

RESEARCH

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Prediction models for risk of developing type 2 diabetes

According to this study reported by Ali Abbasi and colleagues, existing prediction models, even those that incorporate only four to six predictors, are valid tools to identify people at high risk of developing type 2 diabetes. They say that models generally overestimate the actual risk, making it necessary to adapt them to local settings.

Use of population based background rates of disease to assess vaccine safety in childhood and mass immunisation in Denmark

This cohort study of 2 300 227 liveborn infants showed that incorporating exact background rates of disease based on age, sex, and seasonal distribution could strengthen vaccine safety assessment and provides an evidence based focus for discussing the incremental risk of newly introduced vaccines. These data could help distinguish events temporally associated with vaccine exposure from those events caused by such exposure, say the authors.

WHAT OUR READERS ARE SAYING

Lifestyle, social factors, and survival after age 75

In this cohort study (p 17), lifestyle behaviours such as not smoking and physical activity were associated with longer survival, even after age 75. These associations, although attenuated, were also present among people aged 85 or older and in people with chronic conditions, said the authors. Here's what some of our rapid respondents said:

"This study shows the necessity of investing in social medicine. Medical schools will need to respond to social accountability."

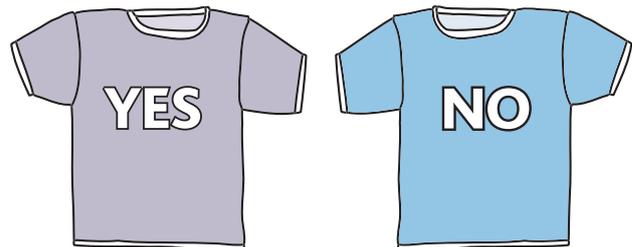


"Prevention and health education is an important aspect in caring for older people."

"Can the authors comment on whether religious activities and the mental, productive, and social stimulation they provide are any more beneficial than non-religious activities?"

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Clinicians' gut feeling about serious infections in children: observational study

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Research: Diagnostic value of laboratory tests in identifying serious infections in febrile children (*BMJ* 2011;342:d3082)

STUDY QUESTION What is the basis and added value of a "gut feeling" that infections in acutely ill children are more serious than suggested by clinical assessment?

SUMMARY ANSWER A gut feeling of something wrong in children despite an otherwise reassuring clinical assessment substantially increased the risk of serious illness (likelihood ratio 25.5, 95% confidence interval 7.9 to 82.0). Clinical features strongly associated with gut feeling were the overall response of the child (decreased consciousness, no laughing) and parental concern that the illness was different from previous experience (odds ratio 36.3, 95% confidence interval 12.3 to 107.07).

WHAT IS KNOWN AND WHAT THIS PAPER ADDS About one in 200 children seen in primary care has a serious illness that is easily missed. In children with a reassuring clinical assessment, serious illness was 25 times more likely with gut feeling; parental concern was one of the features most strongly associated with gut feeling.

Participants and setting

3369 children presenting to general practice or community paediatricians with an acute illness lasting a maximum of five days.

Design

This cross sectional study was originally set up as a diagnostic accuracy study on clinical features. For these secondary analyses, we only included children for whom the clinical presentation was otherwise reassuring.

Primary outcome

The primary outcome was the diagnostic accuracy of gut feeling for serious infections. Secondary outcomes were the features associated with clinicians experiencing a gut feeling.

Main results and the role of chance

In children with an otherwise reassuring clinical presentation, gut feeling was associated with a sensitivity of 33% (95% confidence interval 4% to 78%), specificity of 99% (98% to 99%), and positive likelihood ratio of 25.5 (7.91 to 82). The features most strongly associated with

Features associated with gut feeling

Features	Odds ratio (95% CI)
Presenting symptoms:	
Cough	0.26 (0.09 to 0.74)
Diarrhoea	0.11 (0.02 to 0.69)
Weight loss	10.53 (1.53 to 72.50)
Urinary symptoms	13.51 (3.69 to 49.44)
Convulsions	61.72 (3.56 to 1069.56)
Does not laugh	3.84 (1.47 to 10.04)
Clinical examination findings:	
Tachypnoea	13.64 (3.52 to 52.80)
Decreased consciousness	52.04 (2.73 to 992.18)
Parental concern illness is different	36.26 (12.28 to 107.07)
Years of experience of doctor*	0.95 (0.90 to 1.00)

*Years since graduation from medical school.

gut feeling were decreased consciousness, tachypnoea, and parental concern.

