RESEARCH

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PATRICK DUMAS/LOOK AT SCIENCES/SPL

THIS WEEK'S RESEARCH QUESTIONS

1142 How does continuous positive airway pressure affect blood pressure in patients with systemic hypertension and obstructive sleep apnoea? ▶ See video at bmj.com video

1143 Which bedside test is best for detecting inadvertent endobronchial intubation?

1144 How is age associated with functional outcomes in patients with acute ischaemic stroke undergoing thrombolysis?

1145 Does retirement change the risk of incident chronic disease, depressive symptoms, and fatigue?

1146 How do alcohol consumption patterns relate to incidence of ischaemic heart disease in two countries with contrasting lifestyles?

Could CPAP be used to treat hypertension?

In Joaquín Durán-Cantolla and colleagues' multicentre trial in Spain patients with hypertension and at least moderate sleep apnoea were randomised to continuous positive airway pressure (CPAP) or sham CPAP for three months (p 1142). This was a trial with a great research question and with methods that should prove generalisable, given that the participants were snorers recruited from primary care whose hypertension had been diagnosed recently by their general practitioners. Mean 24 hour ambulatory blood pressures (systolic, diastolic, and night time) fell by around 1.5-2 mm Hg in the CPAP group. But what do these statistically significant primary outcomes mean for clinical practice? In an accompanying video at bmj.com/video the authors and Domhnall MacAuley, *BMJ* primary care editor, discuss the trial and ponder its clinical implications.

R&R: rest and retirement

PHILIPPE DESMAZES/AFP/GETTY IMAGES

Many of us look to retirement as an opportunity to put our feet up and see out our twilight years free from the stress and hassles of the workplace. But does all this relaxation have any tangible benefit on physical or mental health, or would we be better off staying in the office?

Hugo Westerlund and colleagues' 15 year prospective study of 14 000 French men and women before and after retirement found that retirement reduced the prevalence of mental fatigue, physical fatigue, and depression (p 1145). However, retirement had no effect on self reported respiratory disease, diabetes, and coronary heart disease and stroke, which cumulatively increased with age without showing any change in trend around retirement.

Writing in a linked editorial, Alex Burdorf reports that the gap between the common retirement age at 65 and life expectancy at that age has increased substantially in the Netherlands from 6.4 to 13.3 years in the past 50 years (p 1113). Whether retiring or continuing to work is best for the health of over 65s is an important question for governments to consider given the increasing longevity of Western populations.

Drinking patterns and ischaemic heart disease

The relation between alcohol consumption and heart disease is a complicated one, with news reports lurching between saying that alcohol, usually red wine, is good for your heart and that drinking is bad for cardiovascular health.

Jean-Bernard Ruidavets and colleagues have probed this topic by comparing the drinking habits of two countries with contrasting lifestyles: Northern Ireland and France (p 1146). They found that although middle aged men in France were more likely to be drinkers than those in Belfast, and they drank more alcohol a week, the incidence of myocardial infarction and coronary death was higher in Belfast.

Looking closer, the authors discovered that in Belfast most men's alcohol intake was concentrated on one day of the weekend and that binge drinkers were almost 20 times more common in Belfast than in France. Given that binge drinkers were almost twice as likely to develop ischaemic heart disease as those who drank more regularly, the authors suggest that the high prevalence of binge drinking in Belfast might explain some of the higher risk of heart disease in the city.

And, of course, wine drinking was associated with a lower risk of coronary events, irrespective of the country. These analyses were adjusted for classic cardiovascular risk factors.

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Childhood adiposity and cardiovascular risk in adolescence

Cross sectional studies in childhood show associations between body mass index (BMI) and cardiovascular risk factors, but few prospective studies have been published. It's been said that BMI is a poor measure of adiposity, particularly in childhood, and that the magnitude of its association with risk factors might underestimate the true adverse effect of greater adiposity in this age group. In a prospective cohort study of over 5000 children in the UK, Debbie Lawlor and colleagues found that BMI, waist circumference, and total fat mass assessed at age 9-12 were positively associated with cardiovascular risk factors at age 15-16 (doi: 10.1136/bmj.c6224). The size of the associations was similar for all measures of adiposity. Girls who lost weight between childhood and adolescence had cardiovascular risk profiles broadly similar to those who were normal weight at both time points. Boys who lost weight, however, had risk factor profiles that were intermediate between those of boys who were normal weight at both ages and boys who were overweight at both ages.

bmj.com/video
Joaquín Durán-Cantolla and Jose María Montserrat, talk about CPAP as a treatment for systemic hypertension.

