RESEARCH

Compiled by Helen Jaques, Lucy Banham, and Trish Groves

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THIS WEEK'S RESEARCH QUESTIONS

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Alcohol: is it all bad news?

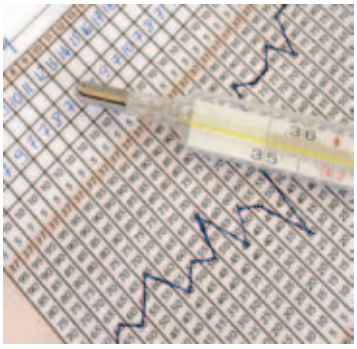
With conflicting messages about the bad and good effects of alcohol often present both in the medical literature and in the general media, what should clinicians be telling their patients? This week's *BMJ* looks at both sides of the coin. The Practice section focuses on the harms of alcohol, with a summary of NICE guidance about risky drinking, accompanied by a patient's story about alcoholism. Meanwhile, Paul Ronksley and colleagues sought answers about the potential benefits of alcohol. Their systematic review and meta-analysis aimed to provide an up to date summary of current knowledge about the effect of drinking on a broad range of clinically important cardiovascular outcomes (p 479). The news was good—for those who consume light to moderate amounts of alcohol (2.5–14.9 g/day, or about ≤1 drink a day). Such consumption was associated with reduced risks of cardiovascular disease compared with non-drinkers. This conclusion was supported by further findings in a second paper by the group (p 480), which showed that moderate alcohol consumption was associated with favourable changes in several biomarkers of coronary heart disease. The evidence of a protective effect of alcohol is compelling, say the authors, and in the full length versions of the papers online they consider how these messages might be integrated into clinical practice and public health messages.

Peer support for type 2 diabetes

Peer support could be a promising approach for diabetes care as it harnesses the ability of patients with diabetes to support each other in managing their everyday lives. However, there is limited evidence supporting its effectiveness. S Smith and colleagues did a pragmatic cluster randomised controlled trial examining the effectiveness of peer support in improving outcomes for people with type 2 diabetes (p 482). The intervention was based on social support and was delivered in groups based in general practices.

They found that although it was feasible to introduce the intervention into this setting, many patients were not interested in participating, and 18% of those who agreed to participate never attended any meetings. For those who took part, there was a trend towards improvements in clinical care but no significant improvements in diabetes or psychosocial outcomes, suggesting that peer support should not be widely adopted in clinical practice until further research is carried out.

Women and infertility: worry away



Women who are struggling to conceive sometimes think that the stress and worry brought on by their infertility problems, or by other things going on in their life such as work or family issues, could be contributing to their lack of natural fertility or lack of success with fertility treatment. Tales of couples who conceive spontaneously on holiday or after adoption, when they aren't under the strain of trying to conceive, only add to this belief.

Thankfully a new meta-analysis has shown that emotional distress has no effect on the likelihood of pregnancy after one cycle of assisted reproductive technology (p 481). The authors of this analysis looked at 14 studies of 3583 infertile women in 10 countries who were undergoing fertility treatment and found no significant difference in subsequent pregnancy between those who were anxious before treatment and those who were not. Whether women were undergoing treatment for the first time or had used an assisted reproductive technology before had no effect on this outcome either.

"This finding provides doctors with the evidence to reassure women that feelings of tension, worry, or depression experienced as a result of their fertility problem, its treatment, or other co-occurring life events are unlikely to further reduce chances of pregnancy," write the authors.

LATEST RESEARCH: For this and other new research articles see www.bmj.com/research

Foundation programmes broaden access to medical school Jonathan Mathers and colleagues did a cross sectional, population based analysis to determine whether new programmes developed to widen access to medicine in the UK have produced more diverse student populations. They report that medical school foundation programmes, which focus on students from ethnic and socioeconomic groups traditionally under-represented in medicine, are more likely to admit non-white students and those from lower socioeconomic classes than are traditional five year undergraduate medical courses (doi:10.1136/bmj.d918). However, foundation programmes are only offered by three of the 31 medical schools in the UK, leading the authors to conclude that "the implementation of 'new' admission routes to the profession does not seem to be bringing significant change." In addition, students on four year graduate entry programmes were older than those on traditional courses but were more likely to be white, suggesting that graduate entry courses aren't changing the socioeconomic profile of the UK medical student population.

