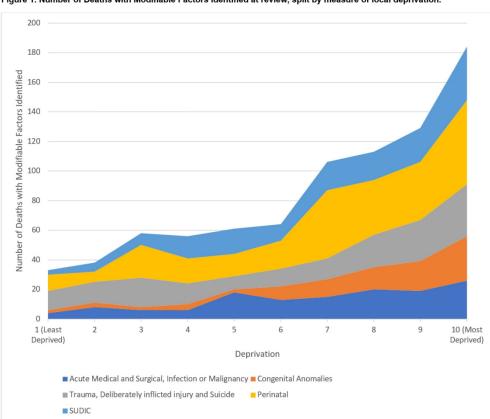
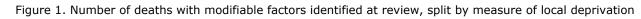


Figure 1. Number of Deaths with Modifiable Factors identified at review, split by measure of local deprivation.



468x407mm (72 x 72 DPI)

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Appendix 1. Sub-domains of deprivation (Weight for the overall IMD in brackets).

Income Deprivation (22.5%)

The Income Deprivation Domain measures the proportion of the population in an area experiencing deprivation relating to low income.

Employment Deprivation (22.5%)

The Employment Deprivation Domain measures the proportion of the working-age population in an area involuntarily excluded from the labour market; this includes people who are unable to work due to unemployment, sickness or disability, or caring responsibilities.

Education, Skills and Training Deprivation (13.5%)

The Education, Skills and Training Domain measures the lack of attainment and skills in the local population. The indicators fall into two sub-domains: one relating to children and young people and one relating to adult skills. The Children and Young People Sub-domain measures the attainment of gualifications and associated measures, while the Adult Skills Sub-domain measures the lack of qualifications in the resident working-age adult population.

Health Deprivation and Disability (13.5%)

The Health Deprivation and Disability Domain measures the risk of premature death and the impairment of quality of life through poor physical or mental health. The domain measures morbidity, disability and premature mortality but not aspects of behaviour or environment that may be predictive of future health deprivation.

Crime (9.3%)

The Crime Domain measures the risk of personal and material victimisation at local level.

Barriers to Housing and Services (9.3%)

The Barriers to Housing and Services Domain measures the physical and financial accessibility of housing and local services. The indicators fall into two sub-domains: the Geographical Barriers Sub-domain, which relates to the physical proximity of local services, and the Wider Barriers Sub-domain which includes issues relating to access to housing such as affordability.

Living Environment Deprivation (9.3%)

The Living Environment Deprivation Domain measures the quality of the local environment. The indicators fall into two sub-domains. The Indoors Sub-domain measures the quality of housing; while the Outdoors Sub-domain contains measures of air quality and road traffic accidents.

Health

Crime

0.800

0.652

0.733

1

1	Appendix 2. W	eights of	each sub-	decile c	lomain t	owards t	he total se	core, and c	orrelatio	ns between	domains.
2					Crime	Child	Adult	Geographic	Wider	Indoor Livina	Outdoor Living
3		Income	Employment	Health		Education	Education	Barriers	Barriers	Environment	Environment
4	Income	1.000									
F											
5	Employment	0.938	1.000								
6											
•	1.1	0.000	0.040	1 000							

1.000

1.00

Wider Barriers 0.539 0.393 0.273 0.512 0.295 0.298 -0.487 1.00 Indoor Living Environment 0.173 0.137 0.168 0.187 0.124 0.047 -0.191 0.133	Geographic Barriers Wider Barriers Indoor Living Environment Outdoor Living Environment	-0.443 0.539 0.173 0.257	-0.380 0.393 0.137 0.153	-0.367 0.273 0.168 0.131	-0.464 0.512 0.187 0.447	-0.228 0.295 0.124 0.009	-0.251 0.298 0.047 0.083	-0.487 -0.191 -0.410	0.133	0
Wider Barriers 0.539 0.393 0.273 0.512 0.295 0.298 -0.487 1.00 Indoor Living Environment 0.173 0.137 0.168 0.187 0.124 0.047 -0.191 0.133 Outdoor Living Environment 0.257 0.153 0.131 0.447 0.009 0.083 -0.410 0.575 0	Wider Barriers Indoor Living Environment Outdoor Living Environment	0.539 0.173 0.257	0.393 0.137 0.153	0.273 0.168 0.131	0.512 0.187 0.447	0.295 0.124 0.009	0.298 0.047 0.083	-0.487 -0.191 -0.410	0.133	
Indoor Living Environment 0.173 0.137 0.168 0.187 0.124 0.047 -0.191 0.133 Outdoor Living Environment 0.257 0.153 0.131 0.447 0.009 0.083 -0.410 0.575 0	Indoor Living Environment Outdoor Living Environment	0.173	0.137	0.168	0.187	0.124	0.047	-0.191 -0.410	0.133	
Environment Outdoor Living 0.257 0.153 0.131 0.447 0.009 0.083 -0.410 0.575 0	Environment Outdoor Living Environment	0.257	0.153	0.131	0.447	0.009	0.083	-0.410	0.575	
Outdoor Living Environment 0.257 0.153 0.131 0.447 0.009 0.083 -0.410 0.575 0	Outdoor Living Environment									0
		<u> </u>	e correlatio	on betwe	een sub-c	leciles of	the IMD.			

0.849

0.607

0.723

1.000

0.591

0.659

1.000

0.456

> > For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

STROBE Statement—Checklist of items that should be included in reports of cohort studies

	Item No	Recommendation	Page No
Title and abstract	1	(<i>a</i>) 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	3
		done and what was found	
T J			
Introduction	2	Europein the acceptific healteneur dand entionals for the investigation hairs	4
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of	5
C		recruitment, exposure, follow-up, and data collection	
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of	5-6
I		participants. Describe methods of follow-up	
		(b) For matched studies, give matching criteria and number of exposed and	
		unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and	5-6
		effect modifiers. Give diagnostic criteria, if applicable	
Data sources/	8*	For each variable of interest, give sources of data and details of methods of	5-6
measurement		assessment (measurement). Describe comparability of assessment methods if	
		there is more than one group	
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable,	5
		describe which groupings were chosen and why	
Statistical methods	12	(a) Describe all statistical methods, including those used to control for	5-6
		confounding	
		(b) Describe any methods used to examine subgroups and interactions	5-6
		(c) Explain how missing data were addressed	5
		(d) If applicable, explain how loss to follow-up was addressed	5
		(<u>e</u>) Describe any sensitivity analyses	6
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers	6
		potentially eligible, examined for eligibility, confirmed eligible, included in	
		the study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	-
		(c) Consider use of a flow diagram	-
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social)	Table
r		and information on exposures and potential confounders	
		(b) Indicate number of participants with missing data for each variable of	Table
		interest	
		(c) Summarise follow-up time (eg, average and total amount)	-

BMJ Open

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

*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 http://www.strobe-statement.org.

BMJ Open

WHAT IS THE RELATIONSHIP BETWEEN DEPRIVATION, MODIFIABLE FACTORS, AND CHILDHOOD DEATHS. A COHORT STUDY USING THE ENGLISH NATIONAL CHILD MORTALITY DATABASE

Journal:	BMJ Open
Manuscript ID	bmjopen-2022-066214.R1
Article Type:	Original research
Date Submitted by the Author:	05-Oct-2022
Complete List of Authors:	Odd, David; Cardiff University, Division of Population Medicine; University of Bristol, National Child Mortality Database Stoianova, Sylvia; University of Bristol, National Child Mortality Database Williams, Tom; University of Bristol, National Child Mortality Database Odd, Dawn; University of the West of England, School of Health and Social Wellbeing Kurinczuk, Jennifer; University of Oxford, National Perinatal Epidemiology Unit Wolfe, Ingrid; King's College London, Department of Women's and Children's Health Luyt, Karen; University of Bristol, National Child Mortality Database
Primary Subject Heading :	Epidemiology
Secondary Subject Heading:	Paediatrics, Public health
Keywords:	EPIDEMIOLOGY, PAEDIATRICS, PUBLIC HEALTH

SCHOLARONE[™] Manuscripts

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our <u>licence</u>.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which <u>Creative Commons</u> licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

review only

WHAT IS THE RELATIONSHIP BETWEEN DEPRIVATION, MODIFIABLE FACTORS, AND CHILDHOOD DEATHS. A COHORT STUDY USING THE ENGLISH NATIONAL CHILD MORTALITY DATABASE

David Odd MD^{1,2}, Sylvia Stoianova MSc², Tom Williams BSc², Dawn Odd³, Jennifer J Kurinczuk⁴, Ingrid Wolfe PhD⁵, Karen Luyt PhD^{2*}

- 1. School of Medicine, Division of Population Medicine, Cardiff University, UK
- 2. National Child Mortality Database, Bristol Medical School, University of Bristol, St Michael's Hospital, Southwell Street, Bristol, UK
- 3. School of Health and Social Wellbeing, University of the West of England, Blackberry Hill, Bristol, UK
- 4. National Perinatal Epidemiology Unit, Nuffield Department of Population Health, University of Oxford, UK

5. School of Life Course Sciences, Department of Women and Children's Health, King's College London, London, UK

elez on

- * Corresponding author
- Dr Karen Luyt
- Email: Karen.Luyt@bristol.ac.uk
- Telephone: +441173425439

Key Words:

deprivation, inequalities, pandemic, mortality, death, child, infant

Word Count: 3700

ABSTRACT

Objectives: The aim of this analysis is to identify the patterns of social deprivation and childhood mortality; and identify potential points where public health, social and education interventions, or health policy may be best targeted.

Design: Decile of deprivation and underlying population distribution was derived using Office for National Statistics data. The risk of death was then derived using a Poisson regression model, calculating the increasing risk of death for each increasing deprivation decile.

Setting: England

Participants: 2688 deaths before 18 years of age reviewed between the April 2019 and March 2020.

Main Outcome Measures: The relationship between deprivation and risk of death; for deaths with, and without modifiable factors.

Results: There was evidence of increasing mortality risk with increase in deprivation decile, with children in the least deprived areas having a mortality of 13.25 (11.78-14.86) per 100000 person-years, compared to 31.14 (29.13-33.25) in the most deprived decile (RR 1.08 (1.07 to 1.10)); with the gradient of risk stronger in children who died with modifiable factors than those without (RR 1.12 (1.09 to 1.15)) vs (RR 1.07 (1.05 to 1.08)). Deprivation sub-domains of Employment, Adult Education, Barriers to Housing and Services, and Indoor Living Environments appeared to be the most important predictors of child mortality

Conclusions: There is a clear gradient of increasing child mortality across England as measures of deprivation increase; with a striking finding that this varied little by area, age or other demographic factor. Over a fifth of all child deaths may be avoided if the most deprived half of the population had the same mortality as the least deprived. Children dying in more deprived areas may have a greater proportion of avoidable deaths. Adult employment, and improvements to housing, may be the most efficient place to target resources to reduce these inequalities.

Strengths and limitations of this study

- Based on statutory death registrations
- High level of data completeness
- Detailed measures on all childhood deaths
- Limited precision due to small numbers of individual events
- Denominators based on population estimates.

BACKGROUND

The death of every child is a devastating loss that profoundly affects bereaved parents as well as siblings, grandparents, extended family members, friends and professionals. The evidence relating to social deprivation and death is strongest for infant mortality however the effects appear measurable across the life course.[1] A systematic review examining the relationship between social factors and early childhood health and developmental outcomes provides strong evidence that factors such as neighbourhood deprivation, lower parental income, unemployment and educational attainment, lower occupational social class, heavy physical occupational demands, lack of housing tenure, and material deprivation in the household are all independently associated with a wide range of adverse health outcomes.[2]

We know that early child development plays a major role in affecting future life chances and health throughout the life course[3] with adverse exposures having greater impacts on younger children.[4] While initiatives have been proposed to reduce the impact of deprivation on health;[5] babies, children, and young people remain the most vulnerable in society. Currently England has one of the highest infant mortality rates in Europe[6, 7] and while much of the variation may be due to socioeconomic factors,[8] it is clear that since infant mortality among the most deprived groups continues to rise,[9] effective policies and other interventions are either lacking or have not been successfully implemented. While the COVID pandemic continues to impact delivery of social and healthcare programs across the world, the longer term impact on economies and social and healthcare budgets is likely to be substantial, and social inequalities even in developed nations, may worsen.

The National Child Mortality Database (NCMD) Programme was established in 2018 to collate and analyse data about all children in England who die before their 18th birthday, with statutory death notifications required within 48 hours[10]. The data are collated from the 58 Child Death Overview Panels (CDOPs) in England who carry out detailed analysis of the circumstances of death and identify the modifiable contributory factors relevant to the death as part of the child death review (CDR) process with the aim of identifying common themes to guide learning and inform actions to reduce future child deaths.[11] The CDR process is statutory, with the Children Act 2004 mandating the review and analysis of all child deaths so the circumstances of death that relate to the welfare of children locally and nationally, or to public health and safety, are identified and understood, and preventive actions established. This work is based on the NCMD Programme's first thematic report.[12]

Aims

The aim of this analysis is to identify and report the patterns of social deprivation, and modifiable factors in relation to childhood mortality, and identify potential intervention points and high risk groups where public health, social and education, or health policy may be best targeted.

METHODS

Three external sources of data were linked to the child death review data using the smallest geographical level of the deprivation index (the Lower Super Output Area (LSOA)). The main measure of deprivation used here is derived from the ONS Index of Multiple Deprivation; which is a complex summary statistic[13] and then split into 10 equal sized (by people) deciles. In this work, a higher decile of deprivation represents a higher level of deprivation in the area where the child lived. The LSOA code also allowed further estimation of the population estimates of age and sex,[14] its rural (Rural town and fringe, Rural village) or urban (Urban city and town, Urban major conurbation) status[15] and its location in England (East Midlands, East of England, London, North East, North West, South East, South West, West Midlands, Yorkshire and the Humber).[16]

Exploratory Variables

For the primary exploratory analysis variables of interest were:

- Age of death (age as a continuous measure) then coded for analysis and presentation as <1 year, 1-4 years, 5-9 years, 10-14 years and 15-17 years).
- Sex (male, female, or missing (including "indeterminate", "not known", "N/A", "NULL" etc)).
- Area of residence: Urban vs Rural[15]
- Region of England.
- Ethnicity was coded as White, Asian or British Asian, Black or British Black, Mixed or Other.

Specific Detailed Data from Child Death Review Process

The CDOP is responsible for identifying any modifiable factors in relation to the child's death. Modifiable factors are those which may have contributed to the death of the child and which might, by means of a locally or nationally achievable intervention, be modified to reduce the risk of future deaths. Factors identified by the CDOP were further classified as (aligning with the statutory Child Death Review categories):

- Characteristics of the child (e.g. loss of key relationships, risk taking behaviour, comorbidity, prematurity, congenital anomaly, learning disability, eating disorder, suicidal ideation or previous suicide attempt)
- Social Environment (e.g. abuse, parenting, consanguinity, financial pressures/hardship)
- Physical Environment (e.g. animal attack, homicide, vehicle related deaths, safety within the home, unsafe infant sleeping practices, and public equipment)
- Service Provision (e.g. gaps in service provision, failure to follow guidelines, poor communication, staffing issues and bed occupancy)

Category of death was allocated by the CDOP while reviewing the case and was categorised as; Acute Medical and Surgical, Congenital Anomalies, Chronic Medical, Deliberately inflicted injury, Infection, Malignancy, Perinatal, Sudden Unexplained Death in Childhood (SUDIC), Suicide or deliberate self-inflicted harm or Trauma.