Bias, confounding, and other reasons for caution

Analysing the components of gut feeling was not the primary aim of the original study. Although 120 children elicited a gut feeling of something wrong, only 21 children were admitted to hospital with a serious infection. Moreover, the analyses may not provide a complete explanation of gut feeling, as a modest amount of variance was shown in the multivariate models.

Generalisability to other populations

Children were recruited consecutively at first contact with healthcare, leading to a representative sample of acutely ill children in Flanders, Belgium. We believe that the results of the study are generalisable to other acutely ill unselected paediatric populations.

Study funding/potential competing interests

The original study was funded by a grant of the Research Foundation-Flanders (FWO) and an unconditional grant from Eurogenerics. The present analyses were done as part of the MaDOx programme, which presents independent research commissioned by the National Institute for Health Research under its programme grants for applied research funding scheme (RP-PG-0407-10347). We have no competing interests.

Cardiovascular disease risk in healthy children and its association with body mass index: systematic review and meta-analysis

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STUDY QUESTION What is the association between categories of body mass index and risk of cardiovascular disease in school aged children in highly developed countries?

SUMMARY ANSWER Having a body mass index above the normal range significantly worsens risk parameters for cardiovascular disease, including blood pressure, fasting insulin, insulin resistance, high density lipoprotein cholesterol, and triglycerides; all of these effects, as well as total cholesterol and low density lipoprotein cholesterol, are increased in obesity.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS Increased weight is associated with a higher risk of abnormal blood pressure and lipid profile, and could contribute to early changes in risk parameters for cardiovascular disease in children. Our results suggest that previous estimates of the effect of excess weight, and in particular obesity, could underestimate the size of the problem; existing definitions of “normal” cardiovascular disease risk parameters should be re-examined to take into account the weight of the child.

Selection criteria for studies

We searched Embase, PubMed, EBSCOHost’s cumulative index to nursing and allied health literature, and the Web of Science between January 2000 and December 2011. We limited searches to studies in healthy children aged 5 to 15 years in highly developed countries, using prospective or retrospective cohort, cross sectional, case-control, or randomised clinical trial designs in school, outpatient, or community settings. Included studies had to report an objective measure of weight and at least one prespecified risk parameter for cardiovascular disease.

Primary outcome(s)

Mean difference in risk parameters for cardiovascular dis-

ease recorded in healthy children compared with those in overweight and obese children.

Main results and role of chance

We included 63 studies of 49 220 children. Compared with normal children, systolic blood pressure was significantly higher by 4.54 mm Hg in overweight children and by 7.49 mm Hg in obese children; we found a similar association in diastolic blood pressure. Obesity adversely affected concentrations of all blood lipids; total cholesterol and triglycerides were 0.15 mmol/L and 0.26 mmol/L higher in obese children, respectively. Fasting insulin and insulin resistance were significantly increased in obese participants compared with normal weight children.

Bias, confounding, and other reasons for caution

Results were limited by the lack of data for age and pubertal status of the included children and the cross-sectional nature of the data. Other limitations included discrepancies in the methods of measurement and reporting in the included studies, and high levels of heterogeneity present in some of the comparisons. Our review only provides a picture of cardiovascular disease risk of children at the time they were measured, and therefore cannot establish the relation between risk parameters for cardiovascular disease and the ongoing changes in weight in the same child, nor can it determine how the disease risk in those children might progress into adulthood.