Continuous positive airway pressure as treatment for systemic hypertension in people with obstructive sleep apnoea: randomised controlled trial

Joaquín Durán-Cantolla,[1 2] Felipe Aizpuru,[3 4] Jose María Montserrat,[5 6] Eugeni Ballester,[5 6] Joaquín Terán-Santos,[6 7] Jose Ignacio Aguirregomoscorta,[8] Mónica Gonzalez,[9] Patricia Lloberes,[6 10] Juan Fernando Masa,[6 11] Mónica De La Peña,[6 12] Santiago Carrizo,[6 13] Mercedes Mayos,[14] Ferrán Barbé,[2 6] Spanish Sleep and Breathing Group

[1]Sleep Unit, Hospital Universitario Txagorritxu, Facultad de Medicina, Universidad del País Vasco, Vitoria 01009, Spain
[2]Department of Respiratory, IRBlleida, Lleida 25198, Spain
[3]Araba Research Unit, Hospital Universitario Txagorritxu
[4]Ciber de Epidemiología y Salud Pública (CiberEsp), Instituto de la Salud Carlos III, Madrid, Spain
[5]Sleep Unit, Department of Respiratory Medicine, Hospital Clínic de Barcelona, Barcelona 08036, Spain
[6]Ciber de Enfermedades Respiratorias (CibeRes), Instituto de la Salud Carlos III, Madrid
[7]Department of Respiratory and Sleep Medicine, Hospital General Yagüe, Burgos 09005, Spain
[8]Sleep Unit, Department of Respiratory Medicine, Hospital de Galdakano, Vizcaya 48960, Spain
[9]Department of Respiratory and Sleep Medicine, Hospital Universitario Marqués de Valdecilla, Santander 39008, Spain
[10]Sleep Unit. Department of Respiratory Medicine, Hospital Valle de Hebrón, Barcelona 08035
[11]Sleep Unit, Department of Respiratory Medicine, Hospital San Pedro de Alcántara, Cáceres 10003, Spain
[12]Sleep Unit, Department of Respiratory Medicine, Hospital Son Dureta, Palma de Mallorca 07014, Spain
[13]Sleep Unit, Department of Respiratory Medicine, Hospital Universitario Miguel Server, Zaragoza 50009, Spain
[14]Sleep Unit, Department of Respiratory Medicine, Hospital de San Pablo, Barcelona 08030
Correspondence to: J Duran-Cantolla joaquin.durancantolla@gmail.com

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STUDY QUESTION

What is the effect of continuous positive airway pressure (CPAP) on 24 hour ambulatory blood pressure monitoring values in a large number of patients with untreated systemic hypertension of new onset and obstructive sleep apnoea?

SUMMARY ANSWER

In patients with both untreated systemic hypertension and obstructive sleep apnoea, CPAP significantly reduces blood pressure, with a greater reduction in patients with systemic hypertension diagnosed by 24 hour ambulatory blood pressure monitoring and in those who used CPAP for more than three hours a night.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Obstructive sleep apnoea is a risk factor for systemic hypertension; whether CPAP can reduce blood pressure in patients with systemic hypertension and obstructive sleep apnoea is an important question. CPAP significantly reduced blood pressure by around 2 mm Hg in patients with untreated systemic hypertension and obstructive sleep apnoea, but an effect of this size may have uncertain clinical relevance.

Design

This was a multicentre, randomised, prospective, double blind, parallel study controlled by placebo with block randomisation and computer generated allocation.

Participants and setting

We included 340 patients recently diagnosed as having systemic hypertension by a general practitioner and with an apnoea-hypopnoea index per hour of sleep of >15 events/hour diagnosed by polysomnography. We assigned them to continuous positive airway pressure (CPAP) (n=169) or a placebo (n=171) of sham CPAP (a very low pressure (<1 cm H_20) without any known therapeutic effect) for three months.