Association of alcohol consumption with selected cardiovascular disease outcomes: a systematic review and meta-analysis

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See also EDITORIAL by Coltart and Gilmore

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Listen to a podcast interview with Paul Ronksley and Susan Brien at www.bmj.com/podcasts

STUDY QUESTION Is alcohol consumption associated with a reduced risk of multiple cardiovascular outcomes?

SUMMARY ANSWER Light to moderate alcohol consumption is associated with a reduced risk of multiple cardiovascular outcomes.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Existing systematic reviews of the association of alcohol consumption with cardiovascular outcomes are somewhat out of date and none has comprehensively studied a broad spectrum of relevant cardiovascular end points. This review provides a summary of current knowledge regarding alcohol associations with five meaningful clinical end points. The results confirm the beneficial effects of moderate alcohol consumption and the need to elucidate the underlying pathophysiological mechanisms.

Selection criteria for studies

A search of databases Medline (1950 through September 2009) and Embase (1980 through September 2009) were supplemented with manual searches of bibliographies and conference proceedings. Two reviewers independently selected prospective cohort studies on the association between alcohol consumption and various cardiovascular outcomes.

Primary outcome(s)

By comparison with a reference group of non-drinkers, we assessed associations of alcohol intake with overall cardiovascular disease mortality, incidence of and mortality from coronary heart disease, and incidence of and mortality from stroke.

Main results and role of chance

Of 4235 citations, 84 unique studies met our criteria for inclusion in the final analysis. The pooled adjusted relative risks for drinkers relative to non-drinkers in random effects models for the outcomes of interest were 0.75 (95% confidence interval 0.70 to 0.80) for cardiovascular disease mortality, 0.71 (0.66 to 0.77) for incident coronary heart disease, 0.75 (0.68 to 0.81) for coronary heart disease mortality, 0.98 (0.91 to 1.06) for incident stroke, and 1.06 (0.91 to 1.23) for stroke mortality. Dose-response analysis revealed that the lowest risk of incident coronary heart disease occurred with 1–2 drinks per day, but for incident stroke it occurred with ≤1 drink per day. When these results are coupled with those of our companion paper, a review of interventional mechanistic studies focusing on biomarkers associated with cardiovascular disease (in particular coronary heart disease), the argument for causation becomes compelling.

Bias, confounding, and other reasons for caution

Our review has some limitations. Firstly, the quality of individual studies varied, with some studies having limited follow-up and adjustment for potential confounding. Secondly, we found limited available information for alcohol and mortality for subtypes of stroke, so this topic continues to be important for large observational cohort studies. Finally, we observed significant heterogeneity across studies for several of our pooled analyses. This is, however, partly due to the large study sample sizes that can confer greater statistical power to heterogeneity tests. The clinical relevance of this heterogeneity may be quite modest.

Study funding/potential competing interests

This review was funded by a contracted operating grant from Program of Research Integrating Substance Use Information into Mainstream Healthcare funded by the Robert Wood Johnson Foundation with co-funding by the Substance Abuse and Mental Health Services and the Administration Center for Substance Abuse Treatment. These sources had no involvement in the conduct of the study or preparation of the manuscript.

