Global determinants of mortality in under 5s: 10 year worldwide longitudinal study

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STUDY QUESTION What is the impact of a large set of determinants on mortality in under 5s at country level?
SUMMARY ANSWER Major determinants of mortality in under 5s were identified. Retrieved relations with such mortality were often non-linear and potentially mediated by lag effects.
WHAT IS KNOWN AND WHAT THIS PAPER ADDS Several studies have already explored global determinants that might have an influence on the mortality rate in under 5s. Most previous studies were cross sectional, assumed linear relations between log mortality in under 5s and its determinants, and focused on immediate action of determinants. By providing a unified framework for mortality in under 5s, encompassing both high and low income countries, this longitudinal study showed non-linear behaviours and lag effects of known or suspected determinants of mortality in under 5s.

Participants and setting

Yearly data on 12 world development indicators from 193 United Nations member countries, 2000-09.

Methods

We fitted a multivariable general additive mixed model allowing for lag effects to the data.

Primary outcomes

The logarithm of mortality in under 5s in 193 countries between 2000 and 2009 compiled by the UN. Such mortality was defined as the national rate of deaths in under 5s per 1000 live births.

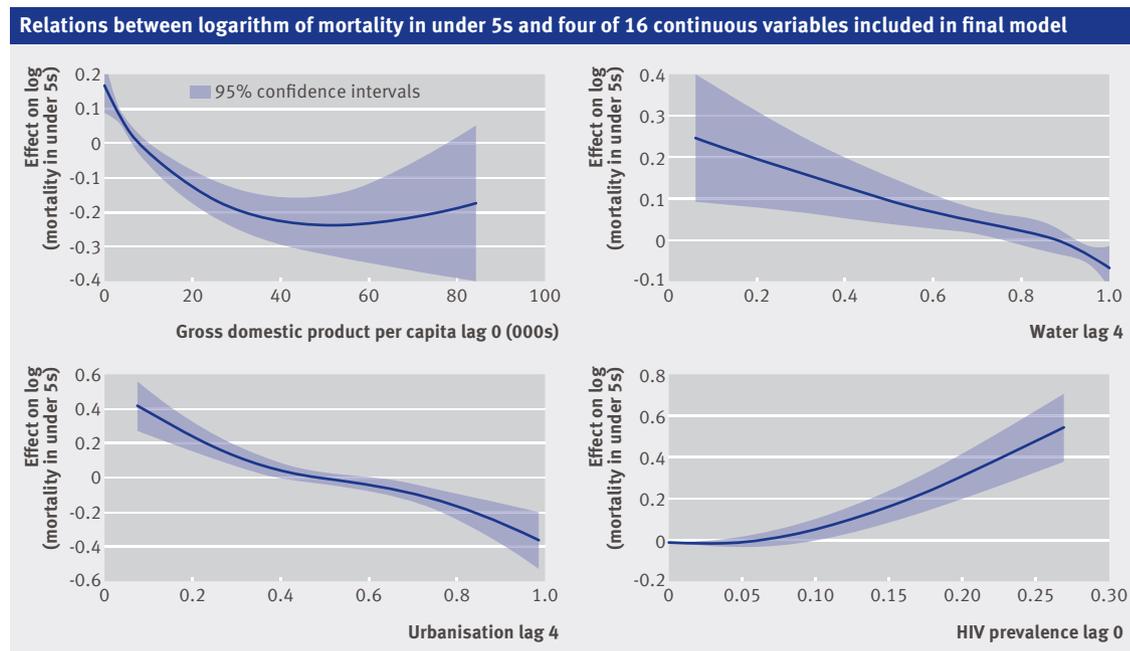## Main results and the role of chance

The model retained the variables: gross domestic product per capita; percentage of population having access to improved water sources, having access to improved sanitation facilities, and living in urban areas; adolescent fertility rate; public health expenditure per capita; HIV prevalence; perceived level of corruption and of violence; and mean number of years in school for women of reproductive age. Some of these variables presented a linear action on log mortality in under 5s indicating that whatever the context, acting on them would be a pertinent strategy to reduce mortality. Others had a threshold based relation potentially mediated by lag effects. The figure shows four retrieved relations and associated lags (in years).