Study funding/potential competing interests

No support was received specifically for this review. CF is funded by the Medical Research Council. The University Department of Primary Care Health Sciences is part of the National Institute for Health Research School of Primary Care Research, which provides financial support for senior staff who contributed to this paper. The authors declare no other conflicts.

Association between child weight and risk parameter for cardiovascular disease

Risk parameter	Overweight v normal weight		Obese v normal weight	
	Mean difference (99% CI)	P	Mean difference (99% CI)	P
Systolic blood pressure (mm Hg)	4.54 (2.44 to 6.64)	<0.001	7.49 (3.36 to 11.62)	<0.001
Diastolic blood pressure (mm Hg)	2.57 (1.55 to 3.58)	<0.001	4.06 (2.05 to 6.08)	<0.001
Fasting insulin (pmol/L)	21.82 (−1.44 to 45.08)	0.02	48.47 (31.96 to 64.97)	<0.001
Insulin resistance (Homeostasis Model Assessment of Insulin Resistance)	0.88 (−0.08 to 1.85)	0.02	1.32 (0.83 to 1.82)	<0.001
Total cholesterol	0.02 (−0.21 to 0.17)	0.77	0.15 (0.04 to 0.25)	<0.001
Low density lipoprotein cholesterol	−0.02 (−0.41 to 0.37)	0.91	0.18 (0.09 to 0.26)	<0.001
High density lipoprotein cholesterol	−0.17 (−0.22 to −0.13)	<0.001	−0.22 (−0.39 to −0.06)	<0.001
Triglycerides	0.21 (0.14 to 0.27)	<0.001	0.26 (0.13 to 0.39)	<0.001

Data are mmol/L unless stated otherwise.

Effectiveness of intervention on physical activity of children: systematic review and meta-analysis of controlled trials with objectively measured outcomes (EarlyBird 54)

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EDITORIAL by Hamer and Fisher

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STUDY QUESTION How effective are physical activity interventions at increasing the activity of children?

SUMMARY ANSWER Physical activity interventions achieve a small to negligible increase in total activity, with a small improvement in the time spent at moderate or vigorous intensities amounting to around four more minutes walking or running per day.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Physical activity interventions have little effect on the prevention of childhood obesity, but the reasons for this have been unclear. The finding that physical activity interventions have little effect on the overall activity of children provides one explanation.

Selection criteria for studies

We searched Embase, Medline, PsycINFO, and SPORTDiscus electronic databases up to March 2012 for trials that sought to increase the physical activity of children/adolescents. To be included, the trials needed to have measured whole day physical activity objectively with accelerometers at both baseline and follow-up. They also needed to have been at least four weeks in duration and to have incorporated a control group.

Primary outcomes

We focused on the total amount of physical activity and the time spent in moderate or vigorous physical activity. Both outcomes were expressed as standardised mean differences.

