# RESEARCH

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## THIS WEEK'S RESEARCH QUESTIONS

**1229** What happens to health and socioeconomic determinants of health in host cities after major multi-sport events?
**1230** Do geriatric rehabilitation programmes improve outcomes for inpatients?
**1231** Is QRISK2 better than NICE's Framingham score at predicting 10 year risk of cardiovascular disease?
**1232** What are the unintended effects of statins?
**1233** Is spironolactone associated with increased renal toxicity in patients with and without heart failure?

### Effects of statins—mostly good; some bad

STEVE PERCIVAL/SPL

Julia Hippisley-Cox, Carol Coupland, and colleagues' cohort study using the QResearch database examined the unintended effects of statins in nearly 226 000 users of statins and more than one million non-users in English and Welsh general practices (p 1232). On the basis of a 20% threshold for cardiovascular risk, the number needed to treat (NNT) with any statin to prevent one case of cardiovascular disease over five years was 37 (95% confidence interval 27 to 64) for women and 33 (24 to 57) for men.

The potential harms of statins have been much debated, and this study adds robust and largely reassuring quantification of these risks. There was no significant association of statins with risk of Parkinson's disease, rheumatoid arthritis, venous thromboembolism, dementia, osteoporotic fracture, or several common cancers—indeed, the risk of oesophageal cancer was significantly lower in statin users, with an NNT of 1266 (850 to 3460) in women and 1082 (711 to 2807) in men.

But the news wasn't all good. In women, the number needed to harm (NNH) for an additional case of acute renal failure over five years was 434 (284 to 783), for moderate or severe myopathy was 259 (186 to 375), for moderate or severe liver dysfunction was 136 (109 to 175), and for cataract was 33 (28 to 38). The numbers for men were similar, but they had a higher risk of myopathy (NNH 91, 74 to 112). If you would like to monitor such risks in your patients, a sister paper in *Heart*, published with open access, presents the authors' open source algorithms for predicting acute renal failure, moderate to serious myopathy, and cataract (http://heart.bmj.com/content/early/2010/05/20/hrt.2010.199034.short?q=w_heart_ahead_tab) and an online risk calculator (http://www.qintervention.org/).

Unsurprisingly, the *BMJ* paper was widely reported, and on the Canadian Broadcasting Company's website it garnered nearly 200 responses in the first week and was recommended 77 times (http://www.cbc.ca/health/story/2010/05/21/statin-cholesterol-side-effects.html).

### Benefits (or not) of hosting large international sports events

Hosting the Olympic Games in 2012 is set to cost the United Kingdom £9.3bn (€10.7bn; $13.3bn), roughly £150 for every man, woman, and child in the country. And what does the population get in return for this investment? Potentially nothing, according to Gerry McCartney and colleagues' systematic review of the health and socioeconomic effects of major multi-sport events (p 1229).

Their search for studies that assessed the "legacy" of big sports events turned up 54 poor quality studies, 18 of which reported economic outcomes and only five of which looked at health outcomes. Collectively, neither the studies that examined health legacies nor those that looked for financial benefits showed a clear positive or negative effect of these events on the host population. Dr McCartney talks about these findings in more detail in a *BMJ* podcast called "Legacy of the games" (www.bmj.com/podcasts).

So what is the outlook for Londoners during and after the 2012 games? Labour MP Kate Hoey, the mayor of London's commissioner for sport, recently told the *London Evening Standard* that "there has been a government failure on legacy" (http://www.thisislondon.co.uk/standard-sport/interviews/article-23813274-the-big-interview-kate-hoey.do).

Editorialist Mike Weed is more optimistic and thinks the London Olympic Games is a good opportunity to robustly measure the population outcomes of large sports events and find out, for better or worse, what the legacy of such events really is (p 1205). However, the organisers need to improve their study designs and the proposed outcome measures first, he says, otherwise "the risk for the UK population is not that we will not get the benefits we want for our £150 a head investment in London 2012, but that there will be no robust evidence of what we have paid for."