RESULTS OF 24 HOUR AMBULATORY BLOOD PRESSURE MONITORING BY CHANGES AT 12 WEEKS FOR ALL FULLY EVALUABLE PATIENTS

Blood pressure measurement	Difference* (95% CI)	P value†
Daytime systolic blood pressure	1.6 (−0.2 to 3.3)	0.07
Daytime diastolic blood pressure	1.1 (−0.1 to 2.3)	0.07
Night-time systolic blood pressure	3.1 (0.9 to 5.2)	0.005
Night-time diastolic blood pressure	1.5 (0.1 to 3.0)	0.03
Mean systolic blood pressure	2.1 (0.4 to 3.7)	0.01
Mean diastolic blood pressure	1.3 (0.2 to 2.3)	0.02

*Differences (reductions) in blood pressure (mm Hg) between continuous positive airway pressure (n=169) and sham (n=171) groups.
†Calculated by *t* test; compares treatment effects.

Primary outcome(s)

The main outcomes were net changes in the different 24 hour ambulatory blood pressure monitoring values from baseline to three months of optimal or sham CPAP.

Main results and the role of chance

Of the 340 patients randomised, 277 (81%) were men; the patients had a mean age of 52.4 (SD 10.5) years, a body mass index of 31.9 (5.7), an Epworth sleepiness scale score of 10.1 (4.3), and an apnoea-hypopnoea index of 43.5 (24.5). No differences between groups were seen at baseline. Compared with placebo and analysed by intention to treat, the mean 24 hour ambulatory blood pressure of the CPAP group decreased by 1.5 (95% confidence interval 0.4 to 2.7) mm Hg (P=0.01). Mean daytime blood pressure decreased by 1.3 (−0.1 to 2.5) mm Hg, and mean night-time blood pressure decreased by 2.1 (0.5 to 3.6) mm Hg (P=0.01).

Harms

Compliance with CPAP and sham treatments was similar and we found no differences between the groups. Some secondary effects occurred in 259 (76%) patients; 12 patients in the CPAP group and 10 in the sham group discontinued the treatment because of poor tolerance.

Bias, confounding, and other reasons for caution

We have no data on the 94 patients who refused to participate, and we cannot be sure about the magnitude of potential bias. The 12 week follow-up may not be representative of longer periods. The effect size was small, and did not achieve the 3 mm Hg drop in mean 24 hour ambulatory blood pressure that the trial was powered to detect, although decreases of around 2 mm Hg, as seen in our study, might reduce cardiovascular risk.

Generalisability to other populations

All patients were habitual snorers, had just been diagnosed as having systemic hypertension, and had received no treatment other than conservative measures. They were therefore the kind of patients that general practitioners usually treat, not filtered by sleep clinics or hospitals.

Study funding/potential competing interests

The study was sponsored by the Spanish Ministry of Health (PI041110), the Basque Government's Department of Health (20031103), and the Spanish Respiratory Society (SEPAR 2005).

Trial registration number

Clinical trials NCT00202527.

Endobronchial intubation detected by insertion depth of endotracheal tube, bilateral auscultation, or observation of chest movements: randomised trial

Christian Sitzwohl,[1] Angelika Langheinrich,[1] Andreas Schober,[1] Peter Krafft,[2] Daniel I Sessler,[3] Harald Herkner,[4] Christopher Gonano,[1] Christian Weinstabl,[2] Stephan C Kettner[2]

EDITORIAL by O'Connor

[1]Department of Anaesthesiology, General Intensive Care, and Pain Control, Medical University of Vienna General Hospital, A-1090 Vienna, Austria
[2]Department of Anaesthesiology, General Intensive Care, and Pain Control, Medical University of Vienna General Hospital
[3]Department of Outcomes Research, Cleveland Clinic, Ohio, USA
[4]Department of Emergency Medicine, Medical University of Vienna General Hospital
Correspondence to: C Sitzwohl christian.sitzwohl@meduniwien.ac.at

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STUDY QUESTION

Which bedside test is best for detecting inadvertent endobronchial intubation?