Analysis

Initially the characteristics of all child deaths reviewed between April 2019 and March 2020 were derived, stratified by the available covariates (listed above). Next we derived the proportion of deaths in each deprivation decile. Evidence of any trend in proportions by increasing deprivation decile were tested using a nonparametric test for trend across ordered groups.[17] This was then repeated for each category of death.

Second, to assess any association between deprivation and the risk of death, the population distribution was derived using ONS data for each LSOA producing a dataset with the predicted numbers of children of each age, sex, rural/urban status and region. The risk of death was then derived using a Poisson regression model, calculating the increasing risk of death for each increasing deprivation decile, with the model then adjusted for the other known underlying population characteristics or possible confounders (sex, age, rural/urban area and region). Lastly both the unadjusted and adjusted model were repeated for each reported category of death and tested (using the likelihood ratio test) to assess if the association between deprivation measures and overall mortality was modified by sex, age category, region, rural/urban status or local population density (total population per 100 m²). Finally for overall mortality a separate model was derived for those children in the lowest five vs the highest five deciles of deprivation, and used to estimate the population attributable risk fraction for those children living the in the most deprived five deciles.

Next, to interrogate the possible causes we initially derived the number, proportion and evidence of trend of modifiable factors identified at the CDOP review across each deprivation decile. We then calculated the increasing risk of death

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

for each increasing deprivation decile separately for those deaths with, or without, modifiable factors identified. The analyses were repeated, stratified by the sub-categories of modifiable factors, and by the category of death.

Role of Funding Source

NHS England provided additional funding to the NCMD to enable rapid set up of the real-time surveillance system and staff time to support its function.

Patient and public involvement

Parent and public involvement is at the heart of the NCMD programme. We are indebted to Charlotte Bevan (Sands -Stillbirth and Neonatal Death Charity), Therese McAlorum (Child Bereavement UK) and Jenny Ward (Lullaby Trust), who represent bereaved families on the NCMD programme steering group.

Data availability

Aggregate data may be available on request to the corresponding author, and subject to approval by HQIP.

RESULTS

A total of 2688 childhood deaths were reviewed by CDOPs between April 2019 and March 2020 and linked to deprivation measures (Table 1).

29	Table 1. Characteristics of the pop	oulations of c	hild deaths reviewed by CDOPs in England during 2019/202
30	Measure	Ν	Child deaths reviewed 2019/2020
31	All Deaths	2688	-
32	Age of Death	2688	
33	<1 year		1675 (62.3%)
34	1-4 Years		322 (12.0%)
35	5-9 Years		211 (7.9%)
36	10-14 Years		227 (8.4%)
37	15-17 Years		253 (9.4%)
38	Sex	2670	
39	Male		1505 (56.4%)
40	Female		1165 (43.6%)
41	Area of residence	2688	
42	Rural		328 (12.2%)
43	Urban		2360 (87.8%)
44	Ethnicity	2390	
45	White		1554 (65.0%)
46	Asian or British Asian		427 (17.9%)
47	Black or British Black		188 (7.9%)
48	Mixed		136 (5.7%)
49	Other		85 (3.6%)
50	Region of residence	2688	
51	East Midlands		214 (8.0%)
52	East of England		211 (8.2%)
53	London		473 (17.6%)
54	North East		109 (4.1%)
55	North West		362 (13.5%)
56	South East		336 (12.5%)
57	South West		232 (8.6%)
58	West Midlands		400 (12.9%)
59	Yorkshire and the Humber		341 (12.7%)
60			

The most common age at death was less than 1 year (62.3%) and more boys than girls died (56.5 vs 43.6% respectively). The majority lived in areas defined as urban (87.8%) and most were of a white ethnic background (65.0%). The number of deaths (p_{trend} =0.003), and the risk of death (p_{trend} <0.001) was more common for children in the most deprived deciles (Table 2). Children in the least deprived two deciles had a mortality risk of 13.25 (95% CI 11.78-14.86) per 100,00 person-years, compared to 31.14 (95% CI 29.13-33.25) in the most deprived 2 deciles.

Table 2. Deaths and risk of death by deprivation decile, stratified by the category of death and patient characteristics of child deaths

Measure			Deprivation Decile						
Numbers of Deaths	1/2 (Least Deprived)	3/4	5/6	7/8	9/10 (Most Deprived)				
	N (%)					Median Decile (IQR)			
All Deaths	293 (10.9%)	383 (14.2%)	476 (17.7%)	644 (24.0%)	892 (33.2%)	7 (4-9)			
Category of Death	, ,	, ,	, ,	, ,	, ,	. ,			
Acute Medical and Surgical	22 (12.9%)	30 (17.5%)	28 (16.4%)	46 (27.0%)	45 (26.3%)	7 (4-9)			
Congenital Anomalies	60 (9.0%)	71 (10.7%)	117 (17.6%)	147 (22.1%)	270 (40.6%)	7 (5-9)			
Chronic Medical	15 (11.2%)	16 (11.9%)	30 (22.4%)	31 (23.1%)	42 (31.3%)	7 (5-9)			
Deliberately inflicted injury	8 (13.1%)	8 (13.1%)	8 (13.1%)	16 (26.2%)	21 (34.4%)	8 (4-9)			
Infection	23 (13.4%)	15 (8.7%)	25 (14.5%)	54 (31.4%)	55 (32.0%)	7 (5-9)			
Malignancy	38 (18.1%)	41 (19.5%)	42 (20.0%)	36 (17.1%)	53 (25.2%)	5 (3-8)			
Perinatal	74 (8.8%)	128 (15.1%)	152 (18.0%)	223 (26.4%)	268 (31.7%)	7 (4-9)			
SUDIC	17 (8.0%)	30 (14.2%)	44 (20.8%)	48 (22.6%)	73 (34.4%)	7 (4-9)			
Suicide or deliberate self- inflicted harm	19 (18.6%)	20 (19.6%)	17 (16.7%)	18 (17.7%)	28 (27.5%)	6 (3-9)			
Trauma	17 (14.7%)	24 (20.7%)	13 (11.2%)	25 (21.6%)	37 (31.9%)	7 (3-9)			
	, ,	, ,	, ,	, ,		, ,			
		Risk (per 100,000 children) (95% Cl)							
All Deaths	13.25 (11.78-14.86)	17.78 (16.04-19.65)	21.10 (19.25-23.09)	26.01 (24.04-28.10)	31.14 (29.13-33.25)	26.01 (24.04-28.10)	•		
Category of Death									
Acute Medical and Surgical	1.00 (0.62-1.51)	1.39 (0.94-1.99)	1.24 (0.82-1.79)	1.86 (1.36-2.48)	1.57 (1.15-2.10)	1.43 (1.22-1.66)			
Congenital Anomalies	2.71 (2.07-3.49)	3.30 (2.57-4.16)	5.19 (4.29-6.22)	5.94 (5.02-6.98)	9.43 (8.33-10.62)	5.56 (5.15-6.00)	•		
Chronic Medical	0.68 (0.38-1.12)	0.75 (0.42-1.21)	1.33 (0.90-1.90)	1.25 (0.85-1.78)	1.47 (1.06-1.98)	1.12 (0.94-1.33)			
Deliberately inflicted injury	0.13 (0.16-0.71)	0.37 (0.16-0.73)	0.35 (0.15-0.70)	0.65 (0.37-1.050)	0.73 (0.45-1.12)	0.51 (0.39-0.66)			
Infection	1.04 (0.66-1.56)	0.70 (0.39-1.15)	1.11 (0.72-1.64)	2.18 (1.64-2.85)	1.92 (1.45-2.50)	1.44 (1.23-1.67)	<		
Malignancy	1.72 (1.22-2.36)	1.91 1.37-2.58)	1.86 (1.34-2.52)	1.45 (1.02-2.01)	1.85 (1.39-2.42)	1.76 (1.53-2.01)			
Perinatal	3.35 (2.63-4.20)	5.94 (4.96-7.07)	6.74 (5.71-7.90)	9.01 (7.86-10.27)	9.36 (0.27-10.54)	7.06 (6.60-7.56)	<		
SUDIC	0.77 (0.45-1.23)	1.39 (0.94-1.99)	1.95 (1.42-2.62)	1.94 (1.43-2.57)	2.55 (2.00-3.20)	1.77 (1.54-2.03)	<		
Suicide or deliberate self- inflicted harm	0.86 (0.52-1.34)	0.93 (0.57-1.43)	0.75 (0.44-1.21)	0.73 (0.43-1.15)	0.98 (0.65-1.41)	0.85 (0.70-1.04)			
Trauma	0.77 (0.45-1.23)	1.11 (0.71-1.66)	0.58 (0.31-0.99)	1.01 (0.65- 1.49)	1.29 (0.91-1.78)	0.97 (0.80-1.16)			

N.B. In this work an increase in the deprivation decile indicates a higher level of local deprivation

When looking at the categories of death, deaths due to acute medical or surgical disease ($p_{trend}=0.017$), congenital anomalies ($p_{trend}=0.003$), chronic medical ($p_{trend}=0.006$), deliberate inflicted injury ($p_{trend}=0.025$), infection ($p_{trend}=0.021$), perinatal ($p_{trend}=0.006$), SUDIC ($p_{trend}=0.003$) and trauma ($p_{trend}=0.038$) appeared to be associated with increasing deprivation. There was little evidence of an association between increasing deprivation and deaths from malignancy ($p_{trend}=0.326$) or suicide or deliberate self-inflicted harm ($p_{trend}=0.296$).

Overall, child mortality was estimated at 22.47(95% CI 21.63-23.34) per 100,000 children/year (Table 3). When estimating the relative risk of death using an unadjusted Poisson model, there was an increasing risk of all-cause mortality as measures of deprivation increased (RR 1.11 (95% CI 1.09-1.12), p<0.001); but also for death categorised as acute medical or surgical (RR 1.06 (95% CI 1.01-1.12), p=0.030), congenital anomalies (RR 1.17 (95% CI 1.14-1.21),p<0.001), chronic medical (RR 1.09 (95% CI 1.03-1.16), p=0.004), deliberately inflicted injury (RR 1.13 (95% CI 1.03-1.24), p=0.009), infection (RR 1.13 (95% CI 1.07-1.19), p<0.001), perinatal (RR 1.11 (95% CI 1.09-

1.14),p<0.001), and SUDIC (RR 1.13 (95% CI 1.08-1.19), p<0.001) (Table 3). After adjusting for age, sex, region and rural status, the association with all-cause mortality (RR 1.08 (95% CI 1.07-1.10), p<0.001) and for congenital

anomalies (RR 1.13 (95% CI 1.10-1.17), p<0.001), chronic medical (RR 1.09 (95% CI 1.02-1.17), p=0.007), deliberately inflicted injury (RR 1.11 (95% CI 1.00-1.22), p=0.040), infection (RR 1.11 (95% CI 1.05-1.18), p<0.001), perinatal (RR 1.07 (95% CI 1.04-1.10), p<0.001), and SUDIC (RR 1.10 (95% CI 1.05-1.16), p<0.001) remained. However, in the adjusted analysis, the association between death in the acute medical or surgical category with increasing measures of deprivation weakened slightly (RR 1.06 (95% CI 1.00-1.12), p=0.052). There was little evidence to suggest an association with malignancy (RR 1.00 (95% CI 0.95-1.05), p=0.979), suicide or deliberate self-inflicted harm (RR 1.03 (95% CI 0.96-1.10), p=0.475) or trauma (RR 1.05 (95% CI 0.98-1.12), p=0.174) in the adjusted (or unadjusted) analyses (Table 3).

Table 3. Relative risk of death for increasing deprivation stratified by category of death, and testing for interactions by characteristics of the child deaths

Measure		Unadjusted				Adjusted*					
	n	Risk per 100,00 children/year	RR 95% CI	р		n	RR 95% CI	р			
All Deaths	2688	22.47 (21.63-23.34)	1.11 (1.09-1.12)	<0.001		2670	1.08 (1.07-1.10)	<0.001			
Acute Medical and Surgical	171	1.43 (1.22-1.66)	1.06 (1.01-1.12)	0.030		170	1.06 (1.00-1.12)	0.052			
Congenital Anomalies	665	5.56 (5.15-6.00)	1.17 (1.14-1.21)	<0.001		658	1.13 (1.10-1.17)	<0.001			
Chronic Medical			1.09 (1.03-1.16)	0.004		134	1.09 (1.02-1.17)	0.007			
Deliberately inflicted injury	61	0.51 (0.39-0.66)	1.13 (1.03-1.24)	0.009		61	1.11 (1.00-1.22)	0.040			
Infection	172	1.44 (1.23-1.67)	1.13 (1.07-1.19)	<0.001		172	1.11 (1.05-1.18)	<0.001			
Malignancy	210	1.76 (1.53-2.01)	1.00 (0.95-1.04)	0.868		210	1.00 (0.95-1.05)	0.979			
Perinatal	845	7.06 (6.60-7.56)	1.11 (1.09-1.14)	<0.001		836	1.07 (1.04-1.10)	<0.001			
SUDIC	212	1.77 (1.54-2.03)	1.13 (1.08-1.19)	<0.001		211	1.10 (1.05-1.16)	<0.001			
Suicide or deliberate self- inflicted harm	102	0.85 (0.70-1.04)	1.01 (0.94-1.08)	0.831		102	1.03 (0.96-1.10)	0.475			
Trauma and other external factors	116	0.97 (0.80-1.16)	1.06 (0.99-1.13)	0.075		116	1.05 (0.98-1.12)	0.174			
Interactions			RR 95% CI	р	Pinteraction		RR 95% CI	р	p interacti		
Sex					0.227				0.1		
Female	nale 1165 19.98 (18.85-21.16) 1.11 (1.09-1.13)		1.11 (1.09-1.13)	<0.001		1165	1.07 (1.05-1.09)	<0.001			
Male	150524.55 (23.33-25.83)1.10 (1.08-1.11)		1.10 (1.08-1.11)	<0.001		1505	1.09 (1.07-1.11)	<0.001			
Age					0.003				<0.0		
<1 year	1675	261.81 (249.42-274.66)	1.11 (1.09-1.13)	<0.001		1659	1.10 (1.08-1.12)	<0.001			
1-4 Years	322	11.88 (10.62-13.25)	1.10 (1.06-1.14)	<0.001		321	1.09 (1.05-1.13)	<0.001			
5-9 Years	211	5.99 (5.21-6.85)	1.00 (0.96-1.05)	0.956		210	0.99 (0.95-1.04)	0.785			
10-14 Years	227	6.93 (6.06-7.89)	1.07 (1.03-1.12)	0.002		227	1.07 (1.02-1.11)	0.006			
15-17 Years	253	13.97 (12.30-15.80)	1.06 (1.01-1.10)	0.011		253	1.05 (1.01-1.09)	0.028			
Area					0.616				0.4		
Urban	2360	23.30 (22.37-24.26)	1.10 (1.09-1.12)	<0.001		2342	1.08 (1.06-1.10)	<0.001			
Rural	328	17.89 (16.00-19.93)	1.12 (1.07-1.17)	<0.001		328	1.10 (1.05-1.16)	<0.001			
Region					0.074				0.1		
East Midlands	214	21.47 (18.69-24.54)	1.07 (1.02-1.12)	0.004		214	1.06 (1.01-1.11)	0.023			
East of England	221	16.54 (14.43-18.87)	1.07 (1.02-1.13)	0.005		220	1.06 (1.01-1.11)	0.030			
London	473	23.38 (21.32-25.59)	1.06 (1.02-1.10)	0.003		464	1.06 (1.01-1.10)	0.007			
North East	109	20.56 (16.88-24.80)	1.06 (0.99-1.13)	0.098		109	1.04 (0.97-1.12)	0.233			
North West	362	23.29 (20.95-25.95)	1.10 (1.06-1.14)	<0.001		360	1.08 (1.04-1.12)	<0.001			
South East	336	17.16 (15.37-19.09)	1.11 (1.07-1.15)	<0.001		336	1.09 (1.05-1.14)	<0.001			
South West	232	21.03 (18.41-23.92)	1.10 (1.05-1.16)	<0.001		232	1.09 (1.03-1.14)	0.001			
West Midlands	400	30.93 (27.98-34.12)	1.16 (1.11-1.20)	<0.001		395	1.14 (1.09-1.19)	<0.001			
Yorkshire and the	3411	29.24 (26.22-32.51)	1.10 (1.06-1.14)	<0.001		340	1.09 (1.05-1.13)	<0.001			