## RESEARCH ONLINE Most read research on bmj.com this week http://www.bmj.com/channels/research.dtl

**Unintended effects of statins in men and women in England and Wales: population based cohort study using the QResearch database** (doi:10.1136/bmj.c2197)

**Toothbrushing, inflammation, and risk of cardiovascular disease: results from Scottish Health Survey** (doi:10.1136/bmj.c2451)

**Long term treatment with metformin in patients with type 2 diabetes and risk of vitamin B-12 deficiency: randomised placebo controlled tri**al (doi:10.1136/bmj.c2181)

**Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: systematic review and meta-analysis** (doi:10.1136/bmj.c2096)

**Effect on falls of providing single lens distance vision glasses to multifocal glasses wearers: VISIBLE randomised controlled trial** (doi:10.1136/bmj.c2265)

# The health and socioeconomic impacts of major multi-sport events: systematic review (1978-2008)

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**EDITORIAL** by Weed
**FEATURE,** p 1222
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## STUDY QUESTION

What are the effects of major multi-sport events such as the Olympic Games and the Commonwealth Games on health and socioeconomic determinants of health in the population of the host city?

## SUMMARY ANSWER

There is little or no evidence that major multi-sport events held between 1978 and 2008 had positive health impacts on the populations of cities that hosted these events.

## WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Cities holding major multi-sport events are under increasing pressure to justify expenditure by creating a positive legacy for the host population; for example, in terms of improvements in employment levels and health. Our review indicates that the host population cannot expect positive health or socioeconomic benefits from major multi-sport events. How the impacts of events are evaluated needs to improve to allow decision makers pitching for future events to make informed judgments.

### Selection criteria for studies

We searched the following sources without language restrictions for papers published between 1978 and 2008: Applied Social Science Index and Abstracts; British Humanities Index; Cochrane database of systematic reviews; Econlit database; Embase; Education Resources Information Center database; Health Management Information Consortium database; International Bibliography of the Social Sciences; Medline; PreMedline; PsycINFO; Sociological Abstracts; Sportdiscus; Web of Knowledge; Worldwide Political Science Abstracts; and the grey literature. We excluded studies that used exclusively estimated data rather than actual data. Studies were selected and critically appraised by two independent reviewers. All data extraction was checked by a second reviewer.

### Primary outcomes

We included outcomes relating to health, wellbeing, quality of life, health service use, and physical activity or functioning, and any measures of the socioeconomic determinants of health, such as the environment and access to services.

### Main results and role of chance

Fifty four studies met the review criteria and were included. Fifty one (94%) studies were quantitative, of which 37 (73%) were repeat cross-sectional studies and 3 (6%) were qualitative. Five studies (9%) reported health outcomes, including suicide, paediatric health service demand, presentation of children with asthma, and presentations of problems related to illicit drug use. The data did not indicate clear negative or positive health impacts of major multi-sport events.

Economic outcomes were reported in 18 studies (33%); tourism in nine (17%); transport or environmental outcomes in eight (15%); housing, crime, or demographics in eight (15%); business outcomes in six (11%); recreation in four (7%); culture in four (7%), and volunteering outcomes in three (6%). The overall impact of major multi-sport events on economic growth and employment was unclear. Two thirds of the economic studies reported increased economic growth or employment immediately after the event, but all these studies used some estimated data in their models, failed to account for opportunity costs, or examined only short term effects. For transport outcomes, synthesis suggested that event related interventions—such as restricted car use and public transport promotion—were associated with significant short term reductions in traffic volume, congestion, or pollution in four out of five cities.

### Bias, confounding, and other reasons for caution

Study quality was poor, with 85% of quantitative studies assessed as being below level 2+ (low risk of confounding, bias, or chance) on the Health Development Agency appraisal scale, often because of a lack of comparison group.