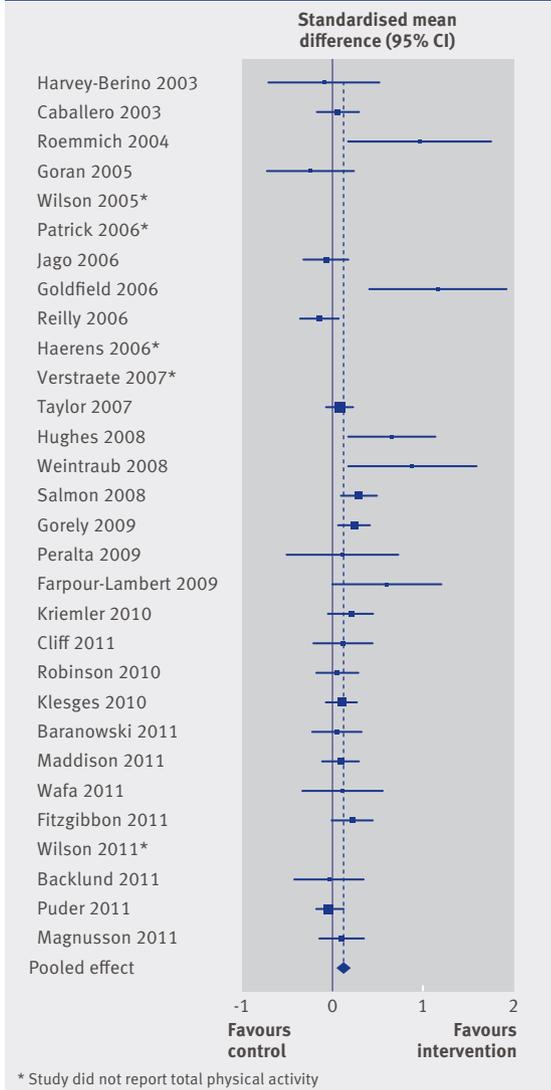
Main results and role of chance

Thirty studies, incorporating 6153 children with accelerometer measured physical activity, met the inclusion criteria. The pooled intervention effect across all studies was small to negligible for total physical activity (standardised mean difference 0.12, 95% confidence interval 0.04 to 0.20; $P < 0.01$) and small for moderate or vigorous physical activity (0.16, 0.08 to 0.24; $P < 0.001$, equivalent to approximately four more minutes walking or running per day). The pooled intervention effect did not differ significantly when restricted to studies of higher methodological quality (standardised mean difference 0.09 for total physical activity and 0.11 for moderate or vigorous physical activity).

Bias, confounding, and other reasons for caution

Not all of the included studies reported both of the outcome measures of interest, yet both are likely to have been collected. This may have led to reporting bias whereby, for example, authors selected the outcome measure that showed the greatest effect. We cannot rule out publication bias either. The absence of small “unsuccessful” trials in

Effects of interventions on total physical activity of children (standardised mean difference and 95% CI)



the presence of small “successful” trials may reflect the reluctance of editors to publish negative results. Both sources of bias may have caused us to overestimate the true effect of the interventions.

Study funding/potential competing interests

EarlyBird (BM and TW) is supported by the Bright Future Trust, the Kirby Laing Foundation, the Peninsula Foundation and the EarlyBird Diabetes Trust. WH is supported by the National Institute for Health Research (NIHR) Collaborations for Leadership in Applied Health Research and Care (CLAHRC).

Lifestyle, social factors, and survival after age 75: population based study

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STUDY QUESTION Do lifestyle and social factors after ages 75 and 85 years affect longevity?

SUMMARY ANSWER Lifestyle behaviours such as not smoking and physical activity were associated with longer survival, even after age 75. A low risk profile added five years to women's lives and six to men's lives. These associations, although attenuated, were also present among the oldest old (≥ 85 years) and in people with chronic health conditions.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

It is uncertain whether lifestyle and social factors predict mortality among the oldest old because of mixed results. The associations of leisure activity and not smoking with increased life expectancy are still present among the oldest old and those with chronic conditions.

Participants and setting

Participants, aged 75 years or more, in the Kungsholmen Project, Stockholm, Sweden.

Design, size, and duration

A longitudinal study of 1810 participants followed up for 18 years. Data included lifestyle factors (smoking, alcohol, and body mass index), social networks, and leisure activities (mental, physical, social, and productive activities). We grouped lifestyle and social factors into four risk profile groups: high risk (unhealthy lifestyle, limited or poor social network, and no leisure activities), moderately high (two of the three risk factors), moderately low (one risk factor), and low (healthy lifestyle, a rich or moderate

social network, and at least one leisure activity). The main outcome measure was median age at death.

Main results and the role of chance

Half of the current smokers died one year earlier than non-smokers. Physical activity had the strongest association with survival; participants who regularly swam, walked, or did gymnastics had a median age at death two years older than those who did not. Median survival of people with a low risk compared with high risk profile was 5.4 years longer. Even among the oldest old and people with chronic conditions, the median age at death was four years higher for those with a low risk compared with high risk profile.