N.B. In this work an increase in the deprivation decile indicates a higher level of local deprivation For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open

* Adjusted for age, sex, region and rural/urban area

There was strong evidence that the association between number of deaths and the deprivation index was modified by age (fully adjusted; p_{interaction}<0.001), but not sex (fully adjusted; p_{interaction}=0.196) or rural/urban status (fully adjusted; p_{interaction}=0.463). In the unadjusted model there was some weak evidence that the relationship may be modified by the region of England (p_{interaction}=0.0743) and population density (p_{interaction}=0.022) although both measures weakened in the adjusted model further (Region; p_{interaction}=0.165, Population Density; p_{interaction}=0.281). In the final, adjusted, regression model, estimating the risk of death (adjusted for age, sex and rural/urban area),

in the final, adjusted, regression model, estimating the risk of death (adjusted for age, sex and rural/urban area),
 comparing the risk of death in the most deprived five deciles with the least deprived five deciles, gave compatible
 results to those from the main analysis (RR 1.47 (95% Cl 1.35-1.60), p<0.001), and a population attributable risk
 fraction of 21.2% (95% Cl 16.7%-25.4%).

The absolute number of deaths where modifiable factors were identified increased as measures of deprivation increased (Figure 1), with additional strong evidence that the proportion of deaths with modifiable contributory factors identified at the CDOP review increased with increasing measures of deprivation; with 24.2% of deaths in the least deprived, compared with 35.1% of deaths in the most (p_{trend}<0.001) (Table 4).

Table 4. The number of deaths, in each deprivation decile with identified modifiable factors; and the relative risk of death for each increasing deprivation decile with, or without them; split by category of death.

Category of Death		Perce	ntage of de			risk of death f ng deprivation			
	All deciles	eciles							
		1/2 N (%) (Least Deprived)	3/4 N (%)	5/6 N (%)	7/8 N (%)	9/10 N (%) (Most Deprived)	P _{trend}	Death without Modifiable Factors	Deaths with Modifiab Factors
All Deaths	842 (31.3%)	71 (24.2%)	114 (29.8%)	125 (26.3%)	219 (34.0%)	313 (35.1%)	<0.001	1.07 (1.05- 1.08)	1.12 (1.0 1.15)
Split by type of Modifiable Factors				•					
Characteristics of the child	70 (2.6%)	9 (3.1%)	14 (3.7%)	6 (1.3%)	15 (2.3%)	26 (2.9%)	0.797	1.08 (1.07- 1.10)	1.10 (1.0 1.21)
Physical Environment	185 (6.9%)	18 (6.1%)	30 (7.8%)	29 (6.1%)	41 (6.4%)	67 (7.5%)	0.764	1.08 (1.07- 1.10)	1.08 (1.0 1.14)
Service Provision	243 (7.9%)	26 (8.9%)	43 (11.2%)	47 (9.9%)	57 (8.9%)	70 (7.9%)	0.131	1.08 (1.07- 1.10)	1.07 (1.0 1.12)
Social Environment	416 (15.5%)	29 (9.9%)	46 (12.0%)	51 (10.7%)	106 (16.5%)	184 (20.6%)	<0.001	1.07 (1.05- 1.09)	1.15 (1.1 1.20)
Split by Category of Death									
Acute Medical and Surgical	42 (24.6%)	5 (22.7%)	8 (26.7%)	7 (25.0%)	9 (20.0%)	13 (29.0%)	0.815	1.05 (0.98- 1.12)	1.10 (0.9 1.24)
Congenital Anomalies	99 (14.9%)	5 (8.3%)	6 (8.5%)	11 (9.4%)	27 (18.4%)	50 (18.5%)	0.001	1.11 (1.07- 1.15)	1.27 (1.1 1.40)
Chronic Medical	21 (15.7%)	1 (6.7%)	2 (12.5%)	6 (20.0%)	4 (12.9%)	8 (19.1%)	0.597	1.09 (1.01- 1.17)	1.14 (0.9 1.35)
Deliberately inflicted injury	43 (70.5%)	4 (50.0%)	7 (87.5%)	6 (75.0%)	12 (75.0%)	14 (66.7%)	0.911	1.08 (0.90- 1.29)	1.12 (0.9 1.26)
Infection	61 (35.5%)	6 (26.1%)	1 (6.7%)	13 (52.0%)	20 (37.0%)	21 (38.2%)	0.126	1.07 (1.00- 1.15)	1.20 (1.0 1.33)
Malignancy	11 (5.2%)	0 (0.0%)	1 (2.4%0	5 (11.9%)	2 (5.6%)	3 (5.7%)	0.181	0.99 (0.94- 1.05)	1.15 (0.9 1.46)
Perinatal	270 (32.0%)	18 (24.3%)	39 (30.5%)	34 (22.4%)	83 (37.2%)	96 (35.8%)	0.015	1.06 (1.03- 1.10)	1.09 (1.0 1.14)
SUDIC	157 (75.1%)	9 (52.9%)	23 (76.7%)	28 (63.6%)	38 (79.2%)	59 (80.8%)	0.045	1.02 (0.92- 1.12)	1.14 (1.0 1.21)
Suicide	59 (57.8%)	12 (63.2%)	9 (45.0%)	8 (47.1%)	9 (50.00%)	21 (75.0%)	0.317	1.01 (0.90- 1.12)	1.04 (0.9 1.14)
Trauma	79 (68.1%)	11 (64.7%)	18 (75.0%)	7 (53.9%)	15 (60.0%)	28 (75.7%)	0.743	1.00 (0.89- 1.12)	1.07 (0.9 1.17)

N.B. In this work an increase in the deprivation decile indicates a higher level of local deprivation * Adjusted for age, sex, region and rural/urban area

Children who died with modifiable factors showed a stronger gradient with increasing deprivation (RR 1.12 (1.09-1.15)) compared to those who died without (RR 1.07 (1.05-1.08)). Individually, only those modifiable factors relating to social environment appeared to show this gradient (p_{trend} <0.001), with less evidence (but small numbers) for those factors around the child, services, or their physical environment. When stratifying by the category of death there was evidence that modifiable factors were more commonly identified in deaths in areas or greater deprivation for congenital anomalies (p_{trend} =0.001), perinatal (p_{trend} =0.045) and SUDIC (p_{trend} =0.045) deaths; with corresponding greater relative risks with deprivation compared to deaths without modifiable factors identified (e.g. Relative risk of death from a congenital abnormality with increasing deprivation was 1.11 (95% Cl 1.07-1.15) for deaths without modifiable factors, and 1.27 (95% Cl 1.16-1.40) for those with).

When analysing the associations between the risk of childhood death and the deprivation sub-domains (Appendix 1), many of the components of the IMD appeared to be closely correlated, with Income and Employment the highest correlation of 0.939 (Appendix 2). The sub-domains selected by the adaptive model, as the strongest associations with childhood deaths (and each categories of death), are shown in Table 5.

	1												
	Category of Death												
IMD Sub-decile	All Deaths	Acute Medical and Surgical All Deaths		Chronic Medical	Deliberately inflicted injury	Infection	Malignancy	Perinatal		Suicide or deliberate self- harm	Trauma		
Income					$\mathbf{N}_{\mathbf{i}}$								
Employment	1.04 (1.01-1.07)							1.04 (1.01-1.07)		1.12 (1.02-1.23)			
Child Education						1.11 (1.05-1.18)							
Adult Education	1.03 (1.00-1.05)		1.12 (1.08-1.16)										
Health		1.07 (1.01-1.14)		1.13 (1.05-1.21)									
Crime	0.97 (0.95-0.99)		0.95 (0.91-0.99)							0.90 (0.82-0.99)			
Geographic Barriers													
Wider Barriers	1.06 (1.03-1.08)		1.07 (1.02-1.12)					1.06 (1.02-1.11)					
Outdoor Living Environment			1.04 (1.01-1.07)				5						
Indoor Living Environment	1.03 (1.01-1.05)		1.05 (1.01-1.09)										

Table 5. Sub-domain measures identified as stongest associations with childhood death

 * Adjusted for age, sex, region and rural/urban area Red boxes show measures where increase in deprivation measures are associated with high risks of death Green boxes show measures where increase in deprivation measures are associated with lower risks of death
 Measures of deprivation in the domains of Employment, Adult Education, Wider barriers (includes issues relating to housing such as affordability and homelessness) and Indoor Living Environments were identified as most correlated with all-cause mortality. Crime also appeared correlated, but in the opposite direction to the others (i.e. increasing

measures of deprivation was associated with lower mortality). There was no clear association of any sub-domain and death by malignancy or deliberately inflicted injury; while in contrast the model for perinatal deaths (the single most common category of death) identified measures of Employment and Wider Barriers as possible predictors. Due to the unexpected association between measures of Crime and reductions in risk of death in the adaptive models, a post-hoc analysis was performed to assess the association between this measure and overall mortality. In this model (without the other sub-domain measures of deprivation), increases in measures of deprivation related to crime were associated with increased child mortality (RR 1.06 (95% CI 1.03-1.09), p<0.001).

Repeating the main analysis but using the Income Deprivation Affecting Children Index (IDACI), a metric for the proportion of all children (aged 0 to 15) living in income deprived families, gave similar results to the main analysis (unadjusted RR 1.10 (95% CI 1.09-1.12), p<0.001)); fully adjusted RR 1.08 (95% CI 1.06-1.09), p<0.001).

DISCUSSION

Key Findings

Over a fifth of all child deaths may be avoided if the most deprived half of the population had the same mortality as the least deprived, alongside pervasive evidence of a clear gradient of increasing childhood mortality across England as measures of deprivation increase; with a striking finding that this varied little by area, age or other demographic factors. While we acknowledge this gradient is not new[9], the magnitude of the associations is sobering and this study adds detail around the social patterning of potentially modifiable factors. The proportion of modifiable factors increased with increasing deprivation; and this appeared to be restricted to social factors such as financial difficulties, homelessness or poor maternal nutrition. In this detailed analysis an association was seen in most of the categories of death (including the largest category, perinatal); with only causation of death by malignancies, suicide or deliberate self-inflicted harm, and trauma not having clear evidence of an association.

Strengths and Limitations

Chance and statistical power are always potential limitations in any statistical analysis, although results in this work were relatively precise. NCMD data is likely to have captured the vast majority of deaths, as child death notifications in England to the NCMD are a statutory requirement, and comparisons with ONS child mortality data for 0-15 year olds in England in 2020, show that there were 1% more deaths reported in NCMD.[18] However, we acknowledge that some deaths may not have been reported. In addition, postcode data may not have been the child's only residence; so other influences, unmeasured in this work, may have also impacted on their outcome. However this seems unlikely to have introduced significant bias, and the population nature of the index may be more likely to reduce any direct effect of inequalities than introduce a false association at the individual level. It is important to note that measures of deprivation are derived from neighbourhood measures, and even if directly relevant to the child, assumptions of causality are complex. In contrast, the relative increase in reported modifiable factors, as the index of deprivation increases does suggest that some of the excess mortality estimated here maybe avoidable. This work is novel, with the ability to report and review an individual/record level cohort of childhood mortality, alongside the detailed information obtained at the multi-agency review of every death.

Results in Context

The population attributable risk (of 20%) identifed here is crude, but a worrying estimate of the impact of deprivation in child mortality in England; and would equate to over 700 excess deaths a year in England. It highlights the importance of future work to identify the causal pathways involved and to develop interventions that effectively address the causes and improve survival. While some areas appear relatively unrelated to deprivation (e.g. malignancy) most of these represent relatively uncommon categories of death. Perinatal events, which was the most prevalent, were strongly associated with deprivation and modifiable factors. We did identify some levels of variation of this association across some measures available to us, but overall the increasing risk with deprivation and child mortality was seen across the whole of England, in all age groups, and communities. Children under 1 living in areas of greater deprivation did appear to have the highest risk of death and this needs further analysis and exploration of potential causal mechanisms but may be due to different disease processes affecting children at different ages, or the differential

impact of deprivation at critical periods of the children's lives. This finding is consistent with the findings from the national perinatal mortality surveillance data, which reported that women living in the most deprived areas are at an 80% higher risk of stillbirth and neonatal death compared to women living in the least deprived areas.[19] Given that death caused by perinatal events also represents the biggest number of childhood deaths in England,[20] these findings provide further evidence for the importance of prioritising interventions around pregnancy and the start of life when parents are especially open to support, and targeting families at higher risk.[1] The Marmot review and subsequent reviews recommend that equity be placed at the heart of national decisions about education policy and funding.[1] This study provides further evidence for continued investment in current policies such as the National Healthy Child Programme which are based in the concept of proportionate universalism and designed to address health inequalities for children aged 0-19.[21]

Like the wider association with all deaths, the mechanisms are likely to be highly complex, and a combination of the intergenerational impact of poverty on family health and lifestyle choices such as maternal diet and family nutrition,[22] parental smoking,[23] as well as the environmental impacts of deprivation, such as housing quality, road traffic pollution, and access to health and social care services which create intersectional disadvantage. Further evaluation of community level interventions is needed, for example there is evidence that programmes such as Sure Start reduced the likelihood of hospitalisation among children of primary school age with greater impact on children living in the most deprived areas.[24]

Wider Implications

Reviewing the components which make up the deprivation index, it should be noted that many of the measures remain very inter-dependent (e.g. income and education) and interpretation should be cautious. Despite universal healthcare, employment was a key association for several of the cause of death categories, and access to care is likely to be an important mediating factor that is amenable to change.[25] A strong association between child mortality and income inequality has been reported amongst the wealthier OECD countries[26] and the UK has among the highest levels of income inequality in Europe.[27] The highest reported measure of income inequality in the UK over the last decade was in the period April 2019 to March 2020[28] and impacts from the COVID pandemic are likely to have worsened this trend. It is notable that Employment, Adult Education, Wider barriers and Indoor Living Environments appear important predictors of child mortality suggesting that adult employment and education opportunities, and access and improvements to housing, may be the most efficient place to target resources in order to reduce these inequalities. This triangulates with qualitative work which identified the lack of cleanliness, unsuitable accommodation (e.g. overcrowding or damp/mould) and financial issues being commonly reported modifiable factors after a child dies.[12] Some component of reverse causality is possible, with households moving to more deprived areas due to family impact of childhood ill health and disability; although children with chronic health conditions may find accessing services or housing/financial support more difficult than others. [12] The unexpected association, in the multivariable model, was that of an inverse relationship (compared to the other data) with measures of crime. While it should be noted that before adjusting for other, correlated, measures of deprivation, increasing measures of crime remained associated with increased risk of childhood death; the finding is interesting, and some component measured in the crime metric provides additional and novel information in this area.