Bias, confounding, and other reasons for caution

The analysis had several limitations. Firstly, ecological studies are known to be prone to bias. Secondly, this study relied on aggregated data estimated by the UN. Other estimations relying on different assumptions and data sources could be considered. Thirdly, some effects might be biased by not considering important but unavailable factors, such as breast feeding or inequality in income. Fourthly, given the definition of lag effects of determinants of mortality in under 5s, the identified lags were only rough indicators and did not perfectly reflect the temporal gradient of determinant relation to outcome. The robustness of results was assessed by performing separate analyses for low income and high income countries.

Study funding/potential competing interests

See bmj.com.

Relations between logarithm of mortality in under 5s and four of 16 continuous variables included in final model

Physical activity and risk of inflammatory bowel disease: prospective study from the Nurses' Health Study cohorts

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STUDY QUESTION
What is the association between physical activity and risk of ulcerative colitis and Crohn's disease?

SUMMARY ANSWER
Physical activity was inversely associated with risk of Crohn's disease but not of ulcerative colitis.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS
Many previous studies have limited information on physical activity and lifestyle factors that can influence or modify the association between physical activity and risk of inflammatory bowel disease. Our data show that increased physical activity is associated with a lower risk of Crohn's disease but not of ulcerative colitis. Taken together with previous observations that physical activity may induce autophagy and modulate innate immunity, our findings suggest that such pathways may play a stronger role in the cause of both diseases.

Participants and setting
Women enrolled in the US Nurses' Health Study and Nurses' Health Study II who provided updated data on physical activity and other risk factors.

Design, size, and duration
We prospectively examined 194 711 women who provided data on physical activity and other risk factors, every two to four years since 1984 in the Nurses' Health Study and since 1989 in the Nurses' Health Study II and followed up through 2010.

Main results and the role of chance
During 3 421 972 person years of follow-up, we docu-mented 284 cases of Crohn's disease and 363 cases of ulcerative colitis. The absolute risk of ulcerative colitis and Crohn's disease among women in the highest fifth of physical activity was 8 and 6 events per 100 000 per-son years compared with 11 and 16 events per 100 000 person years among women in the lowest fifth, respec-tively. The risk of Crohn's disease was inversely associ-ated with physical activity (P for trend 0.02). Compared with women in the lowest fifth of physical activity, the multivariate adjusted hazard ratio of Crohn's disease among women in the highest fifth was 0.64 (95% confi-dence interval 0.44 to 0.94). Active women with at least 27 metabolic equivalent task (MET) hours per week of physical activity had a 44% reduction (hazard ratio 0.56, 95% confidence interval 0.37 to 0.84) in risk of develop-ing Crohn's disease compared with women with <3 MET h/wk. Physical activity was not associated with risk of ulcerative colitis (P for trend 0.46).

Bias, confounding, and other reasons for caution
Although we had prospectively collected detailed data on a broad range of potential risk factors for both diseases, our study is observational and we cannot exclude the possibil-ity of residual confounding.

Generalisability to other populations
Our data should be generalisable to older women. It is unclear if these findings apply to other racial/ethnic groups, younger women, or men.

Study funding/potential competing interests
All researchers are independent of the study funders, the National Institute of Health, and the American Gastroen-terological Association.