POOLED RELATIVE RISKS FOR CARDIOVASCULAR AND STROKE OUTCOMES ASSOCIATED WITH ALCOHOL CONSUMPTION

	Cardiovascular disease mortality	Incident coronary heart disease	Coronary heart disease mortality	Incident stroke	Stroke mortality
No of studies (No of participants)	21 (1 184 956)	29 (549 504)	31 (1 925 106)	17 (458 811)	10 (723 571)
Relative risk estimate (95% CI)					
Active drinkers *v* non-drinkers	0.75 (0.70 to 0.80)	0.71 (0.66 to 0.77)	0.75 (0.68 to 0.81)	0.98 (0.91 to 1.06)	1.06 (0.91 to 1.23)
Alcohol intake (g/day) *v* none*:					
<2.5	0.71 (0.57 to 0.89)	0.96 (0.86 to 1.06)	0.92 (0.80 to 1.06)	0.81 (0.74 to 0.89)	1.00 (0.75 to 1.34)
2.5–14.9	0.77 (0.71 to 0.83)	0.75 (0.65 to 0.88)	0.79 (0.73 to 0.86)	0.80 (0.74 to 0.87)	0.86 (0.75 to 0.99)
15–29.9	0.75 (0.70 to 0.80)	0.66 (0.59 to 0.75)	0.79 (0.71 to 0.88)	0.92 (0.82 to 1.04)	1.15 (0.86 to 1.54)
30–60	0.85 (0.73 to 0.98)	0.67 (0.56 to 0.79)	0.77 (0.72 to 0.83)	1.15 (0.98 to 1.35)	1.10 (0.85 to 1.45)
>60	0.99 (0.84 to 1.17)	0.76 (0.52 to 1.09)	0.75 (0.63 to 0.89)	1.62 (1.32 to 1.98)	1.44 (0.99 to 2.10)

*12.5 g alcohol = a single standard drink, so intake categories roughly equivalent to <0.5, 0.5–1, 1–2.5, 2.5–5, and >5 drinks per day.

Effect of alcohol consumption on biological markers associated with risk of coronary heart disease: systematic review and meta-analysis of interventional studies

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Listen to a podcast interview with Paul Ronksley and Susan Brien at www.bmj.com/podcasts

STUDY QUESTION What is the effect of alcohol use on circulating biomarkers associated with risk for coronary heart disease in adults?

SUMMARY ANSWER Moderate alcohol consumption produced favourable changes for selected biomarkers, significantly increasing circulating levels of high density lipoprotein cholesterol and adiponectin and decreasing levels of fibrinogen.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS Observational studies have shown moderate alcohol consumption to be associated with a lower risk of specific cardiovascular diseases, particularly coronary heart disease. This systematic review and meta-analysis of interventional studies determined that moderate alcohol consumption results in favourable changes in certain biomarkers associated with risk of coronary heart disease.

Selection criteria for studies

Medline (1950 to October 2009) and Embase (1980 to October 2009) were searched without limits. Two independent reviewers selected interventional studies of adults without known cardiovascular disease comparing fasting, circulating levels of specific biomarkers associated with coronary heart disease after alcohol use with a period of no alcohol use (controls).

Primary outcome(s)

The mean change in biomarker levels after a period of alcohol use compared with a period of no alcohol use.

Main results and role of chance

Of 4690 citations, 44 studies contained data that could be meta-analysed. We used either random or fixed effects models to pool mean changes in biomarker levels for 13 biomarkers. After alcohol use, significant changes occurred in levels of high density lipoprotein cholesterol (0.094 mmol/L, 95% confidence interval 0.064 to 0.123), apolipoprotein A1 (0.101 g/L, 0.073 to 0.129), fibrinogen (−0.20 g/L, −0.29 to −0.11), and adiponectin (0.56 mg/L, 0.39 to 0.72). A significant dose-response change in high density lipoprotein levels occurred—for alcohol 12.5-29.9 g/day (1 or 2 drinks, n=7), mean difference 0.072 mmol/L (0.024 to 0.119); for 30-60 g/day (2-4 drinks, n=24), mean difference 0.103 mmol/L (0.065 to 0.141); and for >60 g/day (>4 drinks, n=2), mean difference 0.141 mmol/L (0.042 to 0.240; P for trend 0.013). No differential effects were found of alcohol beverage type on pooled mean changes in biomarkers.

Bias, confounding, and other reasons for caution

The pooled studies lacked uniformity. In particular, duration and dosing of the alcohol interventions differed, as did the characteristics of the participants. Furthermore, stable circulating cellular and molecular biomarkers associated with coronary heart disease were evaluated, whereas more variable measures, such as blood pressure, were not. Other biomarkers may be of relevance to the effects of alcohol on other conditions, such as cancer, that were not evaluated. Lastly, the favourable effects of alcohol use on some of the biomarkers associated with coronary heart disease still can be characterised only as indirect evidence for a causal mechanism by which alcohol may be cardioprotective.