⁵⁷ Currently the child death review data collection form contains a free text area where social deprivation related factors
 ⁵⁸ are noted if considered relevant by the CDOP review panel. The form does not include specific and prompting
 ⁶⁰ questions for possible factors relating to social deprivation, and improvements in collecting these data in a
 ⁶¹ standardised format would assist in more detailed analysis of future deaths; and comparisons with control population

BMJ Open

would be vital in placing future work in context. Any future analyses should explore the information collected about the circumstances of death and modifiable factors in greater detail while analyses following on from this will also need to interpret the results in the context of the economic and social impact of the COVID-19 pandemic.

Conclusion

<text> There is evidence of a clear gradient of increasing child mortality across England as measures of deprivation increase; with a striking finding that this varied little by area, age or other demographic factor. Over a fifth of all child deaths may be avoided if the most deprived half of the population had the same mortality as the least deprived. Children dying in more deprived areas may have a greater proportion of avoidable deaths, while adult employment and education opportunities, and access and improvements to housing, may be the most efficient place to target resources in order to reduce these inequalities.

Acknowledgements

1

2

3 4

5

6 7

8

9

29 30 31

32

54

We thank all Child Death Overview Panels (CDOPs) who submitted data for the purposes of this report and all child death review professionals for submitting data and providing additional information when requested.

Parent and public involvement is at the heart of the NCMD programme. We are indebted to Charlotte Bevan (Sands -

Stillbirth and Neonatal Death Charity), Therese McAlorum (Child Bereavement UK) and Jenny Ward (Lullaby Trust),

who represent bereaved families on the NCMD programme steering group.

We thank the NCMD team for technical and administrative support.

¹⁴ Ethics approval and consent to participate

The NCMD legal basis to collect confidential and personal level data under the Common Law Duty of Confidentiality has been established through the Children Act 2004 Sections M - N, Working Together to Safeguard Children 2018 (https://consult.education.gov.uk/child-protection-safeguarding-and-family-law/working-together-to-safeguard-childrenrevisions-t/supporting_documents/Working%20Together%20to%20Safeguard%20Children.pdf) and associated Child Death Review Statutory & Operational

22 Detail review statutory a operational
 23 Guidance <u>https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/859302/c</u>
 24 <u>hild-death-review-statutory-and-operational-guidance-england.pdf</u>).

The NCMD legal basis to collect personal data under the General Data Protection Regulation (GDPR) without consent is defined by GDPR Article 6 (e) Public task and 9 (h) Health or social care (with a basis in law).

Authors Contributions

33 David O: I declare that I participated in the study concept and design, contributed to acquisition, analysis and

interpretation of data, drafting and review of the manuscript and that I have seen and approved the final version.

SS: I declare that I participated in the study design, contributed to data acquisition, linkage, analysis and interpretation
 of analysis, drafting and review of the manuscript; and that I have seen and approved the final version.

TW: I declare that I participated in the study design, contributed to data acquisition, linkage, analysis and interpretation
 of data analyses, reviewing the manuscript; and that I have seen and approved the final version.

Dawn O: I declare that I contributed to study design, interpretation of data analysis, reviewing the manuscript; and that
 I have seen and approved the final version.

JK: I declare that I contributed to study design, interpretation of data analysis, reviewing the manuscript; and that I
 have seen and approved the final version.

IW: I declare that I contributed to study design, interpretation of data analysis, reviewing the manuscript; and that I
 have seen and approved the final version.

KL: I declare that I obtained funding for this work, participated in the study concept and design, contributed to data
 acquisition and interpretation of data, drafting and reviewing the manuscript; and that I have seen and approved the
 final version.

55 56 **Competing Interests**

57 David O: I have no conflicts of interest.

59 SS: I have no conflicts of interest.

⁶⁰ TW: I have no conflicts of interest.

Dawn O: I have no conflicts of interest.

- JK: I have no conflicts of interest.
- IW: I have no conflicts of interest.
- KL: I have no conflicts of interest.

Funding

The National Child Mortality Database (NCMD) Programme is commissioned by the Healthcare Quality Improvement Partnership (HQIP) as part of the National Clinical Audit and Patient Outcomes Programme (NCAPOP). HQIP is led by a consortium of the Academy of Medical Royal Colleges, the Royal College of Nursing, and National Voices. Its aim is to promote quality improvement in patient outcomes. HQIP holds the contract to commission, manage and develop the National Clinical Audit and Patient Outcomes Programme (NCAPOP), comprising around 40 projects covering care provided to people with a wide range of medical, surgical and mental health conditions. NCAPOP is funded by NHS England, the Welsh Government and, with some individual projects, other devolved administrations and crown dependencies www.hgip.org.uk/national-programmes. NHS England provided additional funding to the NCMD to enable rapid set up of the real-time surveillance system and staff time to support its function but had no input into the data analysis or interpretation.

Availability of data

Aggregate data may be available on request to the corresponding author, and subject to approval by HQIP.

REFERENCES

4	
5	1. Marmot M. Fair society, healthy lives: the Marmot review. Strategic Review of Health Inequalities in England
6	Post 2010. 2010.
7	
8 9	
9 10	and development: a European-wide systematic review. Pediatric research. 2014;76(5):418-24.
11	3. Marmot M, Friel S, Bell R, Houweling TAJ, Taylor S. Closing the gap in a generation: health equity through
12	action on the social determinants of health. Lancet (London, England). 2008;372(9650):1661-9.
13	4. Bundy DAP, de Silva N, Horton S, Patton GC, Schultz L, Jamison DT. Investment in child and adolescent health
14	and development: key messages from Disease Control Priorities, 3rd Edition. Lancet (London, England).
15	2018;391(10121):687-99.
16	5. The NHS long term plan. 2019. <u>https://www.longtermplan.nhs.uk/</u>
17	6. MacDorman MF, Matthews TJ, Mohangoo AD, Zeitlin J. International comparisons of infant mortality and
18	related factors: United States and Europe, 2010. National vital statistics reports : from the Centers for Disease
19 20	Control and Prevention, National Center for Health Statistics, National Vital Statistics System. 2014;63(5):1-6.
20 21	7. Lozano R, Fullman N, Mumford JE, Knight M, Barthelemy CM, Abbafati C, et al. Measuring universal health
22	coverage based on an index of effective coverage of health services in 204 countries and territories,
23	1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. The Lancet.
24	2020;396(10258):1250-84.
25	8. Zylbersztejn A, Gilbert R, Hjern A, Wijlaars L, Hardelid P. Child mortality in England compared with Sweden: a
26	birth cohort study. Lancet (London, England). 2018;391(10134):2008-18.
27	9. Taylor-Robinson D, Lai ETC, Wickham S, Rose T, Norman P, Bambra C, et al. Assessing the impact of rising
28	child poverty on the unprecedented rise in infant mortality in England, 2000-2017: time trend analysis. BMJ open.
29 30	2019;9(10):e029424-e.
31	10. National Child Mortality Database.
32	11. Child Death Review: Statutory and Operational Guidance (England). HM Government (UK). London; 2018.
33	https://www.gov.uk/government/publications/child-death-review-statutory-and-operational-guidance-england
34	12. Odd D, Stoianova S, Sleap V, Williams T, Cook N, McGeehan L, et al. Child Mortality and Social Deprivation.
35	National Child Mortality Database (UK). 2021. https://www.ncmd.info/2021/05/13/dep-report-2021/
36	13. McLennan D, Noble S, Noble M, Plunkett E, Wright G, Gutacker N. The English Indices of Deprivation 2019:
37	Technical Report. Ministry of Housing, Communities and Local Government. 2019.
38 39	14. Lower layer Super Output Area population estimates (supporting information). 2020.
40	15. Rural Urban Classification (2011) of Lower Layer Super Output Areas in England and Wales. 2018.
41	16. Population estimates for the UK, England and Wales, Scotland and Northern Ireland: mid-2019. Office for
42	National Statistics (UK). 2020.
43	17. Cuzick J. A Wilcoxon-type test for trend. Statistics in medicine. 1985;4(1):87-90.
44	18. Child mortality (death cohort) tables in England and Wales. Office for National Statistics (UK); 2022.
45	https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/datasets/childmortalit
46 47	ystatisticschildhoodinfantandperinatalchildhoodinfantandperinatalmortalityinenglandandwales
47 48	19. UK Perinatal Deaths for Births from January to December 2018. 2020.
49	https://www.npeu.ox.ac.uk/assets/downloads/mbrrace-uk/reports/perinatal-surveillance-report-2018/MBRRACE- UK Perinatal Surveillance Report 2018 - final v3.pdf
50	20. Williams T, Sleap V, Stoianova S, Rossouw G, Cook N, Odd D, et al. NCMD second annual report. National
51	Child Mortliaty Database (UK). 2021. https://www.ncmd.info/wp-
52	
53	 <u>content/uploads/2021/06/NCMD_2nd_Annual_Report_June-2021_web-FINAL.pdf</u> Healthy child programme 0 to 19: health visitor and school nurse commissioning. 2021.
54	
55 56	https://www.gov.uk/government/publications/healthy-child-programme-0-to-19-health-visitor-and-school-nurse- commissioning#full-publication-update-history
50 57	22. Growing Up in the UK. 2013. <u>https://www.bma.org.uk/media/2049/growingupinuk_may2013.pdf</u>
58	 PHE Strategy 2020-25. 2019. <u>https://www.gov.uk/government/publications/phe-strategy-2020-to-2025</u>
59	 23. Cattan S, Conti G, Farquharson C, Ginja R. The Health Effects of Sure Start. Institute for Fiscal Studies. 2019.
60	https://www.ifs.org.uk/publications/14139

1 2	25. Dixon-Woods M, Cavers D, Agarwal S, Annandale E, Arthur A, Harvey J, et al. Conducting a critical interpretive synthesis of the literature on access to healthcare by vulnerable groups. BMC medical research
3 4	methodology. 2006;6:35
5	26. Collison D, Dey C, Hannah G, Stevenson L. Income inequality and child mortality in wealthy nations. Journal
6 7	of public health (Oxford, England). 2007;29(2):114-7. 27. Francis-Devine B. Income inequality in the UK. 2020.
8	https://researchbriefings.files.parliament.uk/documents/CBP-7484/CBP-7484.pdf
9	28. Household income inequality, UK: financial year ending 2020. Office of National Statistics (UK). 2021.
10 11	https://www.ons.gov.uk/peoplepopulationandcommunity/personalandhouseholdfinances/incomeandwealth/bulleti
12	ns/householdincomeinequalityfinancial/financialyearending2020
13 14	
15	
16	
17 18	
19	
20 21	
22	
23 24	
24 25	
26	
27 28	
29	
30 31	
32	
33 34	
35	
36 37	
38	
39 40	
40 41	
42	
43 44	
45	
46 47	
48	
49 50	
51	
52 53	
54	
55 56	
57	
58 59	
60	

Figure 1. Number of deaths with modifiable factors identified at review, split by measure of local deprivation

for peer teriew only

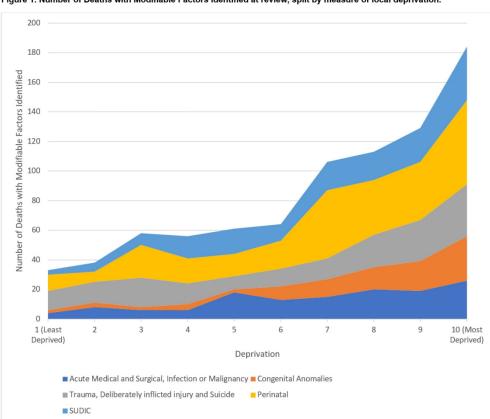
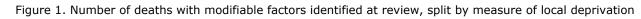


Figure 1. Number of Deaths with Modifiable Factors identified at review, split by measure of local deprivation.



468x407mm (72 x 72 DPI)

Appendix 1. Sub-domains of deprivation (Weight for the overall IMD in brackets).

Income Deprivation (22.5%)

The Income Deprivation Domain measures the proportion of the population in an area experiencing deprivation relating to low income.

Employment Deprivation (22.5%)

The Employment Deprivation Domain measures the proportion of the working-age population in an area involuntarily excluded from the labour market; this includes people who are unable to work due to unemployment, sickness or disability, or caring responsibilities.

Education, Skills and Training Deprivation (13.5%)

The Education, Skills and Training Domain measures the lack of attainment and skills in the local population. The indicators fall into two sub-domains: one relating to children and young people and one relating to adult skills. The Children and Young People Sub-domain measures the attainment of gualifications and associated measures, while the Adult Skills Sub-domain measures the lack of qualifications in the resident working-age adult population.

Health Deprivation and Disability (13.5%)

The Health Deprivation and Disability Domain measures the risk of premature death and the impairment of quality of life through poor physical or mental health. The domain measures morbidity, disability and premature mortality but not aspects of behaviour or environment that may be predictive of future health deprivation.

Crime (9.3%)

The Crime Domain measures the risk of personal and material victimisation at local level.

Barriers to Housing and Services (9.3%)

The Barriers to Housing and Services Domain measures the physical and financial accessibility of housing and local services. The indicators fall into two sub-domains: the Geographical Barriers Sub-domain, which relates to the physical proximity of local services, and the Wider Barriers Sub-domain which includes issues relating to access to housing such as affordability.

Living Environment Deprivation (9.3%)

The Living Environment Deprivation Domain measures the quality of the local environment. The indicators fall into two sub-domains. The Indoors Sub-domain measures the quality of housing; while the Outdoors Sub-domain contains measures of air quality and road traffic accidents.