SUMMARY ANSWER

Depth of endotracheal tube insertion and a combination of three clinical tests (chest auscultation, observation and palpation of chest excursion, and depth of endotracheal tube insertion) are most sensitive for detection of inadvertent endobronchial intubation.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

The recommended method for prevention of misplacement of an endotracheal tube, and potential serious complications, is bilateral auscultation of the lungs. With this technique, clinicians with limited experience detected endobronchial intubation in only 45% (nine) of cases. Detection improved to 85% (17) when they used estimated tube insertion depth.

Design

Patients were randomly assigned to eight study groups. In four groups, an endotracheal tube was fibreoptically positioned 2.5-4.0 cm above the carina, whereas in the other four groups the tube was positioned in the right mainstem bronchus. To determine whether the tube was properly positioned in the trachea, first year residents and experienced anaesthetists were randomly assigned to independently perform bilateral auscultation of the chest (auscultation); observation and palpation of symmetrical chest movements (observation); estimation of the position of the tube by the insertion depth (tube depth); or a combination of all three (all three).

Participants and setting

160 consecutive patients (American Society of Anesthesiologists category I or II), aged 19-75, scheduled for elective gynaecological or urological surgery.

Primary outcome

Correct and incorrect judgments of position of endotracheal tube.

Main results

Patients underwent 320 observations by experienced and inexperienced anaesthetists. First year residents missed endobronchial intubation by auscultation in 11 (55%) cases and performed significantly worse than experienced anaesthetists (3 (15%) missed) with this bedside test (odds ratio 10.0, 95% confidence interval 1.4 to 434). Tube depth and the three tests combined were more sensitive for detecting endobronchial intubation than auscultation. The four tested methods had the same specificity for ruling out endobronchial intubation (that is, confirming correct tracheal intubation). The average correct tube insertion depth was 21 cm in women and 23 cm in men. By inserting the tube to these distances, however, the distal tip of the tube was less than 2.5 cm away from the carina in 20% (24/118) of women and 18% (7/42) of men. Therefore an insertion depth of 20 cm in women and 22 cm in men provides a better safety margin.

Harms

There were no harms associated with the intervention.

Bias, confounding, and other reasons for caution

A possible weakness of this study is the relatively small number of patients within each of the eight groups and the difference in female and male patients included (74% *v* 26%). It is well documented, however, that the incidence of inadvertent endobronchial intubation is higher in women than in men and we thus considered the imbalance towards more women acceptable.

Generalisability to other populations

The morphometric characteristics of our study patients were typically for a western white population. For other populations different tube insertion depths might be appropriate.

Study funding/potential competing interests

None declared.

Trial registration number

NCT 01232166

DETECTION OF INADVERTENT ENDOBRONCHIAL INTUBATION BY DIFFERENT METHODS

	Bilateral auscultation	Observation of symmetrical chest movements	Depth of tube	All three
Sensitivity* (95% CI)	65 (49 to 81)	43 (25 to 60)	88 (75 to 100)	100
Specificity (95% CI)	93 (84 to 100)	90 (81 to 100)	98 (93 to 100)	95 (88 to 100)

*P<0.001 for difference between methods.

CME

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Thrombolysis in very elderly people: controlled comparison of SITS International Stroke Thrombolysis Registry and Virtual International Stroke Trials Archive

Nishant K Mishra,[1] Niaz Ahmed,[2] Grethe Andersen,[3] José A Egido,[4] Perttu J Lindsberg,[5] Peter A Ringleb,[6] Nils G Wahlgren,[2] Kennedy R Lees,[1] for the VISTA and SITS collaborators

EDITORIAL by Derex

[1]Acute Stroke Unit, University Department of Medicine and Therapeutics, Gardiner Institute, Western Infirmary and Faculty of Medicine, University of Glasgow, Glasgow G11 6NT, UK
[2]Department of Neurology, Karolinska University Hospital, Karolinska Institutet 171 76 Stockholm, Sweden
[3]Department of Neurology, Aarhus University Hospital, Aarhus, Denmark
[4]Department of Neurology, Hospital San Carlos, Spain
[5]Department of Neurology, Helsinki University Central Hospital, and Program of Molecular Neurology, University of Helsinki, Helsinki, Finland
[6]Department of Neurology, University Hospital of Heidelberg, Heidelberg, Germany
Correspondence to: K R Lees
k.r.lees@clinmed.gla.ac.uk

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STUDY QUESTION:
What effect does age have on functional outcomes in patients with acute ischaemic stroke undergoing thrombolysis, and is withholding such treatment from patients aged over 80 justified?

