The impact of antibiotics on growth in children in low and middle income countries: systematic review and meta-analysis of randomised controlled trials

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STUDY QUESTION Does antibiotic treatment lead to improvements in growth in prepubertal children (1 month to 12 years old) in low and middle income countries?
SUMMARY ANSWER Antibiotics have a growth promoting effect in prepubertal children in low and middle income countries. This effect was more pronounced for ponderal growth. Effects on height were larger in younger populations, and the effects on weight were larger in African studies versus those from other regions, after adjusting for age.
WHAT IS KNOWN AND WHAT THIS PAPER ADDS Antibiotics have shown variable effects on growth in humans but are currently recommended by the World Health Organization for severely malnourished children and those infected with or exposed to HIV to reduce morbidity and mortality. Evidence from these trials shows that antibiotic use in prepubertal children from undernourished populations leads to clinically relevant growth gains, particularly for weight.

Selection criteria for studies
We searched Medline, Embase, Scopus, the Cochrane central register of controlled trials, and Web of Science to 12 December 2013. Eligible studies were randomised controlled trials conducted in low or middle income countries in which an orally administered antibacterial agent was allocated by randomisation or minimisation, and growth was measured as an outcome. Participants 1 month to 12 years old were included. Control was placebo or non-antimicrobial intervention.

Primary outcome
Treatment effect was defined as the difference in mean height (cm) or weight (g) between treated and control children for each month of follow-up.

Main results and role of chance
Antibiotic use increased height by 0.04 cm/month (95% confidence interval 0.00 to 0.07) and weight by 23.8 g/month (95% confidence interval 4.3 to 43.3).

Bias, confounding, and other reasons for caution
Included trials were conducted over a 60 year period and covered a wide range of antibiotics, treatment regimens, and indications for treatment. Trial effects were heterogeneous, and growth gains may vary with antibiotic used and target population. The small number of trials limited our power to identify moderators of treatment effect and to fully investigate trial level confounding with multivariable meta-regression. Finally, we cannot rule out cross level bias in our analyses of treatment effect moderators, particularly with respect to age.

Study funding/potential competing interests
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Antibiotic treatment effects, and effect moderators adjusted for mean population age

Effect estimated	Effect size (95% CI)
Height effects (8 trials, 4247 participants)	
Difference in mean height (treated *v* control patients)	0.04 cm/month (0.00 to 0.07)
Change in treatment effects on height per additional day of treatment	0.007 cm/month (0.00 to 0.01)
Change in treatment effects on height per 1 month increase in mean population age	−0.001 cm/month (−0.002 to 0.00)
Weight effects (10 trials, 4316 participants)	
Difference in mean weight (treated *v* control patients)	23.80 g/month (4.29 to 43.31)
Difference in treatment effects on weight by geographical region of trial (Africa *v* other)	33.2 g/month (5.3 to 61.2)
Change in treatment effects on weight per 1 month increase in mean population age (months)	−0.2 g/month (−0.4 to −0.1)

Chronic hypertension and pregnancy outcomes: systematic review and meta-analysis

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STUDY QUESTION What are the pregnancy complications in women with chronic hypertension, and how common are they in comparison with the general pregnancy population in the US?

SUMMARY ANSWER Chronic hypertension is associated with a high incidence of adverse pregnancy outcomes compared with a general population, as exemplified in this report by US data.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS Women with chronic hypertension have worse pregnancy outcomes, but the magnitude of pregnancy risk for women with chronic hypertension is uncertain from pre-existing data. Compared with a separate dataset from the US general pregnancy population, women with chronic hypertension in US studies have a nearly eightfold higher pooled incidence of superimposed pre-eclampsia than pre-eclampsia, an approximately threefold increased risk of preterm delivery before 37 weeks' gestation, birth weight <2500 g, and neonatal intensive care admission, and a fourfold increased risk of perinatal death.