Study funding/potential competing interests

This review was supported by a contracted operating grant from Program of Research Integrating Substance Use Information into Mainstream Healthcare (PRISM) funded by the Robert Wood Johnson Foundation project No 58529, with cofunding by the Substance Abuse and Mental Health Services and the Administration Center for Substance Abuse Treatment. These sources had no involvement in the conduct of the study or preparation of the manuscript.

SUMMARY OF POOLED MEAN DIFFERENCE IN BIOMARKER LEVEL AFTER ALCOHOL USE COMPARED WITH PERIOD OF NO USE

Biomarker	No of studies (participants) pooled	Pooled mean difference in biomarker level (95% CI)
High density lipoprotein cholesterol (mmol/L)	33 (796)	0.09 (0.06 to 0.12)*†
Low density lipoprotein cholesterol (mmol/L)	24 (513)	−0.11 (−0.22 to 0.01)†
Total cholesterol (mmol/L)	26 (596)	0.00 (−0.07 to 0.07)
Triglycerides (mmol/L)	31 (752)	0.02 (−0.02 to 0.05)
Apolipoprotein A1 (g/L)	16 (374)	0.10 (0.07 to 0.13)*†
Lp(a) lipoprotein (mg/dL)	3 (114)	0.80 (−4.2 to 5.8)
C reactive protein (mg/L)	5 (186)	−0.11 (−0.31 to 0.10)
Interleukin 6 (pg/mL)	2 (144)	0.50 (−3.48 to 4.49)
Tumour necrosis factor α (pg/mL)	3 (121)	−0.47 (−32.02 to 31.08)
Plasminogen activator inhibitor 1 (ng/mL)	3 (67)	3.29 (−0.90 to 7.47)
Tissue plasminogen activator (ng/mL)	3 (67)	0.75 (−0.13 to 1.64)
Fibrinogen (g/L)	7 (387)	−0.20 (−0.29 to −0.11)*
Adiponectin (mg/L)	4 (108)	0.56 (0.39 to 0.72)*

*Significant (P<0.01) change in biomarker level after alcohol use compared with period of no use.
†Heterogeneity detected across pooled studies, where Q statistic P<0.10.

Emotional distress in infertile women and failure of assisted reproductive technologies: meta-analysis of prospective psychosocial studies

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STUDY QUESTION Does pretreatment emotional distress affect the likelihood of achieving pregnancy in women undergoing a single cycle of treatment with assisted reproductive technologies?

SUMMARY ANSWER Pretreatment emotional distress is unlikely to affect subsequent pregnancy in a single cycle of treatment with assisted reproductive technology.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS
Many infertile women believe that emotional distress (for example, tension or worry) is a contributing factor to their lack of success with assisted reproductive technologies, but existing human studies on this topic are inconclusive because of significant heterogeneity in study designs. This meta-analysis of 14 prospective studies confirms that distress is unlikely to affect chances of pregnancy after a single cycle of treatment with assisted reproductive technologies.

Selection criteria for studies

PubMed, Medline, Embase, PsycINFO, PsychNET, ISI Web of Knowledge, and ISI Web of Science were searched for articles published from 1985 to March 2010 (inclusive) using the terms "assisted reproductive technologies" and "emotional distress" and their variants. The selection criteria were that emotional distress (anxiety or depression) in women was measured before the start of stimulation; the outcome (pregnant or not pregnant) was reported for a single cycle of treatment with an assisted reproductive technology (in vitro fertilisation, intracytoplasmic sperm injection, or gamete intrafallopian transfer); the pregnancy outcome was based on laboratory or clinical evidence; and means and standard deviations for pretreatment emotional distress (anxiety or depression) were available for pregnant and not pregnant groups in the publication or through additional contact with the author.

Primary outcome(s)

The primary outcome measure was the standardised mean difference (adjusted for small sample size) in pretreatment anxiety or depression (priority on anxiety where both measured) between women who achieved pregnancy with assisted reproductive technology (defined as a positive pregnancy test or positive fetal heart scan or live birth) and women who did not.