Health

Crime

0.800

0.652

0.733

1

1	Appendix 2. W	eights of	each sub-	decile c	lomain t	owards t	he total se	core, and c	orrelatio	ns between	domains.
2					Crime	Child	Adult	Geographic	Wider	Indoor Livina	Outdoor Living
3		Income	Employment	Health		Education	Education	Barriers	Barriers	Environment	Environment
4	Income	1.000									
F											
5	Employment	0.938	1.000								
6											
•	1.1	0.000	0.040	1 000							

1.000

1.00

Wider Barriers 0.539 0.393 0.273 0.512 0.295 0.298 -0.487 1.00 Indoor Living Environment 0.173 0.137 0.168 0.187 0.124 0.047 -0.191 0.133	Geographic Barriers Wider Barriers Indoor Living Environment Outdoor Living Environment	-0.443 0.539 0.173 0.257	-0.380 0.393 0.137 0.153	-0.367 0.273 0.168 0.131	-0.464 0.512 0.187 0.447	-0.228 0.295 0.124 0.009	-0.251 0.298 0.047 0.083	-0.487 -0.191 -0.410	0.133	0
Wider Barriers 0.539 0.393 0.273 0.512 0.295 0.298 -0.487 1.00 Indoor Living Environment 0.173 0.137 0.168 0.187 0.124 0.047 -0.191 0.133 Outdoor Living Environment 0.257 0.153 0.131 0.447 0.009 0.083 -0.410 0.575 0	Wider Barriers Indoor Living Environment Outdoor Living Environment	0.539 0.173 0.257	0.393 0.137 0.153	0.273 0.168 0.131	0.512 0.187 0.447	0.295 0.124 0.009	0.298 0.047 0.083	-0.487 -0.191 -0.410	0.133	
Indoor Living Environment 0.173 0.137 0.168 0.187 0.124 0.047 -0.191 0.133 Outdoor Living Environment 0.257 0.153 0.131 0.447 0.009 0.083 -0.410 0.575 0	Indoor Living Environment Outdoor Living Environment	0.173	0.137	0.168	0.187	0.124	0.047	-0.191 -0.410	0.133	
Environment Outdoor Living 0.257 0.153 0.131 0.447 0.009 0.083 -0.410 0.575 0	Environment Outdoor Living Environment	0.257	0.153	0.131	0.447	0.009	0.083	-0.410	0.575	
Outdoor Living Environment 0.257 0.153 0.131 0.447 0.009 0.083 -0.410 0.575 0	Outdoor Living Environment									0
		<u> </u>	e correlatio	on betwe	een sub-c	leciles of	the IMD.			

0.849

0.607

0.723

1.000

0.591

0.659

1.000

0.456

STROBE Statement—Checklist of items that should be included in reports of cohort studies

	Item No	Recommendation	Page No
Title and abstract	1	(<i>a</i>) 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	3
		done and what was found	
T			
Introduction	2	Europein the acceptific healteneur dand entionals for the investigation hairs	4
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of	5
C		recruitment, exposure, follow-up, and data collection	
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of	5-6
I		participants. Describe methods of follow-up	
		(b) For matched studies, give matching criteria and number of exposed and	
(b) For matched studies, give unexposed Variables 7 Clearly define all outcomes, e effect modifiers. Give diagnos Data sources/ 8* For each variable of interest, assessment (measurement). D there is more than one group Bias 9 Study size 10 Explain how the study size ward Quantitative variables 11	Clearly define all outcomes, exposures, predictors, potential confounders, and	5-6	
		effect modifiers. Give diagnostic criteria, if applicable	
Data sources/	8*	For each variable of interest, give sources of data and details of methods of	5-6
measurement		assessment (measurement). Describe comparability of assessment methods if	
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable,	5
		describe which groupings were chosen and why	
Statistical methods	12	(a) Describe all statistical methods, including those used to control for	5-6
		confounding	
		(b) Describe any methods used to examine subgroups and interactions	5-6
		(c) Explain how missing data were addressed	5
		(d) If applicable, explain how loss to follow-up was addressed	5
		(<u>e</u>) Describe any sensitivity analyses	6
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers	6
		potentially eligible, examined for eligibility, confirmed eligible, included in	
		the study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	-
		(c) Consider use of a flow diagram	-
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social)	Table
r		and information on exposures and potential confounders	
		(b) Indicate number of participants with missing data for each variable of	Table
		interest	
		(c) Summarise follow-up time (eg, average and total amount)	-

BMJ Open

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

*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 http://www.strobe-statement.org.

BMJ Open

WHAT IS THE RELATIONSHIP BETWEEN DEPRIVATION, MODIFIABLE FACTORS, AND CHILDHOOD DEATHS. A COHORT STUDY USING THE ENGLISH NATIONAL CHILD MORTALITY DATABASE

Journal:	BMJ Open
Manuscript ID	bmjopen-2022-066214.R2
Article Type:	Original research
Date Submitted by the Author:	20-Oct-2022
Complete List of Authors:	Odd, David; Cardiff University, Division of Population Medicine; University of Bristol, National Child Mortality Database Stoianova, Sylvia; University of Bristol, National Child Mortality Database Williams, Tom; University of Bristol, National Child Mortality Database Odd, Dawn; University of the West of England, School of Health and Social Wellbeing Kurinczuk, Jennifer; University of Oxford, National Perinatal Epidemiology Unit Wolfe, Ingrid; King's College London, Department of Women's and Children's Health Luyt, Karen; University of Bristol, National Child Mortality Database
Primary Subject Heading :	Epidemiology
Secondary Subject Heading:	Paediatrics, Public health
Keywords:	EPIDEMIOLOGY, PAEDIATRICS, PUBLIC HEALTH

SCHOLARONE[™] Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our <u>licence</u>.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which <u>Creative Commons</u> licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

review only

WHAT IS THE RELATIONSHIP BETWEEN DEPRIVATION, MODIFIABLE FACTORS, AND CHILDHOOD DEATHS. A COHORT STUDY USING THE ENGLISH NATIONAL CHILD MORTALITY DATABASE

David Odd MD^{1,2}, Sylvia Stoianova MSc², Tom Williams BSc², Dawn Odd³, Jennifer J Kurinczuk⁴, Ingrid Wolfe PhD⁵, Karen Luyt PhD^{2*}

- 1. School of Medicine, Division of Population Medicine, Cardiff University, UK
- 2. National Child Mortality Database, Bristol Medical School, University of Bristol, St Michael's Hospital, Southwell Street, Bristol, UK
- 3. School of Health and Social Wellbeing, University of the West of England, Blackberry Hill, Bristol, UK
- 4. National Perinatal Epidemiology Unit, Nuffield Department of Population Health, University of Oxford, UK

5. School of Life Course Sciences, Department of Women and Children's Health, King's College London, London, UK

eliezoni

- * Corresponding author
- Dr Karen Luyt
- Email: Karen.Luyt@bristol.ac.uk
- Telephone: +441173425439

Key Words:

deprivation, inequalities, pandemic, mortality, death, child, infant

Word Count: 3700

ABSTRACT

Objectives: The aim of this analysis is to identify the patterns of social deprivation and childhood mortality; and identify potential points where public health, social and education interventions, or health policy may be best targeted.

Design: Decile of deprivation and underlying population distribution was derived using Office for National Statistics data. The risk of death was then derived using a Poisson regression model, calculating the increasing risk of death for each increasing deprivation decile.

Setting: England

Participants: 2688 deaths before 18 years of age reviewed between the April 2019 and March 2020.

Main Outcome Measures: The relationship between deprivation and risk of death; for deaths with, and without modifiable factors.

Results: There was evidence of increasing mortality risk with increase in deprivation decile, with children in the least deprived areas having a mortality of 13.25 (11.78-14.86) per 100000 person-years, compared to 31.14 (29.13-33.25) in the most deprived decile (RR 1.08 (1.07 to 1.10)); with the gradient of risk stronger in children who died with modifiable factors than those without (RR 1.12 (1.09 to 1.15)) vs (RR 1.07 (1.05 to 1.08)). Deprivation sub-domains of Employment, Adult Education, Barriers to Housing and Services, and Indoor Living Environments appeared to be the most important predictors of child mortality

Conclusions: There is a clear gradient of increasing child mortality across England as measures of deprivation increase; with a striking finding that this varied little by area, age or other demographic factor. Over a fifth of all child deaths may be avoided if the most deprived half of the population had the same mortality as the least deprived. Children dying in more deprived areas may have a greater proportion of avoidable deaths. Adult employment, and improvements to housing, may be the most efficient place to target resources to reduce these inequalities.

Strengths and limitations of this study

- Based on statutory death registrations
- High level of data completeness
- Detailed measures on all childhood deaths
- Limited precision due to small numbers of individual events
- Denominators based on population estimates.

BACKGROUND

The death of every child is a devastating loss that profoundly affects bereaved parents as well as siblings, grandparents, extended family members, friends and professionals. The evidence relating to social deprivation and death is strongest for infant mortality however the effects appear measurable across the life course.[1] A systematic review examining the relationship between social factors and early childhood health and developmental outcomes provides strong evidence that factors such as neighbourhood deprivation, lower parental income, unemployment and educational attainment, lower occupational social class, heavy physical occupational demands, lack of housing tenure, and material deprivation in the household are all independently associated with a wide range of adverse health outcomes.[2]

We know that early child development plays a major role in affecting future life chances and health throughout the life course[3] with adverse exposures having greater impacts on younger children.[4] While initiatives have been proposed to reduce the impact of deprivation on health;[5] babies, children, and young people remain the most vulnerable in society. Currently England has one of the highest infant mortality rates in Europe[6, 7] and while much of the variation may be due to socioeconomic factors,[8] it is clear that since infant mortality among the most deprived groups continues to rise,[9] effective policies and other interventions are either lacking or have not been successfully implemented. While the COVID pandemic continues to impact delivery of social and healthcare programs across the world, the longer term impact on economies and social and healthcare budgets is likely to be substantial, and social inequalities even in developed nations, may worsen.

The National Child Mortality Database (NCMD) Programme was established in 2018 to collate and analyse data about all children in England who die before their 18th birthday, with statutory death notifications required within 48 hours[10]. The data are collated from the 58 Child Death Overview Panels (CDOPs) in England who carry out detailed analysis of the circumstances of death and identify the modifiable contributory factors relevant to the death as part of the child death review (CDR) process with the aim of identifying common themes to guide learning and inform actions to reduce future child deaths.[11] The CDR process is statutory, with the Children Act 2004 mandating the review and analysis of all child deaths so the circumstances of death that relate to the welfare of children locally and nationally, or to public health and safety, are identified and understood, and preventive actions established. This work is based on the NCMD Programme's first thematic report.[12]

Aims

The aim of this analysis is to identify and report the patterns of social deprivation, and modifiable factors in relation to childhood mortality, and identify potential intervention points and high risk groups where public health, social and education, or health policy may be best targeted.

METHODS

Three external sources of data were linked to the child death review data using the smallest geographical level of the deprivation index (the Lower Super Output Area (LSOA)). The main measure of deprivation used here is derived from the ONS Index of Multiple Deprivation; which is a complex summary statistic[13] and then split into 10 equal sized (by people) deciles. In this work, a higher decile of deprivation represents a higher level of deprivation in the area where the child lived. The LSOA code also allowed further estimation of the population estimates of age and sex,[14] its rural (Rural town and fringe, Rural village) or urban (Urban city and town, Urban major conurbation) status[15] and its location in England (East Midlands, East of England, London, North East, North West, South East, South West, West Midlands, Yorkshire and the Humber).[16]

Exploratory Variables

For the primary exploratory analysis variables of interest were:

- Age of death (age as a continuous measure) then coded for analysis and presentation as <1 year, 1-4 years, 5-9 years, 10-14 years and 15-17 years).
- Sex (male, female, or missing (including "indeterminate", "not known", "N/A", "NULL" etc)).
- Area of residence: Urban vs Rural[15]
- Region of England.
- Ethnicity was coded as White, Asian or British Asian, Black or British Black, Mixed or Other.

Specific Detailed Data from Child Death Review Process

The CDOP is responsible for identifying any modifiable factors in relation to the child's death. Modifiable factors are those which may have contributed to the death of the child and which might, by means of a locally or nationally achievable intervention, be modified to reduce the risk of future deaths. Factors identified by the CDOP were further classified as (aligning with the statutory Child Death Review categories):

- Characteristics of the child (e.g. loss of key relationships, risk taking behaviour, comorbidity, prematurity, congenital anomaly, learning disability, eating disorder, suicidal ideation or previous suicide attempt)
- Social Environment (e.g. abuse, parenting, consanguinity, financial pressures/hardship)
- Physical Environment (e.g. animal attack, homicide, vehicle related deaths, safety within the home, unsafe infant sleeping practices, and public equipment)
- Service Provision (e.g. gaps in service provision, failure to follow guidelines, poor communication, staffing issues and bed occupancy)

Category of death was allocated by the CDOP while reviewing the case and was categorised as; Acute Medical and Surgical, Congenital Anomalies, Chronic Medical, Deliberately inflicted injury, Infection, Malignancy, Perinatal, Sudden Unexplained Death in Childhood (SUDIC), Suicide or deliberate self-inflicted harm or Trauma.

Analysis

Initially the characteristics of all child deaths reviewed between April 2019 and March 2020 were derived, stratified by the available covariates (listed above). Next we derived the proportion of deaths in each deprivation decile. Evidence of any trend in proportions by increasing deprivation decile were tested using a nonparametric test for trend across ordered groups.[17] This was then repeated for each category of death.

Second, to assess any association between deprivation and the risk of death, the population distribution was derived using ONS data for each LSOA producing a dataset with the predicted numbers of children of each age, sex, rural/urban status and region. The risk of death was then derived using a Poisson regression model, calculating the increasing risk of death for each increasing deprivation decile, with the model then adjusted for the other known underlying population characteristics or possible confounders (sex, age, rural/urban area and region). Lastly both the unadjusted and adjusted model were repeated for each reported category of death and tested (using the likelihood ratio test) to assess if the association between deprivation measures and overall mortality was modified by sex, age category, region, rural/urban status or local population density (total population per 100 m²). Finally for overall mortality a separate model was derived for those children in the lowest five vs the highest five deciles of deprivation, and used to estimate the population attributable risk fraction for those children living the in the most deprived five deciles.

Next, to interrogate the possible causes we initially derived the number, proportion and evidence of trend of modifiable factors identified at the CDOP review across each deprivation decile. We then calculated the increasing risk of death

for each increasing deprivation decile separately for those deaths with, or without, modifiable factors identified. The analyses were repeated, stratified by the sub-categories of modifiable factors, and by the category of death.

NHS England provided additional funding to the NCMD to enable rapid set up of the real-time surveillance system and staff time to support its function.

Patient and public involvement

Parent and public involvement is at the heart of the NCMD programme. We are indebted to Charlotte Bevan (Sands -Stillbirth and Neonatal Death Charity), Therese McAlorum (Child Bereavement UK) and Jenny Ward (Lullaby Trust), who represent bereaved families on the NCMD programme steering group.

Data availability

Aggregate data may be available on request to the corresponding author, and subject to approval by HQIP.

RESULTS

A total of 2688 childhood deaths were reviewed by CDOPs between April 2019 and March 2020 and linked to deprivation measures (Table 1).