Selection criteria for studies

We searched Embase, Medline, and Web of Science, without language restrictions, from the time of first publication until June 2013. We identified studies involving pregnant women with chronic hypertension, including retrospective and prospective cohorts, population studies, and appropriate arms of randomised controlled trials.

Primary outcomes

We extracted data and used mixed methods logistic regression to calculate estimated pooled incidences of the following adverse outcomes of pregnancy: superimposed pre-eclampsia, caesarean section, preterm delivery before 37 weeks' gestation, birth weight below 2500 g, perinatal death (fetal death after 20 weeks' gestation including stillbirth and neonatal death up to 1 month), and admission to a neonatal unit (neonatal intensive care or special care baby unit).

Main results and role of chance

Women with chronic hypertension had high pooled average incidences of all adverse pregnancy outcomes (see table). Comparison of pooled average incidences from US studies with the US general population dataset showed that women with chronic hypertension had worse pregnancy outcomes. Relative risks 7.7 (95% confidence interval 5.7 to 10.1) for superimposed pre-eclampsia compared with pre-eclampsia, 1.3 (1.1 to 1.5) for caesarean section, 2.7 (1.9 to 3.6) for preterm delivery before 37 weeks' gestation, 2.7 (1.9 to 3.8) for birth weight below 2500 g, 3.2 (2.2 to 4.4) for neonatal unit admission, and 4.2 (2.7 to 6.5) for perinatal death. These findings emphasise a need for heightened antenatal surveillance. They should inform counselling and contribute to optimisation of maternal health, drug treatment, and pre-pregnancy management in women affected by chronic hypertension.

Bias, confounding, and other reasons for caution

Predicted 95% interval ranges were wide, and considerable heterogeneity existed in the reported incidence of all outcomes (τ^2=0.286 to 0.766), which was not reduced by subsequent subgroup analysis including the following groupings: country's economic wealth according to World Bank classification (gross national income per capita), study period, inclusion or exclusion of multiple pregnancies, inclusion or exclusion of congenital abnormalities, inclusion or exclusion of women with secondary hypertension, study design, and study definition of chronic hypertension. Meta-regression to identify the influence of potential modifiers of outcome including parity, maternal age, and ethnicity did not identify an underlying cause, suggesting that either populations with chronic hypertension are varied or determination of chronic hypertension and outcomes may not be consistent.

Study funding/potential competing interests

KB's salary is funded by a National Institute of Health Research doctoral fellowship.

Estimated incidence and prediction intervals of adverse pregnancy outcomes for women with chronic hypertension

Outcome	No of studies	Estimated incidence (%) (95% CI)	Prediction intervals (95%)
Superimposed pre-eclampsia	38	25.9 (21.0 to 31.5)	5.5 to 67.2
Caesarean section	27	41.4 (35.5 to 47.7)	15.5 to 73.2
Preterm delivery (<37 weeks)	30	28.1 (22.6 to 34.4)	6.8 to 67.6
Birth weight <2500 g	14	16.9 (13.1 to 21.5)	5.7 to 40.6
Neonatal intensive care	16	20.5 (15.7 to 26.4)	5.9 to 51.3
Perinatal death	27	4.0 (2.9 to 5.4)	0.9 to 16.4

95% prediction intervals show uncertainty of range of possible incidence percentages for new study population, whereas 95% confidence intervals show uncertainty about estimate of average percentage incidence across study populations.

Global, regional, and national consumption levels of dietary fats and oils in 1990 and 2010: a systematic analysis including 266 country-specific nutrition surveys

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STUDY QUESTION What are the global consumption levels of key dietary fats and oils by region, country, age, and sex in 1990 and 2010?

SUMMARY ANSWER Dietary surveys covered 82% of the global population and showed both similarities and substantial diversity across regions and nations.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS Dietary fats and oils are major contributors to risk of non-communicable chronic diseases, but the patterns and distributions of their consumption by region, country, age, and sex are not well established. The present findings can help inform national and global efforts to alter diet and improve population health.