SUMMARY ANSWER:
After acute ischaemic stroke patients aged >80 derive similar benefits from thrombolysis (with intravenous alteplase) to those aged ≤80.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS
Currently, use of intravenous thrombolysis with alteplase has marketing approval in Europe only for patients aged under 80, and despite encouragement from clinical guidelines, access to this treatment by very elderly patients varies because of limited evidence on safety and efficacy. This large non-randomised controlled analysis shows that use of alteplase is also associated with similarly improved outcomes in patients aged >80.

Participants and setting

We compared 23 062 patients who underwent thrombolysis and were enrolled in the SITS-International Stroke Thrombolysis Registry from December 2002 to November 2009 and 6166 controls from neuroprotection trials recorded in the Virtual International Stroke Trials Archive (VISTA) during 1998-2007. Of the 29 228 patients, 3439 were aged over 80 (mean 85 years) and 210 were aged over 90.

Design, size, and duration

This was a non-randomised controlled comparison of outcomes between patients who did and did not undergo thrombolysis, classified by age categories (≤80 and >80, and 10 year age bands).

Primary outcomes, risks, and exposures

Our primary outcome measure was the distribution of scores on the modified Rankin scale at 90 days. We examined patients treated with alteplase compared with controls separately for patients aged >80 (very elderly) and patients aged ≤80. We used ordinal analysis to compare distributions, adjusting for age and baseline severity. In secondary analyses we adjusted for all variables that differed at baseline and examined dichotomised scores.

Main results and the role of chance

The common odds for better outcomes favouring alteplase were 1.4 (95% confidence interval 1.3 to 1.6; P<0.001) in the very elderly and 1.6 (1.5 to 1.7; P<0.001) in younger patients, after adjustment for age and baseline severity.

Under secondary analysis, in which we also adjusted for age, sex, history of diabetes or previous stroke, previous use of antithrombotics, baseline score on National Institutes of Health stroke scale, and hypertension, the common odds ratio was 1.5 (1.3 to 1.8; P=0.003) among very elderly patients. Dichotomisation delivered comparable results with the ordinal analyses. The results indicate that 8.2 patients aged >80 need to be treated for one more patient to achieve a modified Rankin scale score of 0-2 (no symptoms to slight disability).

Bias, confounding, and other reasons for caution

Selection for treatment with alteplase was not random. Although analyses were adjusted for known confounders and results are consistent with existing evidence from randomised trials and other controlled comparisons, we cannot exclude bias causing overestimation of benefit across all age groups.

Generalisability to other populations

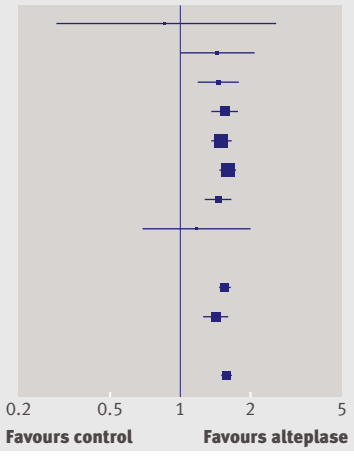
As patients treated with alteplase in this study were registered as part of routine clinical care, the results are generalisable to patients treated according to European Stroke Organisation guidelines.

Study funding/potential competing interests

NKM is supported by scholarships from the University of Glasgow, an overseas research studentship, and the European Stroke Organisation. The SITS-MOST registry was supported by Boehringer Ingelheim as a condition of EMEA approval for intravenous alteplase. KRL, GA, JAE, NGW, and NA have received support from Boehringer Ingelheim (see online publication for full disclosures).