### Study funding/potential competing interests

GMcC, ST, HT, VH, and LB were funded by the Chief Scientist Office at the Scottish Government Health Directorate, JS and DSM were funded by NHS Greater Glasgow and Clyde, and PH and DSM were funded by the University of Glasgow. GMcC is a member of the Scottish Socialist Party and was previously involved in a project to have a velodrome built in the west of Scotland. All other authors declare no competing interests.

**IMPACTS OF MAJOR MULTI-SPORTS EVENTS ON HEALTH OUTCOMES**

| Study | Sporting Event | Health Outcome | Impact* |
|---|---|---|---|
| Lee (2007) | 2002 Asian Games Busan, South Korea | Childhood asthma hospital admissions | ↔ |
| Friedman (2001) | 1996 Olympic Games Atlanta, GA, USA | Childhood asthma acute care events | ↓ |
| Simon (1998) | 1996 Olympic Games Atlanta | Paediatric health service demand | ↑ |
| Indig (2003) | 2000 Olympic Games Sydney, Australia | Hospital presentations related to illicit drugs | ↑ |
| Shin (2000) | 1988 Olympic Games Seoul, South Korea | Suicide rates | ↔ |

See the full paper for impacts on recreation, transport, crime, volunteers, and culture.
*↑=increase; ↓=decrease; ↔=no change.

# Inpatient rehabilitation specifically designed for geriatric patients: systematic review and meta-analysis of randomised controlled trials

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**STUDY QUESTION** Do inpatient rehabilitation programmes specifically designed for geriatric patients improve outcomes?

**SUMMARY ANSWER** Inpatient rehabilitation specifically designed for geriatric patients has beneficial short term effects and less pronounced longer term effects over usual care for all outcomes measured.

**WHAT IS KNOWN AND WHAT THIS PAPER ADDS** Inpatient rehabilitation programmes specifically designed for patients with cardiac, neurological, pulmonary, or musculoskeletal problems have been shown to improve patient outcomes. Inpatient rehabilitation programmes specifically designed for geriatric patients also improve outcomes.


### Selection criteria for studies

This systematic review and meta-analysis included randomised controlled trials on the short or longer term effects of inpatient rehabilitation specifically designed for geriatric patients. Rehabilitation was defined as inpatient multidisciplinary programmes with active physiotherapy or occupational therapy, or both, according to the World Health Organization's international classification of functioning, disability, and health (ICF) framework. Published studies were identified through searches in Medline, Embase (1 January 1970 to 31 July 2008) and the Cochrane Central Register of Controlled Trials (Clinical Trials; CENTRAL) database and by screening reference lists. No language restrictions were applied. Trials had to report at least one of the primary outcomes at one time point.

### Primary outcomes

Functional status, admissions to nursing homes, and mortality at discharge and at the end of follow-up (range 3-12 months).

### Main results and role of chance

We included 17 trials with 4780 patients that compared the effects of general or orthopaedic geriatric rehabilitation programmes with usual care. Meta-analyses of effects indicated an overall benefit in short term outcomes (at discharge) (odds ratio 1.75 (95% confidence interval 1.31 to 2.35) for function, relative risk 0.64 (0.51 to 0.81) for admissions to nursing homes, relative risk 0.72 (0.55 to 0.95) for mortality), and longer term (at the end of follow-up) (1.36 (1.07 to 1.71), 0.84 (0.72 to 0.99), 0.87 (0.77 to 0.97), respectively). Compared with patients in the control groups, the weighted mean length of hospital stay after randomisation was longer in patients allocated to general geriatric rehabilitation (24.5 *v* 15.1 days) and shorter in patients with orthopaedic rehabilitation (24.6 *v* 28.9 days). Multiple stratified analyses according to characteristics of the programme, patients, and quality of the methods showed only two significant differences in effects between study subgroups: orthopaedic intervention programmes were more likely to be associated with functional improvement at discharge (odds ratio 2.33 (1.62 to 3.34), P=0.04) and at the end of follow-up (1.79 (1.24 to 2.60), P=0.01), and there was a more beneficial short term effect for admissions to nursing homes in study populations with a younger mean age (<80) compared with populations with a higher mean age (relative risk 0.75 (0.58 to 0.96), P=0.045).