Measure	pulations of c	child deaths reviewed by CDOPs in England during 2019/2 Child deaths reviewed 2019/2020
		Child deaths reviewed 2019/2020
All Deaths	2688	-
Age of Death	2688	
<1 year		1675 (62.3%)
1-4 Years		322 (12.0%)
5-9 Years		211 (7.9%)
10-14 Years		227 (8.4%)
15-17 Years		253 (9.4%)
Sex	2670	
Male		1505 (56.4%)
Female		1165 (43.6%)
Area of residence	2688	
Rural		328 (12.2%)
Urban		2360 (87.8%)
Ethnicity	2390	
White		1554 (65.0%)
Asian or British Asian		427 (17.9%)
Black or British Black		188 (7.9%)
Mixed		136 (5.7%)
Other		85 (3.6%)
Region of residence	2688	
East Midlands		214 (8.0%)
East of England		211 (8.2%)
London		473 (17.6%)
North East		109 (4.1%)
North West		362 (13.5%)
South East		336 (12.5%)
South West		232 (8.6%)
West Midlands		400 (12.9%)
Yorkshire and the Humber		341 (12.7%)
		··· (·=·· ··)

The most common age at death was less than 1 year (62.3%) and more boys than girls died (56.5 vs 43.6% respectively). The majority lived in areas defined as urban (87.8%) and most were of a white ethnic background (65.0%). The number of deaths (p_{trend} =0.003), and the risk of death (p_{trend} <0.001) was more common for children in the most deprived deciles (Table 2). Children in the least deprived two deciles had a mortality risk of 13.25 (95% CI 11.78-14.86) per 100,00 person-years, compared to 31.14 (95% CI 29.13-33.25) in the most deprived 2 deciles.

Table 2. Deaths and risk of death by deprivation decile, stratified by the category of death and patient characteristics of child deaths

Measure			Deprivation Decile				
Numbers of Deaths	1/2 (Least Deprived)	3/4	5/6	7/8	9/10 (Most Deprived)		
	N (%)					Median Decile (IQR)	
All Deaths	293 (10.9%)	383 (14.2%)	476 (17.7%)	644 (24.0%)	892 (33.2%)	7 (4-9)	
Category of Death	, ,	, ,	, ,	, ,	, ,		
Acute Medical and Surgical	22 (12.9%)	30 (17.5%)	28 (16.4%)	46 (27.0%)	45 (26.3%)	7 (4-9)	
Congenital Anomalies	60 (9.0%)	71 (10.7%)	117 (17.6%)	147 (22.1%)	270 (40.6%)	7 (5-9)	
Chronic Medical	15 (11.2%)	16 (11.9%)	30 (22.4%)	31 (23.1%)	42 (31.3%)	7 (5-9)	
Deliberately inflicted injury	8 (13.1%)	8 (13.1%)	8 (13.1%)	16 (26.2%)	21 (34.4%)	8 (4-9)	
Infection	23 (13.4%)	15 (8.7%)	25 (14.5%)	54 (31.4%)	55 (32.0%)	7 (5-9)	
Malignancy	38 (18.1%)	41 (19.5%)	42 (20.0%)	36 (17.1%)	53 (25.2%)	5 (3-8)	
Perinatal	74 (8.8%)	128 (15.1%)	152 (18.0%)	223 (26.4%)	268 (31.7%)	7 (4-9)	
SUDIC	17 (8.0%)	30 (14.2%)	44 (20.8%)	48 (22.6%)	73 (34.4%)	7 (4-9)	
Suicide or deliberate self- inflicted harm	19 (18.6%)	20 (19.6%)	17 (16.7%)	18 (17.7%)	28 (27.5%)	6 (3-9)	
Trauma	17 (14.7%)	24 (20.7%)	13 (11.2%)	25 (21.6%)	37 (31.9%)	7 (3-9)	
	, ,	, ,	, ,	, ,			
		Risk (per	100,000 children)	(95% CI)		Overall Risk (95% Cl)	
All Deaths	13.25 (11.78-14.86)	17.78 (16.04-19.65)	21.10 (19.25-23.09)	26.01 (24.04-28.10)	31.14 (29.13-33.25)	26.01 (24.04-28.10)	•
Category of Death							
Acute Medical and Surgical	1.00 (0.62-1.51)	1.39 (0.94-1.99)	1.24 (0.82-1.79)	1.86 (1.36-2.48)	1.57 (1.15-2.10)	1.43 (1.22-1.66)	
Congenital Anomalies	2.71 (2.07-3.49)	3.30 (2.57-4.16)	5.19 (4.29-6.22)	5.94 (5.02-6.98)	9.43 (8.33-10.62)	5.56 (5.15-6.00)	•
Chronic Medical	0.68 (0.38-1.12)	0.75 (0.42-1.21)	1.33 (0.90-1.90)	1.25 (0.85-1.78)	1.47 (1.06-1.98)	1.12 (0.94-1.33)	
Deliberately inflicted injury	0.13 (0.16-0.71)	0.37 (0.16-0.73)	0.35 (0.15-0.70)	0.65 (0.37-1.050)	0.73 (0.45-1.12)	0.51 (0.39-0.66)	
Infection	1.04 (0.66-1.56)	0.70 (0.39-1.15)	1.11 (0.72-1.64)	2.18 (1.64-2.85)	1.92 (1.45-2.50)	1.44 (1.23-1.67)	<
Malignancy	1.72 (1.22-2.36)	1.91 1.37-2.58)	1.86 (1.34-2.52)	1.45 (1.02-2.01)	1.85 (1.39-2.42)	1.76 (1.53-2.01)	
Perinatal	3.35 (2.63-4.20)	5.94 (4.96-7.07)	6.74 (5.71-7.90)	9.01 (7.86-10.27)	9.36 (0.27-10.54)	7.06 (6.60-7.56)	<
SUDIC	0.77 (0.45-1.23)	1.39 (0.94-1.99)	1.95 (1.42-2.62)	1.94 (1.43-2.57)	2.55 (2.00-3.20)	1.77 (1.54-2.03)	4
Suicide or deliberate self- inflicted harm	0.86 (0.52-1.34)	0.93 (0.57-1.43)	0.75 (0.44-1.21)	0.73 (0.43-1.15)	0.98 (0.65-1.41)	0.85 (0.70-1.04)	
Trauma	0.77 (0.45-1.23)	1.11 (0.71-1.66)	0.58 (0.31-0.99)	1.01 (0.65- 1.49)	1.29 (0.91-1.78)	0.97 (0.80-1.16)	

N.B. In this work an increase in the deprivation decile indicates a higher level of local deprivation

When looking at the categories of death, deaths due to acute medical or surgical disease ($p_{trend}=0.017$), congenital anomalies ($p_{trend}=0.003$), chronic medical ($p_{trend}=0.006$), deliberate inflicted injury ($p_{trend}=0.025$), infection ($p_{trend}=0.021$), perinatal ($p_{trend}=0.006$), SUDIC ($p_{trend}=0.003$) and trauma ($p_{trend}=0.038$) appeared to be associated with increasing deprivation. There was little evidence of an association between increasing deprivation and deaths from malignancy ($p_{trend}=0.326$) or suicide or deliberate self-inflicted harm ($p_{trend}=0.296$).

Overall, child mortality was estimated at 22.47(95% CI 21.63-23.34) per 100,000 children/year (Table 3). When estimating the relative risk of death using an unadjusted Poisson model, there was an increasing risk of all-cause mortality as measures of deprivation increased (RR 1.11 (95% CI 1.09-1.12), p<0.001); but also for death categorised as acute medical or surgical (RR 1.06 (95% CI 1.01-1.12), p=0.030), congenital anomalies (RR 1.17 (95% CI 1.14-1.21),p<0.001), chronic medical (RR 1.09 (95% CI 1.03-1.16), p=0.004), deliberately inflicted injury (RR 1.13 (95% CI 1.03-1.24), p=0.009), infection (RR 1.13 (95% CI 1.07-1.19), p<0.001), perinatal (RR 1.11 (95% CI 1.09-

1.14),p<0.001), and SUDIC (RR 1.13 (95% CI 1.08-1.19), p<0.001) (Table 3). After adjusting for age, sex, region and rural status, the association with all-cause mortality (RR 1.08 (95% CI 1.07-1.10), p<0.001) and for congenital

anomalies (RR 1.13 (95% CI 1.10-1.17), p<0.001), chronic medical (RR 1.09 (95% CI 1.02-1.17), p=0.007), deliberately inflicted injury (RR 1.11 (95% CI 1.00-1.22), p=0.040), infection (RR 1.11 (95% CI 1.05-1.18), p<0.001), perinatal (RR 1.07 (95% CI 1.04-1.10), p<0.001), and SUDIC (RR 1.10 (95% CI 1.05-1.16), p<0.001) remained. However, in the adjusted analysis, the association between death in the acute medical or surgical category with increasing measures of deprivation weakened slightly (RR 1.06 (95% CI 1.00-1.12), p=0.052). There was little evidence to suggest an association with malignancy (RR 1.00 (95% CI 0.95-1.05), p=0.979), suicide or deliberate selfinflicted harm (RR 1.03 (95% CI 0.96-1.10), p=0.475) or trauma (RR 1.05 (95% CI 0.98-1.12), p=0.174) in the adjusted (or unadjusted) analyses (Table 3).

Table 3. Relative risk of death for increasing deprivation stratified by category of death, and testing for interactions by characteristics of the child deaths

Measure			nadjusted				Adjust		
	n	Risk per 100,00 children/year	RR 95% CI	р		n	RR 95% CI	р	
All Deaths	2688	22.47 (21.63-23.34)	1.11 (1.09-1.12)	<0.001		2670	1.08 (1.07-1.10)	<0.001	
Acute Medical and Surgical	171	1.43 (1.22-1.66)	1.06 (1.01-1.12)	0.030		170	1.06 (1.00-1.12)	0.052	
Congenital Anomalies	665	5.56 (5.15-6.00)	1.17 (1.14-1.21)	<0.001		658	1.13 (1.10-1.17)	<0.001	
Chronic Medical	134	1.12 (0.94-1.33)	1.09 (1.03-1.16)	0.004		134	1.09 (1.02-1.17)	0.007	
Deliberately inflicted injury	61	0.51 (0.39-0.66)	1.13 (1.03-1.24)	0.009		61	1.11 (1.00-1.22)	0.040	
Infection	172	1.44 (1.23-1.67)	1.13 (1.07-1.19)	<0.001		172	1.11 (1.05-1.18)	<0.001	
Malignancy	210	1.76 (1.53-2.01)	1.00 (0.95-1.04)	0.868		210	1.00 (0.95-1.05)	0.979	
Perinatal	845	7.06 (6.60-7.56)	1.11 (1.09-1.14)	<0.001		836	1.07 (1.04-1.10)	<0.001	
SUDIC	212	1.77 (1.54-2.03)	1.13 (1.08-1.19)	<0.001		211	1.10 (1.05-1.16)	<0.001	
Suicide or deliberate self- inflicted harm	102	0.85 (0.70-1.04)	1.01 (0.94-1.08)	0.831		102	1.03 (0.96-1.10)	0.475	
Trauma and other external factors	116	0.97 (0.80-1.16)	1.06 (0.99-1.13)	0.075		116	1.05 (0.98-1.12)	0.174	
Interactions			RR 95% CI	р	Pinteraction		RR 95% CI	р	Pinteracti
Sex					0.227				0.1
Female	ale 1165 19.98 (18.85-21.16) 1.11 (1.09-1.13)		<0.001		1165	1.07 (1.05-1.09)	<0.001		
Male	1505	24.55 (23.33-25.83)	(23.33-25.83) 1.10 (1.08-1.11)			1505	1.09 (1.07-1.11)	<0.001	
Age					0.003				<0.0
<1 year	1675	261.81 (249.42-274.66)	1.11 (1.09-1.13)	<0.001		1659	1.10 (1.08-1.12)	<0.001	
1-4 Years	322	11.88 (10.62-13.25)	1.10 (1.06-1.14)	<0.001		321	1.09 (1.05-1.13)	<0.001	
5-9 Years	211	5.99 (5.21-6.85)	1.00 (0.96-1.05)	0.956		210	0.99 (0.95-1.04)	0.785	
10-14 Years	227	6.93 (6.06-7.89)	1.07 (1.03-1.12)	0.002		227	1.07 (1.02-1.11)	0.006	
15-17 Years	253	13.97 (12.30-15.80)	1.06 (1.01-1.10)	0.011		253	1.05 (1.01-1.09)	0.028	
Area					0.616				0.4
Urban	2360	23.30 (22.37-24.26)	1.10 (1.09-1.12)	<0.001		2342	1.08 (1.06-1.10)	<0.001	
Rural	328	17.89 (16.00-19.93)	1.12 (1.07-1.17)	<0.001		328	1.10 (1.05-1.16)	<0.001	
Region					0.074				0.1
East Midlands	214	21.47 (18.69-24.54)	1.07 (1.02-1.12)	0.004		214	1.06 (1.01-1.11)	0.023	
East of England	221	16.54 (14.43-18.87)	1.07 (1.02-1.13)	0.005		220	1.06 (1.01-1.11)	0.030	
London	473	23.38 (21.32-25.59)	1.06 (1.02-1.10)	0.003		464	1.06 (1.01-1.10)	0.007	
North East	109	20.56 (16.88-24.80)	1.06 (0.99-1.13)	0.098		109	1.04 (0.97-1.12)	0.233	
North West	362	23.29 (20.95-25.95)	1.10 (1.06-1.14)	<0.001		360	1.08 (1.04-1.12)	<0.001	
South East	336	17.16 (15.37-19.09)	1.11 (1.07-1.15)	<0.001		336	1.09 (1.05-1.14)	<0.001	
South West	232	21.03 (18.41-23.92)	1.10 (1.05-1.16)	<0.001		232	1.09 (1.03-1.14)	0.001	
West Midlands	400	30.93 (27.98-34.12)	1.16 (1.11-1.20)	<0.001		395	1.14 (1.09-1.19)	<0.001	
Yorkshire and the	341	29.24 (26.22-32.51)	1.10 (1.06-1.14)	<0.001		340	1.09 (1.05-1.13)	<0.001	

N.B. In this work an increase in the deprivation decile indicates a higher level of local deprivation For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open

* Adjusted for age, sex, region and rural/urban area

There was strong evidence that the association between number of deaths and the deprivation index was modified by age (fully adjusted; p_{interaction}<0.001), but not sex (fully adjusted; p_{interaction}=0.196) or rural/urban status (fully adjusted; p_{interaction}=0.463). In the unadjusted model there was some weak evidence that the relationship may be modified by the region of England (p_{interaction}=0.0743) and population density (p_{interaction}=0.022) although both measures weakened in the adjusted model further (Region; p_{interaction}=0.165, Population Density; p_{interaction}=0.281). In the final, adjusted, regression model, estimating the risk of death (adjusted for age, sex and rural/urban area),

in the final, adjusted, regression model, estimating the risk of death (adjusted for age, sex and rural/urban area),
 comparing the risk of death in the most deprived five deciles with the least deprived five deciles, gave compatible
 results to those from the main analysis (RR 1.47 (95% Cl 1.35-1.60), p<0.001), and a population attributable risk
 fraction of 21.2% (95% Cl 16.7%-25.4%).

The absolute number of deaths where modifiable factors were identified increased as measures of deprivation increased (Figure 1), with additional strong evidence that the proportion of deaths with modifiable contributory factors identified at the CDOP review increased with increasing measures of deprivation; with 24.2% of deaths in the least deprived, compared with 35.1% of deaths in the most (p_{trend}<0.001) (Table 4).

Table 4. The number of deaths, in each deprivation decile with identified modifiable factors; and the relative risk of death for each increasing deprivation decile with, or without them; split by category of death.