Physical activity and risk of Crohn's disease and ulcerative colitis

Variables	Updated physical activity* (MET h/wk)					P for trend
	Lowest fifth	2nd fifth	3rd fifth	4th fifth	Highest fifth	
Person years	667 291	684 398	689 222	692 548	688 514	
Crohn's disease:						
No of cases	72	54	63	48	47	
Age adjusted (95% CI)	1.00	0.71 (0.50 to 1.02)	0.83 (0.59 to 1.17)	0.61 (0.42 to 0.88)	0.60 (0.42 to 0.87)	0.005
Multivariable adjusted (95% CI)†	1.00	0.74 (0.52 to 1.05)	0.88 (0.63 to 1.24)	0.65 (0.45 to 0.95)	0.64 (0.44 to 0.94)	0.02
Ulcerative colitis:						
No of cases	74	67	85	63	74	
Age adjusted (95% CI)	1.00	0.88 (0.63 to 1.23)	1.10 (0.80 to 1.51)	0.82 (0.58 to 1.15)	0.96 (0.70 to 1.33)	0.70
Multivariable adjusted (95% CI)†	1.00	0.87 (0.62 to 1.21)	1.06 (0.78 to 1.46)	0.78 (0.56 to 1.10)	0.91 (0.65 to 1.26)	0.46

MET h/wk=metabolic equivalent task hours per week.
*Mean over follow-up.
†Models adjusted for age, smoking, body mass index at baseline, oral contraceptive use, hormone therapy, appendicectomy, geographic latitude of residence at age 30, cohort, and non-steroid anti-inflammatory drug use (full details of variables are in the paper on bmj.com).

Perinatal outcomes after bariatric surgery: nationwide population based matched cohort study

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STUDY QUESTION

Do perinatal outcomes differ in births of women with versus without a history of bariatric surgery?

SUMMARY ANSWER

Women with a history of bariatric surgery are at increased risk of preterm and small for gestational age births but decreased risk of large for gestational age births compared with women with similar characteristics, including early pregnancy body mass index.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Small studies have been inconclusive regarding differences in perinatal outcomes between women with a history of bariatric surgery and obese comparators. This large cohort study found women with a history of bariatric surgery to have a greater risk of preterm and small for gestational age births but lower risk of large for gestational age births than matched controls.

Participants and setting

From the Swedish medical birth register and by linkage with the national patient register we identified 2534 singleton births to women with a history of bariatric surgery. We matched these women to 12 468 controls for maternal age, parity, early pregnancy body mass index, early pregnancy smoking status, educational level, and year of delivery (1992-2009).

Design

Population based matched cohort study. Procedure types included gastric bypass (33%, n=827), gastric banding (27%, n=692), vertical banded gastroplasty (37%, n=949), and other (2.6%, n=66).

Main results and the role of chance

Births in women with a history of bariatric surgery were more often preterm and small for gestational age than in matched controls. Body mass index seemed to be an effect modifier, and the increased risks were observed only in women with a body mass index <35. No effect modification was detected by procedure type or interval between surgery and delivery. A history of bariatric surgery was also associated with a decreased risk of large for gestational age births, whereas no differences were detected for stillbirths or neonatal deaths.

Bias, confounding, and other reasons for caution

Despite the large sample size, the number of stillbirths and neonatal deaths was low, resulting in limited statistical power.

Generalisability to other populations

Given the population based design and the national coverage of this study, the findings may be generalisable to other countries. However, the results may not be generalisable to other types of procedure, although consistent effects were seen for both restrictive and malabsorptive procedures.

Study funding/potential competing interests

Preterm birth and fetal growth outcomes for births of women with a history of bariatric surgery and matched controls

| Outcomes | No of births | | No (%) of cases | | Bariatric surgery *v* matched controls | | |
	Bariatric surgery	Matched controls	Bariatric surgery	Matched controls	Risk difference (95% CI)	Conditional odds ratio (95% CI)*	P value
Preterm birth (<37 weeks)	2511	12 379	243 (9.7)	750 (6.1)	3.6 (2.4 to 4.9)	1.7 (1.4 to 2.0)	P<0.001
Small for gestational age	2507	12 338	131 (5.2)	369 (3.0)	2.2 (1.3 to 3.2)	2.0 (1.5 to 2.5)	P<0.001
Large for gestational age	2507	12 338	105 (4.2)	895 (7.3)	−3.1 (−4.0 to −2.2)	0.6 (0.4 to 0.7)	P<0.001

*Conditioned on matching factors: maternal age, parity, early pregnancy body mass index, early pregnancy smoking status, educational level, and year of delivery.