Selection criteria for studies

We conducted systematic searches (without language or date restrictions) to identify individual-level dietary national surveys worldwide. Surveys with evidence for selection or measurement bias were excluded. Data on dietary fats and oils with the largest public health impact were obtained and assessed among adults in 16 age and sex-specific groups. A multilevel hierarchical Bayesian model accounted for differences in national and regional missingness, measurement incomparability, study representativeness, and sampling and modelling uncertainty.

Primary outcome(s)

Consumption of saturated, omega 6, seafood omega 3, plant omega 3, and trans fats and dietary cholesterol.

Main results and the role of chance

A total of 266 surveys in adults (83% nationally representative) were included, comprising a total of 1 630 069 unique individuals, representing 113 of 187 countries and 82% of the global population. In 2010, global saturated fat consumption was 9.4% of total energy intake (%E) (95% uncertainty interval 9.2 to 9.5); country-specific intakes varied dramatically from 2.3%E to 27.5%E (table). Country-specific consumption of omega 6 fats ranged from 1.2%E to 12.5%E (global mean 5.9%E); corresponding consumption of trans fats was 0.2%E to 6.5%E (mean 1.4%E), of dietary cholesterol 97 to 440 mg/day (228 mg/day); of seafood omega 3 fats 5 to 3886 mg/day (163 mg/day), and of plant omega 3 fats <100 to 5542 mg/day (1371 mg/day). Trans fat intakes were generally higher at younger ages, and dietary cholesterol and seafood omega 3 fats intakes were generally higher at older ages. Intakes were similar by sex. Between 1990 and 2010, global intakes of saturated fat, dietary cholesterol, and trans fat remained stable, whereas intakes of omega 6 and of seafood and plant omega 3 fats increased.

Bias, confounding, and other reasons for caution

Dietary changes over the past 20 years should be interpreted with caution because of limited available data over time. Relatively little data were available for most sub-Saharan African nations, on trans fats, or on plant omega 3 fats.

Study funding/potential competing interests

The study was part of the Global Burden of Disease Study 2010, supported in part by the Bill & Melinda Gates Foundation. DM has received honoraria for scientific presentations, consulting, membership of an advisory board, and an online book chapter from commercial bodies (see full version for details).

Characteristics of adult global consumption of dietary fats and oils with largest public health impact in 2010

Characteristic	Saturated fats (%E)	Omega 6 polyunsaturated fats (%E)	Trans fats (%E)	Dietary cholesterol (mg/day)	Seafood omega 3 fats (mg/day)	Plant omega 3 fats (mg/day)
Global mean consumption (95% UI)	9.4 (9.2 to 9.5)	5.9 (5.7 to 6.1)	1.4 (1.36 to 1.44)	228 (222 to 234)	163 (154 to 172)	1371 (1299 to 1465)
Range across 21 global regions (overall variation)	4.3 to 23.5 (5.5-fold)	2.5 to 8.5 (3.4-fold)	0.6 to 2.9 (4.8-fold)	139 to 328 (2.4-fold)	13 to 710 (55-fold)	302 to 3205 (10.6-fold)
Range across 187 countries (overall variation)	2.3 to 27.5 (12.2-fold)	1.2 to 12.5 (10.5-fold)	0.2 to 6.5 (28.1-fold)	97 to 440 (4.5-fold)	5 to 3886 (840-fold)	2 to 5542 (2731-fold)
Countries achieving optimal mean intake, population (% of global population)	<10%E: 75 countries, 2.73bn people (61.8%)	≥12%E: 1 country, 6.1m people (0.1%)≥5%E: 94 countries, 2.32bn people (52.4%)	≤0.5%E: 12 countries, 24.4m people (0.6%)	<300 mg/day: 155 countries, 3.9bn people (87.6%)	≥250 mg/day: 45 countries, 837m people (18.9%)	≥0.5 %E or ≥1100 mg for a 2000 kcal/day diet: 52 countries, 1.94bn people (43.9%)
Countries not achieving optimal mean intake, population (% of global population)	≥10%E: 112 countries, 1.69bn people (38.2%)	<12%E: 186 countries, 4.42bn people (99.9%)<5%E: 93 countries, 2.1bn people (47.6%)	>0.5%E: 175 countries, 4.42bn people (99.4%)>2.0%E: 12 countries, 644m people (14.6%)	≥300 mg/day: 32 countries, 548m people (12.4%)	<250 mg/d: 142 countries, 3.58bn people (81.1%)<100 mg/day: 100 countries, 2.95bn people (66.8%)	<0.5 %E or <1100 mg for a 2000 kcal/day diet: 135 countries, 2.48bn people (56.1%)<500 mg/day: 61 countries, 789m people (17.8%)