Category of Death		Perce			nodifiable fa	ctors		Relative risk increasing o decile*	
	All deciles		Split b	y Deprivatio	on Decile				
		1/2 N (%) (Least Deprived)	3/4 N (%)	5/6 N (%)	7/8 N (%)	9/10 N (%) (Most Deprived)	P _{trend}	Death without Modifiable Factors	Deaths with Modifiab Factors
All Deaths	842 (31.3%)	71 (24.2%)	114 (29.8%)	125 (26.3%)	219 (34.0%)	313 (35.1%)	<0.001	1.07 (1.05- 1.08)	1.12 (1.0 1.15)
Split by type of Modifiable Factors				•					
Characteristics of the child	70 (2.6%)	9 (3.1%)	14 (3.7%)	6 (1.3%)	15 (2.3%)	26 (2.9%)	0.797	1.08 (1.07- 1.10)	1.10 (1.0 1.21)
Physical Environment	185 (6.9%)	18 (6.1%)	30 (7.8%)	29 (6.1%)	41 (6.4%)	67 (7.5%)	0.764	1.08 (1.07- 1.10)	1.08 (1.0 1.14)
Service Provision	243 (7.9%)	26 (8.9%)	43 (11.2%)	47 (9.9%)	57 (8.9%)	70 (7.9%)	0.131	1.08 (1.07- 1.10)	1.07 (1.0 1.12)
Social Environment	416 (15.5%)	29 (9.9%)	46 (12.0%)	51 (10.7%)	106 (16.5%)	184 (20.6%)	<0.001	1.07 (1.05- 1.09)	1.15 (1.1 1.20)
Split by Category of Death									
Acute Medical and Surgical	42 (24.6%)	5 (22.7%)	8 (26.7%)	7 (25.0%)	9 (20.0%)	13 (29.0%)	0.815	1.05 (0.98- 1.12)	1.10 (0.9 1.24)
Congenital Anomalies	99 (14.9%)	5 (8.3%)	6 (8.5%)	11 (9.4%)	27 (18.4%)	50 (18.5%)	0.001	1.11 (1.07- 1.15)	1.27 (1.1 1.40)
Chronic Medical	21 (15.7%)	1 (6.7%)	2 (12.5%)	6 (20.0%)	4 (12.9%)	8 (19.1%)	0.597	1.09 (1.01- 1.17)	1.14 (0.9 1.35)
Deliberately inflicted injury	43 (70.5%)	4 (50.0%)	7 (87.5%)	6 (75.0%)	12 (75.0%)	14 (66.7%)	0.911	1.08 (0.90- 1.29)	1.12 (0.9 1.26)
Infection	61 (35.5%)	6 (26.1%)	1 (6.7%)	13 (52.0%)	20 (37.0%)	21 (38.2%)	0.126	1.07 (1.00- 1.15)	1.20 (1.0 1.33)
Malignancy	11 (5.2%)	0 (0.0%)	1 (2.4%0	5 (11.9%)	2 (5.6%)	3 (5.7%)	0.181	0.99 (0.94- 1.05)	1.15 (0.9 1.46)
Perinatal	270 (32.0%)	18 (24.3%)	39 (30.5%)	34 (22.4%)	83 (37.2%)	96 (35.8%)	0.015	1.06 (1.03- 1.10)	1.09 (1.0 1.14)
SUDIC	157 (75.1%)	9 (52.9%)	23 (76.7%)	28 (63.6%)	38 (79.2%)	59 (80.8%)	0.045	1.02 (0.92- 1.12)	1.14 (1.0 1.21)
Suicide	59 (57.8%)	12 (63.2%)	9 (45.0%)	8 (47.1%)	9 (50.00%)	21 (75.0%)	0.317	1.01 (0.90- 1.12)	1.04 (0.9 1.14)
Trauma	79 (68.1%)	11 (64.7%)	18 (75.0%)	7 (53.9%)	15 (60.0%)	28 (75.7%)	0.743	1.00 (0.89- 1.12)	1.07 (0.9 1.17)

N.B. In this work an increase in the deprivation decile indicates a higher level of local deprivation * Adjusted for age, sex, region and rural/urban area

Children who died with modifiable factors showed a stronger gradient with increasing deprivation (RR 1.12 (1.09-1.15)) compared to those who died without (RR 1.07 (1.05-1.08)). Individually, only those modifiable factors relating to social environment appeared to show this gradient (p_{trend} <0.001), with less evidence (but small numbers) for those factors around the child, services, or their physical environment. When stratifying by the category of death there was evidence that modifiable factors were more commonly identified in deaths in areas or greater deprivation for congenital anomalies (p_{trend} =0.001), perinatal (p_{trend} =0.045) and SUDIC (p_{trend} =0.045) deaths; with corresponding greater relative risks with deprivation compared to deaths without modifiable factors identified (e.g. Relative risk of death from a congenital abnormality with increasing deprivation was 1.11 (95% Cl 1.07-1.15) for deaths without modifiable factors, and 1.27 (95% Cl 1.16-1.40) for those with).

When analysing the associations between the risk of childhood death and the deprivation sub-domains (Appendix 1), many of the components of the IMD appeared to be closely correlated, with Income and Employment the highest correlation of 0.939 (Appendix 2). The sub-domains selected by the adaptive model, as the strongest associations with childhood deaths (and each categories of death), are shown in Table 5.

					Category of	of Death					
IMD Sub-decile	All Deaths	Acute Medical and Surgical	Congenital Anomalies	Chronic Medical	Deliberately inflicted injury	Infection	Malignancy	Perinatal	SUDIC	Suicide or deliberate self- harm	Trauma
Income					$\mathbf{N}_{\mathbf{i}}$						
Employment	1.04 (1.01-1.07)							1.04 (1.01-1.07)		1.12 (1.02-1.23)	
Child Education						1.11 (1.05-1.18)					
Adult Education	1.03 (1.00-1.05)		1.12 (1.08-1.16)								
Health		1.07 (1.01-1.14)		1.13 (1.05-1.21)							
Crime	0.97 (0.95-0.99)		0.95 (0.91-0.99)							0.90 (0.82-0.99)	
Geographic Barriers											
Wider Barriers	1.06 (1.03-1.08)		1.07 (1.02-1.12)					1.06 (1.02-1.11)			
Outdoor Living Environment			1.04 (1.01-1.07)				5				
Indoor Living Environment	1.03 (1.01-1.05)		1.05 (1.01-1.09)								

Table 5. Sub-domain measures identified as stongest associations with childhood death

 * Adjusted for age, sex, region and rural/urban area Red boxes show measures where increase in deprivation measures are associated with high risks of death Green boxes show measures where increase in deprivation measures are associated with lower risks of death
 Measures of deprivation in the domains of Employment, Adult Education, Wider barriers (includes issues relating to housing such as affordability and homelessness) and Indoor Living Environments were identified as most correlated with all-cause mortality. Crime also appeared correlated, but in the opposite direction to the others (i.e. increasing

measures of deprivation was associated with lower mortality). There was no clear association of any sub-domain and death by malignancy or deliberately inflicted injury; while in contrast the model for perinatal deaths (the single most common category of death) identified measures of Employment and Wider Barriers as possible predictors. Due to the unexpected association between measures of Crime and reductions in risk of death in the adaptive models, a post-hoc analysis was performed to assess the association between this measure and overall mortality. In this model (without the other sub-domain measures of deprivation), increases in measures of deprivation related to crime were associated with increased child mortality (RR 1.06 (95% CI 1.03-1.09), p<0.001).

Repeating the main analysis but using the Income Deprivation Affecting Children Index (IDACI), a metric for the proportion of all children (aged 0 to 15) living in income deprived families, gave similar results to the main analysis (unadjusted RR 1.10 (95% CI 1.09-1.12), p<0.001)); fully adjusted RR 1.08 (95% CI 1.06-1.09), p<0.001).

DISCUSSION

Key Findings

Over a fifth of all child deaths may be avoided if the most deprived half of the population had the same mortality as the least deprived, alongside pervasive evidence of a clear gradient of increasing childhood mortality across England as measures of deprivation increase; with a striking finding that this varied little by area, age or other demographic factors. While we acknowledge this gradient is not new[9], the magnitude of the associations is sobering and this study adds detail around the social patterning of potentially modifiable factors. The proportion of modifiable factors increased with increasing deprivation; and this appeared to be restricted to social factors such as financial difficulties, homelessness or poor maternal nutrition. In this detailed analysis an association was seen in most of the categories of death (including the largest category, perinatal); with only causation of death by malignancies, suicide or deliberate self-inflicted harm, and trauma not having clear evidence of an association.

Strengths and Limitations

Chance and statistical power are always potential limitations in any statistical analysis, although results in this work were relatively precise. NCMD data is likely to have captured the vast majority of deaths, as child death notifications in England to the NCMD are a statutory requirement, and comparisons with ONS child mortality data for 0-15 year olds in England in 2020, show that there were 1% more deaths reported in NCMD.[18] However, we acknowledge that some deaths may not have been reported. In addition, postcode data may not have been the child's only residence; so other influences, unmeasured in this work, may have also impacted on their outcome. However this seems unlikely to have introduced significant bias, and the population nature of the index may be more likely to reduce any direct effect of inequalities than introduce a false association at the individual level. It is important to note that measures of deprivation are derived from neighbourhood measures, and even if directly relevant to the child, assumptions of causality are complex. In contrast, the relative increase in reported modifiable factors, as the index of deprivation increases does suggest that some of the excess mortality estimated here maybe avoidable. This work is novel, with the ability to report and review an individual/record level cohort of childhood mortality, alongside the detailed information obtained at the multi-agency review of every death.

Results in Context

The population attributable risk (of 20%) identifed here is crude, but a worrying estimate of the impact of deprivation in child mortality in England; and would equate to over 700 excess deaths a year in England. It highlights the importance of future work to identify the causal pathways involved and to develop interventions that effectively address the causes and improve survival. While some areas appear relatively unrelated to deprivation (e.g. malignancy) most of these represent relatively uncommon categories of death. Perinatal events, which was the most prevalent, were strongly associated with deprivation and modifiable factors. We did identify some levels of variation of this association across some measures available to us, but overall the increasing risk with deprivation and child mortality was seen across the whole of England, in all age groups, and communities. Children under 1 living in areas of greater deprivation did appear to have the highest risk of death and this needs further analysis and exploration of potential causal mechanisms but may be due to different disease processes affecting children at different ages, or the differential

impact of deprivation at critical periods of the children's lives. This finding is consistent with the findings from the national perinatal mortality surveillance data, which reported that women living in the most deprived areas are at an 80% higher risk of stillbirth and neonatal death compared to women living in the least deprived areas.[19] Given that death caused by perinatal events also represents the biggest number of childhood deaths in England,[20] these findings provide further evidence for the importance of prioritising interventions around pregnancy and the start of life when parents are especially open to support, and targeting families at higher risk.[1] The Marmot review and subsequent reviews recommend that equity be placed at the heart of national decisions about education policy and funding.[1] This study provides further evidence for continued investment in current policies such as the National Healthy Child Programme which are based in the concept of proportionate universalism and designed to address health inequalities for children aged 0-19.[21]

Like the wider association with all deaths, the mechanisms are likely to be highly complex, and a combination of the intergenerational impact of poverty on family health and lifestyle choices such as maternal diet and family nutrition,[22] parental smoking,[23] as well as the environmental impacts of deprivation, such as housing quality, road traffic pollution, and access to health and social care services which create intersectional disadvantage. Further evaluation of community level interventions is needed, for example there is evidence that programmes such as Sure Start reduced the likelihood of hospitalisation among children of primary school age with greater impact on children living in the most deprived areas.[24]

Wider Implications

Reviewing the components which make up the deprivation index, it should be noted that many of the measures remain very inter-dependent (e.g. income and education) and interpretation should be cautious. Despite universal healthcare, employment was a key association for several of the cause of death categories, and access to care is likely to be an important mediating factor that is amenable to change.[25] A strong association between child mortality and income inequality has been reported amongst the wealthier OECD countries[26] and the UK has among the highest levels of income inequality in Europe.[27] The highest reported measure of income inequality in the UK over the last decade was in the period April 2019 to March 2020[28] and impacts from the COVID pandemic are likely to have worsened this trend. It is notable that Employment, Adult Education, Wider barriers and Indoor Living Environments appear important predictors of child mortality suggesting that adult employment and education opportunities, and access and improvements to housing, may be the most efficient place to target resources in order to reduce these inequalities. This triangulates with qualitative work which identified the lack of cleanliness, unsuitable accommodation (e.g. overcrowding or damp/mould) and financial issues being commonly reported modifiable factors after a child dies.[12] Some component of reverse causality is possible, with households moving to more deprived areas due to family impact of childhood ill health and disability; although children with chronic health conditions may find accessing services or housing/financial support more difficult than others. [12] The unexpected association, in the multivariable model, was that of an inverse relationship (compared to the other data) with measures of crime. While it should be noted that before adjusting for other, correlated, measures of deprivation, increasing measures of crime remained associated with increased risk of childhood death; the finding is interesting, and some component measured in the crime metric provides additional and novel information in this area.

⁵⁷ Currently the child death review data collection form contains a free text area where social deprivation related factors
 ⁵⁸ are noted if considered relevant by the CDOP review panel. The form does not include specific and prompting
 ⁶⁰ questions for possible factors relating to social deprivation, and improvements in collecting these data in a
 ⁶¹ standardised format would assist in more detailed analysis of future deaths; and comparisons with control population

BMJ Open

would be vital in placing future work in context. Any future analyses should explore the information collected about the circumstances of death and modifiable factors in greater detail while analyses following on from this will also need to interpret the results in the context of the economic and social impact of the COVID-19 pandemic.

Conclusion

<text> There is evidence of a clear gradient of increasing child mortality across England as measures of deprivation increase; with a striking finding that this varied little by area, age or other demographic factor. Over a fifth of all child deaths may be avoided if the most deprived half of the population had the same mortality as the least deprived. Children dying in more deprived areas may have a greater proportion of avoidable deaths, while adult employment and education opportunities, and access and improvements to housing, may be the most efficient place to target resources in order to reduce these inequalities.

Acknowledgements

1

2

3 4

5

6 7

8

9

29 30 31

32

54

We thank all Child Death Overview Panels (CDOPs) who submitted data for the purposes of this report and all child death review professionals for submitting data and providing additional information when requested.

Parent and public involvement is at the heart of the NCMD programme. We are indebted to Charlotte Bevan (Sands -

Stillbirth and Neonatal Death Charity), Therese McAlorum (Child Bereavement UK) and Jenny Ward (Lullaby Trust),

who represent bereaved families on the NCMD programme steering group.

We thank the NCMD team for technical and administrative support.

¹⁴ Ethics approval and consent to participate

The NCMD legal basis to collect confidential and personal level data under the Common Law Duty of Confidentiality has been established through the Children Act 2004 Sections M - N, Working Together to Safeguard Children 2018 (https://consult.education.gov.uk/child-protection-safeguarding-and-family-law/working-together-to-safeguard-childrenrevisions-t/supporting_documents/Working%20Together%20to%20Safeguard%20Children.pdf) and associated Child Death Review Statutory & Operational

22 Detail review statutory a operational
 23 Guidance <u>https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/859302/c</u>
 24 <u>hild-death-review-statutory-and-operational-guidance-england.pdf</u>).

The NCMD legal basis to collect personal data under the General Data Protection Regulation (GDPR) without consent is defined by GDPR Article 6 (e) Public task and 9 (h) Health or social care (with a basis in law).