Bias, confounding, and other reasons for caution

Survival selection needs to be taken into account, especially for factors showing an inverse association with mortality. The positive associations with mortality are more likely to be underestimated. Alcohol consumption was self reported, which might lead to information bias. We cannot assess the relations between changes in modifiable factors over the lifespan and survival because we assessed exposures only at baseline.

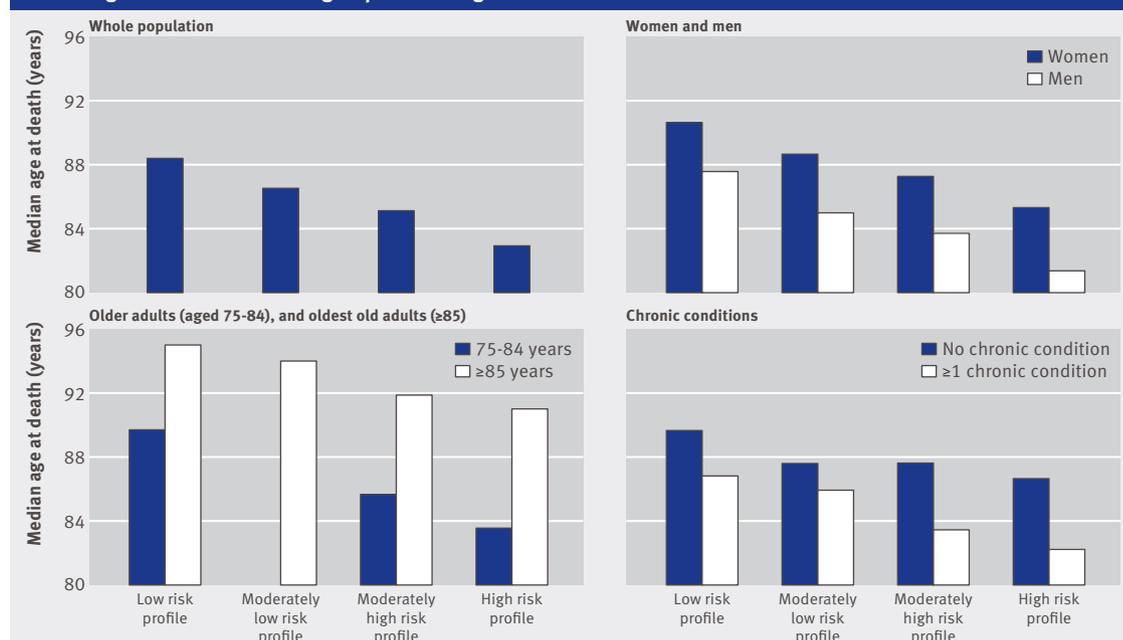
Generalisability to other populations

The findings might be generalised to older urban populations in Western countries.

Study funding/potential competing interests

All researchers are independent of the funders.

Median age at death in four risk groups according to modifiable factors



The health and development of children born to older mothers in the United Kingdom: observational study using longitudinal cohort data

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STUDY QUESTION What is the relation between child health and development and maternal age, controlling for personal characteristics and parity?

SUMMARY ANSWER Increasing maternal age was associated with children having a greater likelihood of being fully immunised by age 9 months as well as fewer hospital admissions and unintentional injuries, better language, and fewer social and emotional difficulties up to age 5 years.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS The trend towards later childbearing is strong. Despite well known antenatal and perinatal risks associated with later motherhood, this research shows that later childbearing is associated with improved outcomes in children up to age 5.

Participants and setting

Millennium Cohort Study and National Evaluation of Sure Start study (random samples of UK children and children in deprived areas of England). We followed up 31 257 children at age 9 months, 24 781 at 3 years, and 22 504 at 5 years.

Design, size, and duration

The longitudinal studies collected information when children were aged 9 months and 3 and 5 years.