UI=uncertainty interval. bn=billion. m=million.

The effect of Massachusetts health reform on 30 day hospital readmissions: retrospective analysis of hospital episode statistics

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STUDY QUESTION Can an expansion of insurance coverage, as has occurred in Massachusetts, reduce overall 30 day readmissions and disparities in this outcome?

SUMMARY ANSWER After adjustment for age, sex, comorbidity, hospital ownership, teaching hospital status, and nurse to census ratio, there was a slightly increased odds of readmission for all causes in Massachusetts compared with control states (New York and New Jersey) post-reform.

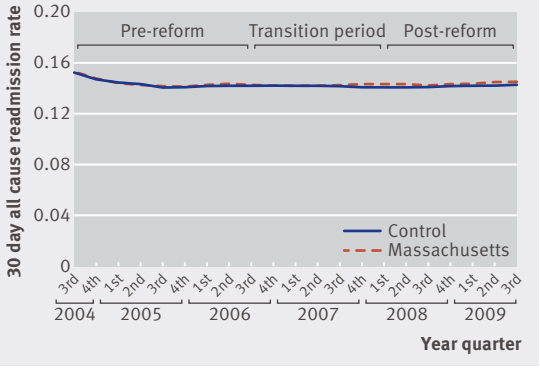
WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Uninsured patients are at increased risk for 30 day hospital readmissions. Extending health insurance coverage alone seems insufficient to improve readmission rates at the population level.

Participants and setting

Adults aged 18-64 admitted to US hospitals 2006-09 in Massachusetts, New York, and New Jersey owing to any cause, excluding obstetrical.

Quarterly readmission rate in Massachusetts *v* control states (New York and New Jersey) among patients aged 18-64



Design

Difference in differences.

Primary outcome

Risk adjusted odds of 30 day readmission for all causes.

Main results and the role of chance

After adjustment for known confounders, including age, sex, comorbidity, hospital ownership, teaching hospital status, and nurse to census ratio, the odds of all cause readmission in Massachusetts was slightly increased compared with control states post-reform (odds ratio 1.02, 95% confidence interval 1.01 to 1.04, P<0.05). Racial and ethnic disparities in all cause readmission rates did not change in Massachusetts compared with control states. In analyses limited to Massachusetts only, there were minimal overall differences in changes in readmission rates between counties with differing baseline uninsurance rates, but black people in counties with the highest uninsurance rates had decreased odds of readmission (0.91, 0.84 to 1.00) compared with black people in counties with lower uninsurance rates. Similarly, white people in counties with the highest uninsurance rates had decreased odds of readmission (0.96, 0.94 to 0.99) compared with white people in counties with lower uninsurance rates.

Bias, confounding, and other reasons for caution

No data were available on utilization of outpatient care or on individual patients' insurance status prior to and subsequent to reform.

Generalisability to other populations

Findings may not be generalizable to all populations expanding insurance coverage.

Study funding/potential competing interests

The study was funded by the United States National Heart, Lung, and Blood Institute. We have no competing interests.