### Bias, confounding, and other reasons for caution

Given the limited number of included studies we might have missed true differences between study subgroups. The pooled effects for function should be interpreted with caution because the true differences in effects between studies might be caused by uncharacterised or unexplained underlying factors or the variability of outcome measures of functional status. Differences in length of stay after randomisation in intervention compared with control patients might have potentially influenced the comparability of outcome data measured at hospital discharge. Longer term effects for all outcomes seemed to be less pronounced than short term effects, which might in part be explained by variable and potentially suboptimal treatments in intervention patients after hospital discharge. Outpatient treatments after the intervention were seldom described, making interpretation of their potential influences on longer term effects impracticable.


**EFFECTS OF INPATIENT REHABILITATION SPECIFICALLY DESIGNED FOR GERIATRIC PATIENTS**

| No of included studies | Outcome | Effect measure (95% CI) | Test of heterogeneity |
|---|---|---|---|
| **Short term effect (at discharge)** | | | |
| 8 | Functional improvement | 1.75* (1.31 to 2.35) | $I^2$=38.4%, P=0.12 |
| 10 | Admission to nursing home | 0.64† (0.51 to 0.81) | $I^2$=14.6%, P=0.31 |
| 12 | Mortality | 0.72† (0.55 to 0.95) | $I^2$=0.0%, P=0.56 |
| **Longer term effect (at end of follow-up)** | | | |
| 12 | Functional improvement | 1.36* (1.07 to 1.71) | $I^2$=51.4%, P=0.02 |
| 13 | Admission to nursing home | 0.84† (0.72 to 0.99) | $I^2$=22.6%, P=0.22, |
| 15 | Mortality | 0.87† (0.77 to 0.97) | $I^2$=0.0%, P=0.60 |

*Odds ratio.
†Relative risk.

### Study funding/potential competing interests

SB was supported by a Forschungskolleg Geriatrie Grant from the Robert Bosch Foundation, Stuttgart, Germany (No 32.5.1141.0021.0).

# An independent and external validation of QRISK2 cardiovascular disease risk score: a prospective open cohort study

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**EDITORIAL by Scott**

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**Response on bmj.com**

**"When would the authors recommend the application of QRISK? Should it be used to assess cardiac risk in the screening of asymptomatic patients without cardiovascular disease or as the best risk score for quantifying risk in patients with cardiovascular disease? And should it be applied in the United Kingdom only or also in areas of the world with limited resources, where finding low cost strategies for scoring risk is essential?"**

Roberto G Carbone, Sergio Rizzo, and Marco Sicuro, Regional Hospital Aosta, Italy; Paolo Paredi, Royal Brompton Hospital, London, United Kingdom

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## STUDY QUESTION

Does QRISK2 provide an improvement over the NICE version of the Framingham risk score for predicting the 10-year risk of cardiovascular disease in the United Kingdom?

## SUMMARY ANSWER

Yes, QRISK2 is more accurate in identifying a high risk population for cardiovascular disease in the United Kingdom than the NICE version of the Framingham equation.

## WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Cardiovascular risk prediction in the United Kingdom has until recently been based on a NICE adjusted version of the US Framingham model that has been shown to over-predict risk. Independent evaluation of QRISK2 shows better performance than NICE Framingham in a large external cohort of UK patients, where QRISK2 identified a group of high risk patients who went on to experience more cardiovascular events over the next 10 years than a similar high risk group identified by NICE Framingham.

### Participants and setting

A total of 365 general practices from the United Kingdom contributing to The Health Improvement Network (THIN) database, contributing 1.58 million patients (9.4 million person years and 71 365 cardiovascular events) aged 35-74 years and registered between 1 January 1993 and 20 June 2008.