Main results and role of chance

This meta-analysis of 14 studies, which sampled 3583 women in 10 countries, did not detect a statistically significant association between pretreatment emotional distress and treatment outcome with assisted reproductive technology (standardised mean difference −0.04, 95% confidence interval CI −0.11 to 0.03, fixed effects model; heterogeneity I^2=14%, P=0.30). Subgroup analyses according to previous experience of assisted reproductive technology, composition of the not pregnant group, and timing of the emotional assessment were not significant.

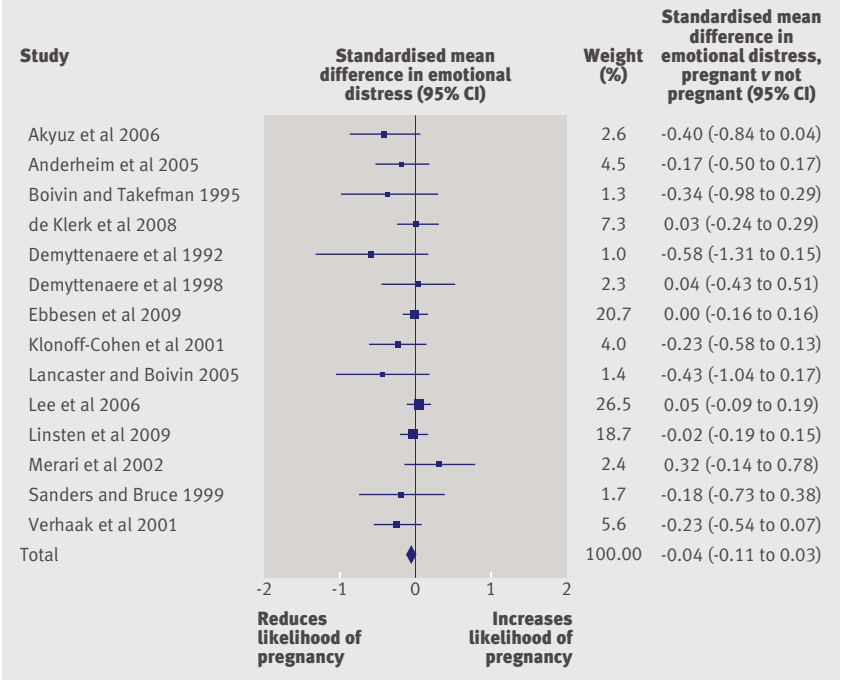
Bias, confounding, and other reasons for caution

A contour enhanced funnel plot and a significant Egger's test indicated the presence of moderate publication bias. This meta-analysis cannot exclude the possibility that psychobiological associations between stress and fertility could be captured using other designs and populations; for example, in people at higher risk for distress or with poorer response to treatment and in women undergoing more than one cycle of treatment.

Study funding and potential competing interests

This study was not funded. EG and CAV declare no financial relationships with any organisations that might have an interest in the submitted work. In the previous three years JB received speaker fees from EMD Serono Inc and Merck & Co (then Schering Plough), and a research grant from Merck Serono SA.

DIFFERENCE IN PRETREATMENT EMOTIONAL DISTRESS IN PREGNANT AND NOT PREGNANT GROUPS IN 14 STUDIES OF ASSISTED REPRODUCTIVE TECHNOLOGY



Peer support for patients with type 2 diabetes: cluster randomised controlled trial

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Find out more about diabetes on the BMJ Group diabetes specialist portal at http://www.bmj.com/site/topics/diabetes

STUDY QUESTION Is group based peer support feasible for patients with type 2 diabetes in general practice and does it improve outcomes?

SUMMARY ANSWER Peer support for patients with type 2 diabetes is feasible in general practice settings but the intervention was not effective when targeted at all patients with type 2 diabetes.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Peer support can harness the ability of patients with diabetes to support each other in managing their everyday lives. In this study of such support, there was a trend towards improvements in clinical care but no significant improvements in diabetes or psychosocial outcomes.