EFFECT OF THROMBOLYSIS ON OUTCOME AFTER ACUTE ISCHAEMIC STROKE BY AGE

Age group	Events: Treated	Events: Control	Odds ratio (95% CI)	Odds ratio (95% CI)
21-30	170	12		0.86 (0.29 to 2.6)
31-40	632	104		1.5 (1.0 to 2.1)
41-50	1642	358		1.5 (1.2 to 1.8)
51-60	3658	830		1.6 (1.4 to 1.8)
61-70	6193	1422		1.5 (1.4 to 1.7)
71-80	8527	2203		1.6 (1.5 to 1.8)
81-90	2069	1158		1.5 (1.3 to 1.7)
91-100	133	77		1.2 (0.69 to 2.0)
≤80	20 860	4929		1.6 (1.5 to 1.7)
>80	2202	1237		1.4 (1.3 to 1.6)
All age groups	23 062	6166		1.6 (1.5 to 1.7)



Effect of retirement on major chronic conditions and fatigue: French GAZEL occupational cohort study

Hugo Westerlund,[1 2] Jussi Vahtera,[3 4] Jane E Ferrie,[2] Archana Singh-Manoux,[2 5] Jaana Pentti,[3] Maria Melchior,[5] Constanze Leineweber,[1] Markus Jokela,[2] Johannes Siegrist,[6] Marcel Goldberg,[5] Marie Zins,[5] Mika Kivimäki[2 3]

EDITORIAL by Burdorf

[1]Stress Research Institute, Stockholm University, SE-106 91 Stockholm, Sweden
[2]Department of Epidemiology and Public Health, University College London, London WC1E 6BT, UK
[3]Finnish Institute of Occupational Health, FI-00250 Helsinki, Finland
[4]Department of Public Health, University of Turku and Turku University Hospital, FI-20520 Turku, Finland
[5]INSERM, U1018, Villejuif, F-94807, France; Université Versailles Saint Quentin en Yvelines, France
[6]Institut für Medizinische Soziologie, Heinrich Heine-Universität Düsseldorf, D-40001 Düsseldorf, Germany
Correspondence to: H Westerlund
hugo.westerlund@stress.su.se

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STUDY QUESTION

Does retirement change the risk of incident chronic disease, depressive symptoms, and fatigue?

SUMMARY ANSWER

Statutory retirement seems not to change the risk of major chronic diseases but is associated with a substantial reduction in mental and physical fatigue and depressive symptoms, particularly among people with pre-existing chronic disease.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Retirement is a major social transition believed to have important consequences for health, but empirical evidence remains contradictory. High levels of fatigue among older workers, largely relieved by retirement, indicate a need for preventive measures, particularly given the drive to raise the retirement age in many countries.

Participants and setting

GAZEL is a prospective cohort study of employees in a French national utility company. We studied the 11 246 men and 2858 women who retired on a statutory basis between 1990 and 2006 and who had returned at least one annual questionnaire before retirement and one after retirement. The mean retirement age in this cohort was 54.8 years.

Design, size, and duration

We used a prospective cohort design with repeat measures from seven years before to seven years after retirement. Respiratory disease, diabetes, coronary heart disease and stroke, mental fatigue, and physical fatigue, were assessed annually by self report over the 15 year observation period, and depressive symptoms were measured at four time points.