Main results and the role of chance

Associations were independent of personal characteristics and parity. The risk of children having unintentional injuries or being admitted to hospital declined with increasing maternal age—at age 3 the risk of unintentional injuries in children born to 20 year olds was 36.6% and in those born to 40 year olds was 28.6%, with hospital admissions declining, respectively, from 27.1% to 21.6%. Immunisations at age 9 months increased with maternal age from 94.6% for

infants born to 20 year olds to 98.1% for infants born to 40 year olds. At three years, excluding combined MMR immunisation resulted in no significant relation with maternal age. An increase in overweight children with increasing maternal age was eliminated once maternal body mass index was included as a covariate. Language development improved with increasing maternal age, with scores for children of 20 year olds being 0.21 to 0.22 SDs below those for children of 40 year olds at ages 3 and 5. Fewer social and emotional difficulties were associated with increasing maternal age. Children of teenage mothers had more difficulties than those of mothers aged 40 (difference 0.28 SDs at age 3 and 0.16 SDs at age 5). The similarity of results across samples and outcomes, and statistical control for a large number of covariates, reduced the likelihood that the results reflected chance.

Bias, confounding, and other reasons for caution

Participants were randomly sampled from child benefit records (97% of population), and response rates ranged from 70% to 90%. Less than 10% of data was missing and possible bias due to missing data was countered by imputation. Many measures were based on maternal report, which may have limited accuracy. It is possible some unmeasured characteristic may have affected the results.

Generalisability

As results were similar for separate analyses of the population representative sample and the deprived sample it is likely that results are applicable to the whole population and across the spectrum of deprivation.

Study funding/potential competing interests

We are independent of the funding agency, the Wellcome Trust.

Summary of significant effects associated with maternal age

Child outcome by age	Maternal age band					Maternal age effect controlling covariates		
	<22	22-26	26-30	30-33	>33	Effect; age 40 v 20 years	Maternal age coefficient in final model	Significance of coefficient
Complete immunisation:								
9 months	93.5	95.3	96.6	96.9	96.8	2.97 (odds ratio)	Age, age ²	<10 ⁻⁴ , 0.0031
Unintentional injury:								
9 months	11.7	9.0	8.0	7.3	6.8	0.62 (odds ratio)	Age	<10 ⁻⁴
3 years	38.9	33.5	33.4	30.7	28.8	0.69 (odds ratio)	Age, age ²	<10 ⁻⁴ , 0.018
5 years	30.7	29.7	28.4	25.7	25.3	0.81 (odds ratio)	Age	0.0026
Admission to hospital:								
9 months	18.8	16.2	13.9	12.3	12.3	0.63 (odds ratio)	Age	<10 ⁻⁴
3 years	33.8	28.5	25.6	23.0	20.8	0.74 (odds ratio)	Age	0.0001
5 years	17.4	16.4	14.1	13.1	13.2	0.88 (odds ratio)	Age	0.17
Mean (SD) vocabulary score:								
3 years	45.3 (10.4)	46.1 (11.3)	48.4 (11.9)	49.8 (11.6)	50.0 (11.5)	0.22 (SD)	Age, age ²	<10 ⁻⁴ , 0.0053
5 years	49.0 (10.5)	49.5 (11.3)	52.2 (11.5)	53.9 (11.5)	54.1 (11.6)	0.21 (SD)	Age, age ²	<10 ⁻⁴ , 0.0032
Mean (SD) strengths and difficulties score:								
3 years	33.3 (5.26)	32.2 (5.24)	31.0 (4.95)	30.2 (4.66)	29.7 (4.70)	-0.28 (SD)	Age, age ²	<10 ⁻⁴ , <10 ⁻⁴
5 years	30.7 (5.23)	29.9 (4.99)	29.0 (4.76)	28.4 (4.42)	28.1 (4.53)	-0.16 (SD)	Age	<10 ⁻⁴

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Mortality and implant revision rates of hip arthroplasty in patients with osteoarthritis: registry based cohort study

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STUDY QUESTION Do mortality and implant revision rates differ in osteoarthritis patients undergoing cemented or uncemented total hip replacement or hip resurfacing?