Design

In this cluster randomised controlled trial practices were stratified by practice size and presence of existing structured diabetes care. A statistician blind to practice identity then used minimisation to allocate them to intervention or control groups. All practices introduced a structured diabetes care system, and the intervention involved nine group meetings facilitated by trained peer supporters based in participants' general practices.

Participants and setting

20 general practices in the east of the Republic of Ireland, 395 patients (192 in intervention group, 203 in control group), and 29 peer supporters with type 2 diabetes. Each practice in the intervention group recruited three peer supporters, at a ratio of one peer supporter to seven or eight patients with type 2 diabetes. The intervention was delivered over a two year period, from May 2007 to April 2009.

Primary outcomes

HbA_{1c}, cholesterol concentration, systolic blood pressure, and wellbeing score, measured at baseline and at two years.

Main results and the role of chance

At two year follow-up, there were no significant differences in HbA_{1c} (mean difference −0.08, 95% confidence interval −0.35 to 0.18), systolic blood pressure (−3.9, −8.9 to 1.1), total cholesterol (−0.03, −0.28 to 0.22), or wellbeing scores (−0.7, −2.3 to 0.8). There was a trend towards decreases in the proportion with poorly controlled risk factors at follow-up, particularly for systolic blood pressure (52% (87/166) >130 mm Hg in intervention *v* 61% (103/169) >130 mm Hg in control), but these changes were not significant. The process evaluation indicated that the intervention was generally delivered as intended, though 18% (35) of patients in the intervention group never attended any group meetings.

Harms

There was some decline in wellbeing in peer supporters, though numbers were small. Providing peer support might be stressful and burdensome.

Bias, confounding, and other reasons for caution

While the study achieved its proposed sample size, diabetes care in general has improved, leaving little room for improvement in mean HbA_{1c}, systolic blood pressure, and total cholesterol in most cases. Certain subgroups of patients, however, did not meet these targets, particularly for systolic blood pressure.

We could not conceal practice allocation before baseline data collection as peer supporters had been identified and trained in intervention practices. This led to a differential recruitment rate with patients in intervention practices being less likely to agree to participate in the study, which could show that group based peer support is not attractive to all patients with type 2 diabetes.

Generalisability to other populations

Practices need financial and organisational assistance in setting up peer support groups and providing ongoing informal support to the peer supporters. If this is not available, our findings might not be applicable.

Study funding/potential competing interests

The study was funded by the Health Research Board of Ireland (Strategic Health Research and Development Research Awards 2004, S/A 009).

Trial registration

Current Controlled Trials ISRCTN42541690.

PRIMARY OUTCOMES IN PARTICIPANTS WITH TYPE 2 DIABETES ALLOCATED TO PEER SUPPORT (INTERVENTION) OR NO PEER SUPPORT (CONTROL)

	No of people (baseline/follow-up)		Mean (SD) outcome at baseline		Mean (SD) outcome at follow-up				
	Intervention	Control	Intervention	Control	Intervention	Control	ICC	Mean difference (95% CI)	P value
HbA_{1c} (%)	187/165	201/170	7.2 (1.4)	7.2 (1.2)	7.1 (1.1)	7.1 (1.2)	0.005	−0.08 (−0.35 to 0.18)	0.64
Systolic blood pressure (mm Hg)	192/166	202/169	146 (21)	144 (18)	136 (19)	137 (15)	0.007	−3.9 (−8.9 to 1.1)	0.12
Cholesterol (mmol/L)	186/164	201/170	4.1 (0.9)	4.5 (1.2)	3.9 (0.9)	4.3 (0.9)	0.004	−0.03 (−0.28 to 0.22)	0.81
Wellbeing score*	192/147	201/157	25.0 (6.8)	23.9 (7.6)	23.7 (5.1)	23.2 (5.8)	0.0001	−0.71 (−2.3 to 0.8)	0.36

ICC=intracluster coefficient.
*Range 0-36 (1-12 low, 13-24 medium, 25-36 high).