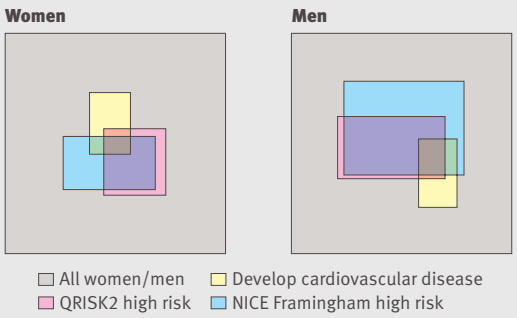
### Design

Prospective cohort study to validate a new cardiovascular risk score, QRISK2, and to compare its performance with the version of the Framingham equation recommended until recently by the National Institute for Health and Clinical Excellence (NICE). QRISK2 includes traditional risk factors included in the Framingham equations (age, sex, systolic blood pressure, smoking status, and total serum cholesterol:high density lipoprotein ratio), but it also includes body mass index, family history of cardiovascular disease, social deprivation, use of antihypertensive treatment, self assigned ethnicity, and conditions associated with cardiovascular risk.

### Main results and the role of chance

The results from this independent and external validation of QRISK2 indicate that QRISK2 offers improved prediction of a patient's 10-year risk of cardiovascular disease over the NICE version of the Framingham equation in the United Kingdom. Discrimination and calibration statistics were better with QRISK2. QRISK2 explained 33% of the variation in men and 40% for women, compared with 29% and 34% respectively for the NICE Framingham. Among the men predicted to be at high risk (≥20% 10-year risk of a cardiovascular event), the incidence rate of cardiovascular disease events (per 1000 person years) was 27.8 (95% confidence interval 27.4 to 28.2) with QRISK2 and 21.9 (21.6 to 22.2) with NICE Framingham. Similarly, the incidence rate of cardiovascular disease events among women in the high risk group was 24.3 (23.8 to 24.9) with QRISK2 compared with 20.6 (20.1 to 21.0) with NICE Framingham. In total, 90 823 men (11.6%) would be reclassified, with 1.8% (11 231) upgraded from low risk with NICE Framingham to high risk with QRISK2. Similarly, 41 126 women (5.2%) would be reclassified, with 15 748 (2.1%) upgraded from low risk with NICE Framingham to high risk with QRISK2. For both men and women, the mean predicted risks in the reclassified patients were more accurate using QRISK2 when compared to the mean observed risks using NICE Framingham.

**PROPORTIONS OF PATIENTS CLASSIFIED AS HIGH RISK BY RISK SCORES WHO HAD A SUBSEQUENT CARDIOVASCULAR EVENT**




### Bias, confounding, and other reasons for caution

There were high levels of missing data for the total serum cholesterol:high density lipoprotein ratio. However, we used multiple imputation with 20 multiple imputed datasets to deal with the missing data. Omitting patients with missing data even in validation will result in performance data that are biased, and so that practice should be avoided.

### Study funding/potential competing interests

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

# Unintended effects of statins in men and women in England and Wales: population based cohort study using the QResearch database

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EDITORIAL
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## STUDY QUESTION

What are the unintended effects of statins?

## SUMMARY ANSWER

Claims of unintended benefits of statins remain unsubstantiated, except for oesophageal cancer. Their adverse effects on hepatic and renal function, muscles and eyes were quantified.

## WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Information on the unintended effects of statins in representative primary care populations is lacking. This study found that the risk of oesophageal cancer was reduced in statin users but the risks of liver dysfunction, acute renal failure, myopathy, and cataract were increased.

### Participants and setting

225 922 new users of statins and 1 778 770 non-users of statins aged 30-84 years from 368 general practices in England and Wales supplying data to the QResearch database.

### Design, size, and duration

We undertook a prospective open cohort study. Cox proportional hazards models were used to estimate the effects of statin type, dose, and duration of use, adjusting for confounders. Outcomes were a range of conditions (see table). The number needed to treat (NNT) or number needed to harm (NNH) was calculated and numbers of additional or fewer cases estimated for 10 000 treated patients.