SUMMARY ANSWER Flexible parametric survival analyses, adjusted for confounding factors, identified a slightly higher mortality rate and a slightly lower revision rate for patients undergoing cemented rather than uncemented total hip replacement. In analyses restricted to men, the mortality rate was lowest for those undergoing Birmingham hip resurfacing.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

The National Joint Registry 2011 report gave only unadjusted mortality rates without consideration of confounding factors. The current analysis shows that small differences in mortality rates still exist between procedure groups, even after adjustment for available confounders, in addition to small differences in implant revision rates.

Participants and setting

All patients undergoing total hip replacement or Birmingham hip resurfacing (Smith and Nephew) in the National Joint Registry of England and Wales.

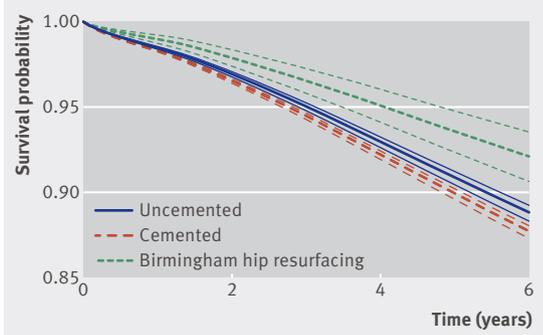
Design, size, and duration

The cohort study comprised about 275 000 patient records from the registry entered in 2003–11. Hip arthroplasty procedures were linked to the time to any subsequent mortality or revision (implant failure). Flexible parametric survival analysis compared mortality and revision rates for procedure groups, adjusting for age, sex, American Society of Anesthesiologists (ASA) grade, and complexity.

Main results and the role of chance

At baseline there were large differences in the characteristics of patients undergoing each procedure, so unadjusted comparisons are inappropriate. Multivariable survival analyses identified a higher mortality rate (adjusted hazard ratio 1.11, 95% confidence interval 1.07 to 1.16) and a lower revision rate (0.53, 0.50 to 0.57) for patients undergoing cemented rather than uncemented total hip replacement. These translate to small predicted differences in population averaged absolute survival probability at all time points. For example, compared with the uncemented group, at eight years after surgery the predicted probability of death in the cemented group was 0.013 higher (0.007 to 0.019) and the predicted probability of revision was 0.015 lower (0.012 to 0.017). In multivariable analyses restricted to men, there was a higher mortality rate in the cemented group and the uncemented group than in the Birmingham hip resurfacing group. In terms

Population averaged (adjusted) survival curves (with 95% confidence intervals) for men comparing cemented, uncemented, and Birmingham hip resurfacing patients with mortality as endpoint



of revision, those undergoing Birmingham hip resurfacing had a similar revision rate to uncemented total hip replacement but both were higher than with cemented total hip replacement.

Bias, confounding, and other reasons for caution

Additional confounding is a potential concern as only a small number of baseline variables are recorded in the National Joint Registry. For instance, there is no measure of physical activity or satisfaction in patients. Revision is only a surrogate marker for time to failure and ASA grade is a surrogate marker of general health. Information on mortality after revision was also unavailable. The maximum follow-up on the registry is eight years.

Generalisability to other populations

The National Joint Registry includes patients from England and Wales; further research in other populations is needed. Even small differences in mortality rates are important given that 1.2 million patients worldwide underwent hip arthroplasty in 2011. If the improved mortality rates with Birmingham hip resurfacing are genuine, our analysis predicts an extra death within six years for every 23 men undergoing cemented total hip replacement rather than Birmingham hip resurfacing.

Study funding/potential competing interests

KIES is funded by the MRC Midlands Hub for Trials Methodology Research at the University of Birmingham (Medical Research Council Grant ID G0800808). RDR is also supported by funding from this Hub. DJWmMcM and RBCT were designers of Birmingham hip resurfacing and were shareholders in Midland Medical Technologies before the company was sold to Smith and Nephew in 2004. DJWmMcM is an unpaid consultant to Smith and Nephew Orthopaedics UK.