Authors Contributions

33 David O: I declare that I participated in the study concept and design, contributed to acquisition, analysis and

interpretation of data, drafting and review of the manuscript and that I have seen and approved the final version.

SS: I declare that I participated in the study design, contributed to data acquisition, linkage, analysis and interpretation
 of analysis, drafting and review of the manuscript; and that I have seen and approved the final version.

TW: I declare that I participated in the study design, contributed to data acquisition, linkage, analysis and interpretation
 of data analyses, reviewing the manuscript; and that I have seen and approved the final version.

Dawn O: I declare that I contributed to study design, interpretation of data analysis, reviewing the manuscript; and that
 I have seen and approved the final version.

JK: I declare that I contributed to study design, interpretation of data analysis, reviewing the manuscript; and that I
 have seen and approved the final version.

IW: I declare that I contributed to study design, interpretation of data analysis, reviewing the manuscript; and that I
 have seen and approved the final version.

KL: I declare that I obtained funding for this work, participated in the study concept and design, contributed to data
 acquisition and interpretation of data, drafting and reviewing the manuscript; and that I have seen and approved the
 final version.

55 56 **Competing Interests**

57 David O: I have no conflicts of interest.

59 SS: I have no conflicts of interest.

⁶⁰ TW: I have no conflicts of interest.

Dawn O: I have no conflicts of interest.

- JK: I have no conflicts of interest.
- IW: I have no conflicts of interest.
- KL: I have no conflicts of interest.

Funding

The National Child Mortality Database (NCMD) Programme is commissioned by the Healthcare Quality Improvement Partnership (HQIP) as part of the National Clinical Audit and Patient Outcomes Programme (NCAPOP). HQIP is led by a consortium of the Academy of Medical Royal Colleges, the Royal College of Nursing, and National Voices. Its aim is to promote quality improvement in patient outcomes. HQIP holds the contract to commission, manage and develop the National Clinical Audit and Patient Outcomes Programme (NCAPOP), comprising around 40 projects covering care provided to people with a wide range of medical, surgical and mental health conditions. NCAPOP is funded by NHS England, the Welsh Government and, with some individual projects, other devolved administrations and crown dependencies www.hgip.org.uk/national-programmes. NHS England provided additional funding to the NCMD to enable rapid set up of the real-time surveillance system and staff time to support its function but had no input into the data analysis or interpretation.

Availability of data

Aggregate data may be available on request to the corresponding author, and subject to approval by HQIP.

REFERENCES

4	
5	1. Marmot M. Fair society, healthy lives: the Marmot review. Strategic Review of Health Inequalities in England
6	Post 2010. 2010.
7	
8 9	
9 10	and development: a European-wide systematic review. Pediatric research. 2014;76(5):418-24.
11	3. Marmot M, Friel S, Bell R, Houweling TAJ, Taylor S. Closing the gap in a generation: health equity through
12	action on the social determinants of health. Lancet (London, England). 2008;372(9650):1661-9.
13	4. Bundy DAP, de Silva N, Horton S, Patton GC, Schultz L, Jamison DT. Investment in child and adolescent health
14	and development: key messages from Disease Control Priorities, 3rd Edition. Lancet (London, England).
15	2018;391(10121):687-99.
16	5. The NHS long term plan. 2019. <u>https://www.longtermplan.nhs.uk/</u>
17	6. MacDorman MF, Matthews TJ, Mohangoo AD, Zeitlin J. International comparisons of infant mortality and
18	related factors: United States and Europe, 2010. National vital statistics reports : from the Centers for Disease
19 20	Control and Prevention, National Center for Health Statistics, National Vital Statistics System. 2014;63(5):1-6.
20 21	7. Lozano R, Fullman N, Mumford JE, Knight M, Barthelemy CM, Abbafati C, et al. Measuring universal health
22	coverage based on an index of effective coverage of health services in 204 countries and territories,
23	1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. The Lancet.
24	2020;396(10258):1250-84.
25	8. Zylbersztejn A, Gilbert R, Hjern A, Wijlaars L, Hardelid P. Child mortality in England compared with Sweden: a
26	birth cohort study. Lancet (London, England). 2018;391(10134):2008-18.
27	9. Taylor-Robinson D, Lai ETC, Wickham S, Rose T, Norman P, Bambra C, et al. Assessing the impact of rising
28	child poverty on the unprecedented rise in infant mortality in England, 2000-2017: time trend analysis. BMJ open.
29 30	2019;9(10):e029424-e.
31	10. National Child Mortality Database.
32	11. Child Death Review: Statutory and Operational Guidance (England). HM Government (UK). London; 2018.
33	https://www.gov.uk/government/publications/child-death-review-statutory-and-operational-guidance-england
34	12. Odd D, Stoianova S, Sleap V, Williams T, Cook N, McGeehan L, et al. Child Mortality and Social Deprivation.
35	National Child Mortality Database (UK). 2021. https://www.ncmd.info/2021/05/13/dep-report-2021/
36	13. McLennan D, Noble S, Noble M, Plunkett E, Wright G, Gutacker N. The English Indices of Deprivation 2019:
37	Technical Report. Ministry of Housing, Communities and Local Government. 2019.
38 39	14. Lower layer Super Output Area population estimates (supporting information). 2020.
40	15. Rural Urban Classification (2011) of Lower Layer Super Output Areas in England and Wales. 2018.
41	16. Population estimates for the UK, England and Wales, Scotland and Northern Ireland: mid-2019. Office for
42	National Statistics (UK). 2020.
43	17. Cuzick J. A Wilcoxon-type test for trend. Statistics in medicine. 1985;4(1):87-90.
44	18. Child mortality (death cohort) tables in England and Wales. Office for National Statistics (UK); 2022.
45	<u>https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/datasets/childmortalitystatisticschildhoodinfantandperinatalchildhoodinfantandperinatalmortalityinenglandandwales</u>
46 47	19. UK Perinatal Deaths for Births from January to December 2018. 2020.
48	https://www.npeu.ox.ac.uk/assets/downloads/mbrrace-uk/reports/perinatal-surveillance-report-2018/MBRRACE-
49	UK Perinatal Surveillance Report 2018 - final v3.pdf
50	20. Williams T, Sleap V, Stoianova S, Rossouw G, Cook N, Odd D, et al. NCMD second annual report. National
51	Child Mortliaty Database (UK). 2021. https://www.ncmd.info/wp-
52	content/uploads/2021/06/NCMD 2nd Annual Report June-2021 web-FINAL.pdf
53	21. Healthy child programme 0 to 19: health visitor and school nurse commissioning. 2021.
54 55	https://www.gov.uk/government/publications/healthy-child-programme-0-to-19-health-visitor-and-school-nurse-
56	commissioning#full-publication-update-history
57	22. Growing Up in the UK. 2013. <u>https://www.bma.org.uk/media/2049/growingupinuk_may2013.pdf</u>
58	 PHE Strategy 2020-25. 2019. <u>https://www.sind.org.uk/metud/2045/growingdpinuk_indy2015.pdf</u>
59	 Cattan S, Conti G, Farquharson C, Ginja R. The Health Effects of Sure Start. Institute for Fiscal Studies. 2019.
60	https://www.ifs.org.uk/publications/14139

1 2	25. Dixon-Woods M, Cavers D, Agarwal S, Annandale E, Arthur A, Harvey J, et al. Conducting a critical interpretive synthesis of the literature on access to healthcare by vulnerable groups. BMC medical research
3 4	methodology. 2006;6:35
5	26. Collison D, Dey C, Hannah G, Stevenson L. Income inequality and child mortality in wealthy nations. Journal
6 7	of public health (Oxford, England). 2007;29(2):114-7. 27. Francis-Devine B. Income inequality in the UK. 2020.
8	https://researchbriefings.files.parliament.uk/documents/CBP-7484/CBP-7484.pdf
9	28. Household income inequality, UK: financial year ending 2020. Office of National Statistics (UK). 2021.
10 11	https://www.ons.gov.uk/peoplepopulationandcommunity/personalandhouseholdfinances/incomeandwealth/bulleti
12	ns/householdincomeinequalityfinancial/financialyearending2020
13 14	
15	
16	
17 18	
19	
20 21	
22	
23 24	
24 25	
26	
27 28	
29	
30 31	
32	
33 34	
35	
36 37	
38	
39 40	
40 41	
42	
43 44	
45	
46 47	
48	
49 50	
51	
52 53	
54	
55 56	
57	
60	
57 58 59	

Figure 1. Number of deaths with modifiable factors identified at review, split by measure of local deprivation

for peer teriew only

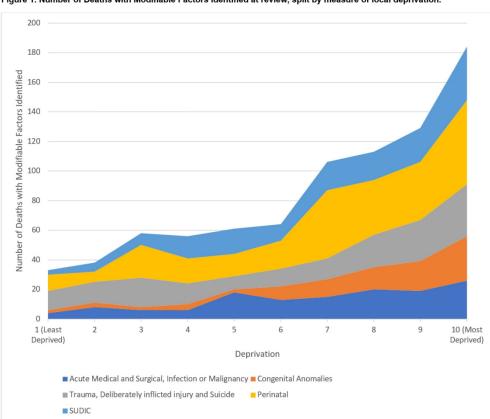
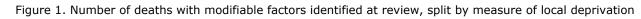


Figure 1. Number of Deaths with Modifiable Factors identified at review, split by measure of local deprivation.



468x407mm (72 x 72 DPI)

Appendix 1. Sub-domains of deprivation (Weight for the overall IMD in brackets).

Income Deprivation (22.5%)

The Income Deprivation Domain measures the proportion of the population in an area experiencing deprivation relating to low income.

Employment Deprivation (22.5%)

The Employment Deprivation Domain measures the proportion of the working-age population in an area involuntarily excluded from the labour market; this includes people who are unable to work due to unemployment, sickness or disability, or caring responsibilities.

Education, Skills and Training Deprivation (13.5%)

The Education, Skills and Training Domain measures the lack of attainment and skills in the local population. The indicators fall into two sub-domains: one relating to children and young people and one relating to adult skills. The Children and Young People Sub-domain measures the attainment of gualifications and associated measures, while the Adult Skills Sub-domain measures the lack of qualifications in the resident working-age adult population.

Health Deprivation and Disability (13.5%)

The Health Deprivation and Disability Domain measures the risk of premature death and the impairment of quality of life through poor physical or mental health. The domain measures morbidity, disability and premature mortality but not aspects of behaviour or environment that may be predictive of future health deprivation.

Crime (9.3%)

The Crime Domain measures the risk of personal and material victimisation at local level.

Barriers to Housing and Services (9.3%)

The Barriers to Housing and Services Domain measures the physical and financial accessibility of housing and local services. The indicators fall into two sub-domains: the Geographical Barriers Sub-domain, which relates to the physical proximity of local services, and the Wider Barriers Sub-domain which includes issues relating to access to housing such as affordability.

Living Environment Deprivation (9.3%)

The Living Environment Deprivation Domain measures the quality of the local environment. The indicators fall into two sub-domains. The Indoors Sub-domain measures the quality of housing; while the Outdoors Sub-domain contains measures of air quality and road traffic accidents.

Health

Crime

0.800

0.652

0.733

1

1	Appendix 2. W	eights of	each sub-	decile c	domain t	owards t	he total se	core, and c	orrelatio	ns between	domains.
2					Crime	Child	Adult	Geographic	Wider	Indoor Livina	Outdoor Living
3		Income	Employment	Health		Education	Education	Barriers	Barriers	Environment	Environment
4	Income	1.000									
5											
5	Employment	0.938	1.000								
6											
-	1.1 141-	0.000	0.040	1 000							(

1.000

1.00

Wider Barriers 0.539 0.393 0.273 0.512 0.295 0.298 -0.487 1.00 Indoor Living Environment 0.173 0.137 0.168 0.187 0.124 0.047 -0.191 0.133	Geographic Barriers Wider Barriers Indoor Living Environment			0.701	0.499	0 769				
Wider Barriers 0.539 0.393 0.273 0.512 0.295 0.298 -0.487 1.00 Indoor Living Environment 0.173 0.137 0.168 0.187 0.124 0.047 -0.191 0.133 Outdoor Living Environment 0.257 0.153 0.131 0.447 0.009 0.083 -0.410 0.575	Wider Barriers Indoor Living Environment	-0.443				0.705	1.00			
Indoor Living Environment 0.173 0.137 0.168 0.187 0.124 0.047 -0.191 0.133 Outdoor Living Environment 0.257 0.153 0.131 0.447 0.009 0.083 -0.410 0.575	Indoor Living Environment		-0.380	-0.367	-0.464	-0.228	-0.251	1.000		
Environment Outdoor Living 0.257 0.153 0.131 0.447 0.009 0.083 -0.410 0.575	Environment	0.539	0.393	0.273	0.512	0.295	0.298	-0.487	1.00	
Outdoor Living Environment 0.257 0.153 0.131 0.447 0.009 0.083 -0.410 0.575		0.173	0.137	0.168	0.187	0.124	0.047	-0.191	0.133	1
		0.257	0.153	0.131	0.447	0.009	0.083	-0.410	0.575	0
	diagonal me	∍asures ar	re correlatio	on betwe	en sub-c	leciles of	the IMD.			

0.849

0.607

0.723

1.000

0.591

0.659

1.000

0.456

STROBE Statement—Checklist of items that should be included in reports of cohort studies

	Item No	Recommendation	Page No
Title and abstract	1	(<i>a</i>) Indicate the study's design with a commonly used term in the title or the abstract	1
			3
		(<i>b</i>) Provide in the abstract an informative and balanced summary of what was done and what was found	
.		uone and what was found	
Introduction	2		4
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	-
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of	5
6		recruitment, exposure, follow-up, and data collection	
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of	5-6
a and parts	Ũ	participants. Describe methods of follow-up	
		(b) For matched studies, give matching criteria and number of exposed and	
		unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and	5-6
v artables	7	effect modifiers. Give diagnostic criteria, if applicable	
Data sources/	8*	For each variable of interest, give sources of data and details of methods of	5-6
measurement	0	assessment (measurement). Describe comparability of assessment methods if	
medsurement		there is more than one group	
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	10	Explain how quantitative variables were handled in the analyses. If applicable,	5
Quantitative variables	11	describe which groupings were chosen and why	
Statistical methods	12	(<i>a</i>) Describe all statistical methods, including those used to control for	5-6
Statistical includes	12	confounding	
		(b) Describe any methods used to examine subgroups and interactions	5-6
		(c) Explain how missing data were addressed	5
		(d) If applicable, explain how loss to follow-up was addressed	5
		(e) Describe any sensitivity analyses	6
D		(<u>e</u>) Describe any sensitivity analyses	-
Results	104		6
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers	0
		potentially eligible, examined for eligibility, confirmed eligible, included in	
		the study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	-
		(c) Consider use of a flow diagram	- Tabla
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social)	Table
		and information on exposures and potential confounders	T-11
		(b) Indicate number of participants with missing data for each variable of	Table
		interest	
		(c) Summarise follow-up time (eg, average and total amount)	-
Outcome data	15*	Report numbers of outcome events or summary measures over time	6

BMJ Open

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

*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 http://www.strobe-statement.org.