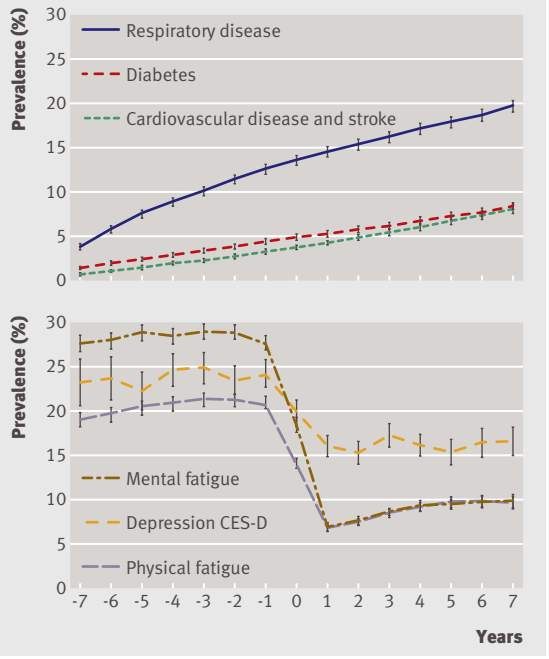
Main results and the role of chance

The average number of repeat measurements per participant was 12.1. Repeated measures logistic regression with generalised estimating equations showed that the cumulative prevalence of self reported respiratory disease, diabetes, and coronary heart disease and stroke increased with age, with no break in the trend around retirement. In contrast, retirement was associated with a substantial decrease in the prevalence of both mental fatigue (odds ratio for fatigue one year after versus one year before the retirement 0.19, 95% confidence interval 0.18 to 0.21) and physical fatigue (0.27, 0.26 to 0.30). A major decrease also occurred in depressive symptoms (0.60, 0.53 to 0.67). The decrease in fatigue around retirement was particularly pronounced among people with chronic disease before retirement.

Bias, confounding, and other reasons for caution

Distinguishing the health effects of retirement from those of age is difficult, but observations of longitudinal health trajectories that change at retirement support a link between retirement and health. We assessed chronic diseases with self reports. These are known to underestimate true prevalences but are unlikely to bias the results of changes in risk of disease in relation to the retirement transition. Observational data cannot prove causality. However, reverse causality is an implausible explanation for the observed reduction in fatigue and depression after statutory retirement.

CHANGES IN PHYSICAL MORBIDITY AND IN DEPRESSION AND FATIGUE IN RELATION TO RETIREMENT (YEAR 0)



Generalisability to other populations

The participants retired relatively young and benefited from good social security, which may limit generalisability to other settings, especially outside of France. As participants retiring on a disability pension were excluded from the analyses, the results may not apply to those who retire on health grounds.

Study funding/potential competing interests

Funding was provided by the Swedish Council for Working Life and Social Research; Academy of Finland; BUPA Foundation and Economic and Social Research Council, UK; National Institutes of Health, USA; and European Science Foundation. The GAZEL cohort was funded by EDF-GDF, INSERM, Agence nationale de la recherché (ANR), and Agence française de sécurité sanitaire de l'environnement et du travail (AFSSET), France.

Patterns of alcohol consumption and ischaemic heart disease in culturally divergent countries: the Prospective Epidemiological Study of Myocardial Infarction (PRIME)

Jean-Bernard Ruidavets,[1] Pierre Ducimetière,[2] Alun Evans,[3] Michèle Montaye,[4] Bernadette Haas,[5] Annie Bingham,[6] John Yarnell,[3] Philippe Amouyel,[4] Dominique Arveiler,[5] Frank Kee,[3] Vanina Bongard,[1] Jean Ferrières[7]

EDITORIAL by Britton

[1]Department of Epidemiology, INSERM U558, Toulouse University School of Medicine, Toulouse, France
[2]INSERM-Paris XI University, Villejuif, France
[3]UK Clinical Research Collaboration Centre of Excellence for Public Health, Queen's University Belfast, Belfast, UK
[4]Department of Epidemiology and Public Health, INSERM U744, Pasteur Institute of Lille, Lille, France
[5]Department of Epidemiology and Public Health, EA 3430, Medical Faculty, University of Strasbourg, Strasbourg, France
[6]INSERM U970, Paul Brousse Hospital, Villejuif, France
[7]Department of Cardiology B and Department of Epidemiology, INSERM U558, Toulouse University Hospital, Toulouse, France
Correspondence to: J-B Ruidavets
jean-bernard.ruidavets@cict.fr

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STUDY QUESTION

How do alcohol consumption patterns influence the incidence of ischaemic heart disease in two countries with contrasting lifestyles, Northern Ireland and France?

SUMMARY ANSWER

Drinking patterns may contribute to the higher incidence of ischaemic heart disease observed in middle aged men in Belfast, Northern Ireland, compared with those in France (Lille, Strasbourg, and Toulouse).