### Main results and the role of chance

Individual statins were not significantly associated with risk of Parkinson's disease, rheumatoid arthritis, venous thromboembolism, dementia, osteoporotic fracture, gastric cancer, colon cancer, lung cancer, melanoma, renal cancer, breast cancer, or prostate cancer. Statin use was associated with decreased risks of oesophageal cancer but increased risks of moderate or serious liver dysfunction, acute renal failure, moderate or serious myopathy, and cataract. Adverse effects were similar across statin types for each outcome except liver dysfunction where risks were highest for fluvastatin. A dose-response effect was apparent for acute renal failure and liver dysfunction, based on the 20% threshold for cardiovascular risk the NNTs and NNHs for men and women are shown in the table.

### Bias, confounding, and other reasons for caution

Observational studies, with their representative and ethnically diverse populations, have limitations, notably bias and unmeasured confounding.

### Generalisability to other populations

Our study has good face validity and is likely to be generalisable as it was done in a large primary care population representative of where most patients in the United Kingdom are assessed, treated, and followed up.

### Study funding/potential competing interests

This study received no external funding. JH-C is codirector of QResearch (a joint partnership between the University of Nottingham and Egton Medical Information System) and director of ClinRisk, which produces software for implementation of clinical risk algorithms to improve patient care. CC is a consultant statistician for ClinRisk.

**POTENTIAL BENEFITS AND HARMS OF STATINS OVER FIVE YEARS IN PATIENTS AGED 35-74 FREE OF CARDIOVASCULAR DISEASE AT BASELINE WITH QRISK2 SCORE OF ≥20%**

| Outcomes | NNH (95% CI) | NNT (95% CI) | Estimated No of cases per 10 000 patients treated (95% CI) | |
|---|---|---|---|---|
| | | | Extra cases | Prevented cases |
| Potential benefits in women: | | | | |
| Cardiovascular disease | — | −37 (−64 to −27) | — | −271 (−374 to −157) |
| Oesophageal cancer | — | −1266 (−3460 to −850) | — | −8 (−12 to −3) |
| Potential harms in women: | | | | |
| Acute renal failure | 434 (284 to 783) | — | 23 (13 to 35) | |
| Cataract | 33 (28 to 38) | — | 307 (260 to 355) | |
| Liver dysfunction | 136 (109 to 175) | — | 74 (57 to 91) | |
| Myopathy | 259 (186 to 375) | — | 39 (27 to 54) | |
| Potential benefits in men: | | | | |
| Cardiovascular disease | — | −33 (−57 to −24) | — | −301 (−417 to −174) |
| Oesophageal cancer | — | −1082 (−2807 to −711) | — | −9 (−14 to −4) |
| Potential harms in men: | | | | |
| Acute renal failure | 346 (245 to 539) | — | 29 (19 to 41) | — |
| Cataract | 52 (44 to 63) | — | 191 (158 to 225) | — |
| Liver dysfunction | 142 (115 to 180) | — | 71 (56 to 87) | — |
| Myopathy | 91 (74 to 112) | — | 110 (90 to 134) | — |

**Response on bmj.com**

**"Comparing cardiovascular outcomes derived from randomised trials with adverse reactions to statins derived from observational studies is like comparing apples and oranges."**
Luca Mascitelli, Comando Brigata alpina Julia, Udine, Italy
To submit a rapid response, go to any article on bmj.com and select "Respond to this article"

# Spironolactone use and renal toxicity: population based longitudinal analysis

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## STUDY QUESTION

Is spironolactone associated with increased renal toxicity in patients with and without heart failure in the setting of the UK National Health Service?

## SUMMARY ANSWER

Despite a marked increased in the use of spironolactone in patients with and without heart failure, no increase in hospital admissions for hyperkalaemia occurred and outpatient hyperkalaemia actually fell.

## WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Doctors are reluctant to use spironolactone because of reports of hyperkalaemia due to spironolactone use in patients with heart failure. No increase in hyperkalaemia related hospital admissions or renal toxicity occurred despite increased use of spironolactone in patients with heart failure, hypertension, or liver disease.

### Participants and setting

We studied all patients resident in Tayside, Scotland, who received one or more dispensed prescriptions for spironolactone between 1994 and 2007.

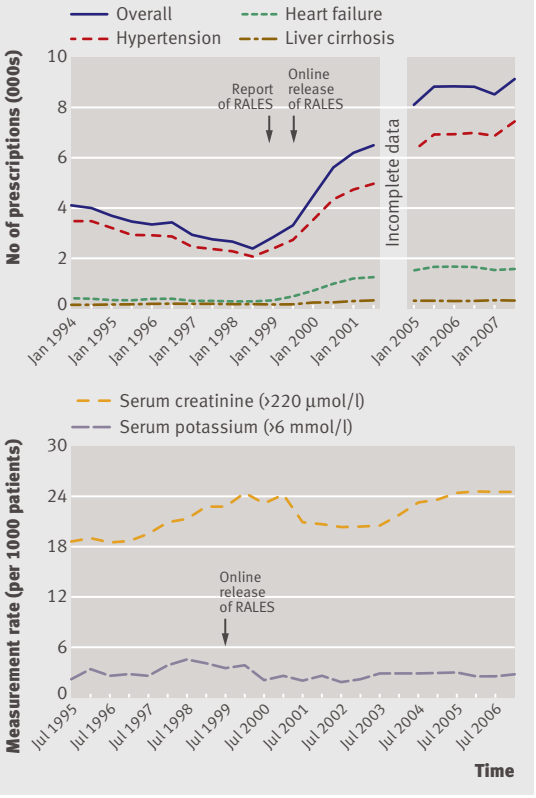
### Design, size, and duration

This was a population based longitudinal analysis using a record linkage database over 14 years. The main outcome measures were the rates of prescribing for spironolactone, hospital admissions for hyperkalaemia, and hyperkalaemia and renal function without admission, before and after the publication of results from the Randomised Aldactone Evaluation Study (RALES).

### Main results and the role of chance

Prescriptions for spironolactone and measurements of serum creatinine and serum potassium all increased in parallel after the release of the RALES results in 1999 (from 2847, 5345, and 5246 in the first half of 1999 to 6582, 10 753, and 10 534 by the second half of 2001, and to 8619, 17 844, and 17 649 by 2007). These increases occurred in patients with and without heart failure (figure). However, the numbers/rates of high serum creatinine measurements (>220 µmol/l) and hyperkalaemia (serum potassium >6 mmol/l) did not increase significantly. Few hospital admissions for hyperkalaemia occurred over this time: three in the first quarter of 1995, two in the last quarter of 2001, and three in 2007. Among patients who were taking angiotensin converting enzyme inhibitors and who had recently been admitted to hospital for heart failure, the rate of spironolactone use was 19.8 per 100 patients in early 1999 rising to 70.1 by late 2001 (P<0.01) and 61.3 by 2007. The rate of outpatient measured hyperkalaemia did not increase (9.9 per 100 patients in early 1999, 6.9 in late 2001, and 2.9 in 2007) despite the increased use of spironolactone.

**SPIRONOLACTONE PRESCRIPTIONS (TOP) AND RATES OF RENAL TOXICITY (BOTTOM) IN TAYSIDE POPULATION**




### Bias, confounding, and other reasons for caution

ICD-9 and ICD-10 codes were used for hospital admission due to heart failure and liver disease, which may be subject to some degree of misclassification because of changes in coding patterns. This was an observational study and did not adjust for other risk factors. Residual confounding cannot be controlled for.

### Generalisability to other populations

The results reflect only one NHS region. We would expect other regions to have similar monitoring systems. Further study on this topic in a large population would strengthen the evidence of safe use of spironolactone in patients with heart failure.

### Study funding/potential competing interests

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