Probiotic supplementation during pregnancy or infancy for the prevention of asthma and wheeze: systematic review and meta-analysis

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STUDY QUESTION

Is probiotic supplementation during pregnancy or infancy safe and protective against the development of asthma and wheeze?

SUMMARY ANSWER

There is currently no clinical evidence to support a protective association between perinatal probiotic supplementation and doctor diagnosed asthma or childhood wheeze.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Recent increases in asthma prevalence could be related to disruption of the infant gut microbiota and associated immune system dysfunction; therefore, perinatal probiotics have been proposed as a novel prevention strategy. This meta-analysis finds that currently, insufficient evidence exists to recommend probiotics for the primary prevention of childhood asthma, wheeze, and lower respiratory tract infection.

Selection criteria for studies

We searched Medline, Embase, and Central (Cochrane Collaboration) from inception to August 2013 for randomised controlled trials evaluating probiotic supplements administered to mothers during pregnancy or to healthy infants during the first year of life. We included trials reporting asthma or related secondary outcomes (wheeze or lower respiratory tract infection).

Primary outcome(s)

Doctor diagnosed asthma.

Main results and role of chance

Of 3011 citations, 20 unique trials enrolling a total of 4866 children met our inclusion criteria. The median age at final follow-up was 24 months and the overall rate of doctor diagnosed asthma was 10.7%. Overall rates of incident wheeze and lower respiratory tract infection were 33.3% and 13.9%, respectively. Among 3257 infants enrolled in nine trials contributing asthma data, the risk ratio of doctor diagnosed asthma after probiotic supplementation was 0.99 (95% confidence interval 0.81 to 1.21, I^2=0%). The risk ratio of incident wheeze associated with probiotic use was 0.97 (0.87 to 1.09, I^2=0%, nine trials, 1949 infants), while the risk ratio of lower respiratory tract infection was 1.26 (0.99 to 1.61, I^2=0%, six trials, 1364 infants).

Bias, confounding, and other reasons for caution

Trials were heterogeneous in the type and duration of probiotic supplementation, and none were designed to detect asthma as the primary outcome. Only five of 20 trials reported outcomes at or beyond six years of participant age, which is considered the minimum age for accurate asthma diagnosis. We adjudicated most trials to be of high (ten trials) or unclear (nine trials) risk of bias, mainly due to attrition. Planned subgroup analyses did not identify significant differences according to these parameters, but were susceptible to type II errors owing to relatively small sample sizes. Further basic and clinical research studies are needed to define the role of probiotics in the prevention of childhood asthma.

Study funding/potential competing interests

Probiotic use during pregnancy or infancy and childhood asthma

Study or subgroup	Risk ratio (95% CI), M-H, random	Weight (%)	Risk ratio (95% CI), M-H, random
Dotterud 2010		5.2	0.64 (0.27 to 1.54)
Ou 2012		7.4	1.29 (0.62 to 2.69)
Taylor 2007		3.4	1.66 (0.56 to 4.91)
Kukkonen 2007		34.9	0.93 (0.66 to 1.30)
Wickens 2008a (HN001)		14.5	0.91 (0.54 to 1.53)
Wickens 2008b (HN019)		16.4	1.04 (0.63 to 1.71)
Niers 2009		3.5	0.63 (0.21 to 1.83)
Kalliomaki 2001		2.5	3.19 (0.90 to 11.37)
Abrahamsson 2007		8.3	0.98 (0.49 to 1.97)
West 2008		4.0	1.01 (0.37 to 2.76)
Total		100.0	0.99 (0.81 to 1.21)

Test for heterogeneity: τ^2=0.00, χ^2=6.57, df=9, P=0.68, I^2=0%

Test for overall effect: z=0.10, P=0.92

Favours probiotic — Favours placebo