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Recent evidence suggests that certain drinking habits, such as binge drinking, might increase the risk of ischaemic heart disease. Heavy or binge drinking is associated with a higher risk of ischaemic heart disease than is regular drinking. A greater proportion of men in Belfast binge drink than in France, which may explain some of the higher risk of ischaemic heart disease in Belfast.

Participants and setting

Participants were men aged 50-59 years who were free of ischaemic heart disease at baseline. Study recruitment took place between 1991 and 1994 in Belfast, Northern Ireland, and in three centres in France (Lille, Strasbourg, and Toulouse).

Design, size, and duration

This study was an observational prospective cohort study of 9778 men followed up for 10 years in the Prospective Epidemiological Study of Myocardial Infarction (PRIME).

Main results and the role of chance

Alcohol consumption patterns at baseline differed radically between Belfast and French centres, with 1456 (60.5%) of the 2405 men in Belfast and 6679 (90.6%) of the 7373 men at the French centres reporting drinking alcohol at least once a week (alcohol <50 g if on only one occasion). However, the alcohol volume consumed by drinkers over a week was similar at inclusion. In Belfast, however, most men's alcohol intake was concentrated on one day of the weekend (on Saturdays drinkers in Belfast consumed on average 91.4 g of alcohol compared with 41. 1 g in France) and binge drinkers (alcohol >50 g on at least one day a week) were almost 20 times more common than in France (9.4% *v* 0.5%). In the French centres, alcohol consumption was more evenly spread throughout the entire week.

Annual incidence of hard coronary events (incident myocardial infarction and coronary death) per 1000 person years during follow-up was 5.63 (95% confidence interval 4.69 to 6.69) in Belfast and 2.78 (95% CI 2.41 to 3.20) in France. Annual incidence of angina pectoris was 5.46 (95% CI 4.53 to 6.54) and 3.49 (95% CI 3.06 to 3.96) per 1000 participants, respectively.

For the whole cohort, adjusted hazard ratios for hard coronary events compared with regular drinkers were 1.97 (95% CI 1.21 to 3.22) for binge drinkers, 2.03 (95% CI 1.41 to 2.94) in never drinkers, and 1.57 (95% CI 1.11 to 2.21) for former drinkers. Hazard ratios were comparable in Belfast and in the French centres. No significant association of angina pectoris with patterns of alcohol consumption was found. The risk of developing hard coronary events in Belfast in comparison with the French centres was 2.03 (95% CI 1.62 to 2.53), although this value gradually decreased after successive adjustment for classic risk factors, patterns of alcohol consumption, and wine drinking.

Bias, confounding, and other reasons for caution

A very high follow-up was achieved over 10 years, with only 5% attrition from the cohort. Validation of ischaemic heart disease outcomes was standardised and completed by the same ad hoc medical committee. A potential weakness of the study is the absence of a detailed history of alcohol consumption behaviour. Alcohol patterns were assessed once at inclusion and were not estimated during the course of the follow-up. Changes in alcohol habits during the follow-up period could have had an effect on the influence of alcohol consumption on the incidence of ischaemic heart disease.

Generalisability to other populations

Demographic factors influence alcohol consumption behaviour and our study investigated a very homogeneous population of men aged 50-59 years, so we cannot generalise our results to women and to other age groups.

Study funding and potential competing interests

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HAZARD RATIOS FOR HARD CORONARY EVENTS IN BELFAST IN RELATION TO THE FRENCH CENTRES

	Hard coronary events	
	Hazard ratio (95% CI)	P value
Non-adjusted	2.03 (1.62 to 2.53)	0.001
Adjusted for classic risk factors*	1.76 (1.37 to 2.67)	0.001
Adjusted for classic risk factors and drinking status†	1.35 (1.02 to 1.80)	0.04
Adjusted for classic risk factors, drinking status, and wine drinking	1.09 (0.79 to 1.50)	0.59

*Adjusted for age, centre, tobacco consumption, years of education, level of physical activity, systolic blood pressure, apolipoprotein A-1 and apolipoprotein B concentration, waist circumference, and treatment for hypertension, diabetes, and dyslipidaemia.
†Drinking status was regular drinker, binge drinker, never drinker, or former drinker.