Association of blood pressure in late adolescence with subsequent mortality: cohort study of Swedish male conscripts

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STUDY QUESTION Do systolic and diastolic blood pressures in young adults contribute equally, and linearly, to risk of death?

SUMMARY ANSWER In more than 1.2 million adolescent men, the relation of diastolic blood pressure to mortality was stronger than that of systolic blood pressure; the relation of diastolic blood pressure to mortality had a threshold at about 90 mm Hg, whereas that of systolic blood pressure was U shaped, with a nadir at about 130 mm Hg.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Because mortality is low in adolescents, previous studies have not been powered to investigate relations of systolic and diastolic blood pressures in adolescence to mortality. In this very large cohort of adolescent men, the relation of diastolic blood pressure to total mortality risk was stronger t han that of systolic blood pressure, which was U shaped.

Participants and setting

We included Swedish men who had military conscription examinations at a mean age of 18.4 years.

Design, size, and duration

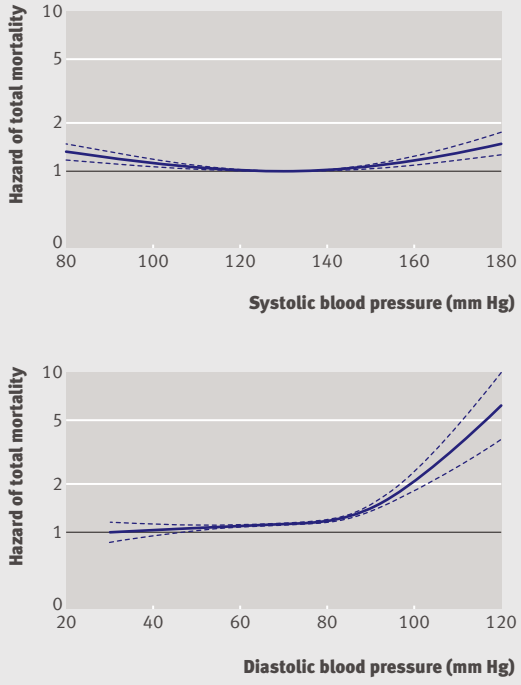
We followed a nationwide cohort of 1 207 141 men with baseline examinations between 1969 and 1995 for a median of 24 (range 0-37) years.

Main results and the role of chance

During follow-up, 28 934 (2.4%) men died. We found a U shaped relation of systolic blood pressure to total mortality, with the lowest risk seen at a systolic blood pressure of about 130 mm Hg. This pattern was driven by the relation to non-cardiovascular mortality, whereas the relation to cardiovascular mortality was monotonically increasing (higher risk with higher blood pressure). The relation of diastolic blood pressure to mortality was monotonically increasing and stronger than that of systolic blood pressure, in terms of both relative risk and population attributable fraction (deaths that could be avoided if blood pressure was in the optimal range).

Relations to cardiovascular and non-cardiovascular mortality were similar, with an apparent risk threshold at a diastolic blood pressure of about 90 mm Hg, below which diastolic blood pressure and mortality were unrelated, and above which a steep risk increase with higher diastolic blood pressures occurred. Because of the large sample size, the results are unlikely to have been produced by chance.

RELATIONS OF SYSTOLIC AND DIASTOLIC BLOOD PRESSURES TO RISK OF DEATH



Solid line represents hazard of total mortality and dashed lines are 95% CI, from multivariable regression spline Cox proportional hazards models adjusted for age, conscription date, conscription centre, socioeconomic position, body mass index, elbow flexion, hand grip, and knee extension strength. Y scale is logarithmic.

Bias, confounding, and other reasons for caution

Random misclassification bias due to baseline measurements made on only one occasion is possible. Although several potential confounders were accounted for in statistical models, residual or unmeasured confounding may exist. In particular, a limited sample with information on smoking rendered models adjusted for smoking imprecise.

Generalisability to other populations

Generalisability to women and ethnic groups other than white Europeans is unknown.

Study funding/potential competing interests

The study was funded by the Swedish Heart-Lung Foundation, the Swedish Research Council (grant 2007-5942), Uppsala University, and Arbetsmarknadens Forsakrings-och Aktiebolag.