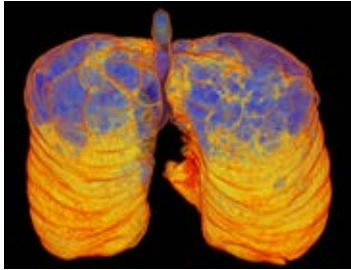


# research



Mortality from respiratory diseases has decreased in the UK and EU15+ countries p 353



Marked increase of imaging, laboratory, and other tests in UK primary care p 354



PPI in clinical trials is likely to improve participant enrolment rates p 356

## ORIGINAL RESEARCH Observational study

### Respiratory disease mortality in the United Kingdom compared with EU15+ countries in 1985-2015

Salciccioli JD, Marshall DC, Shalhoub J, Maruthappu M, De Carlo G, Chung KF

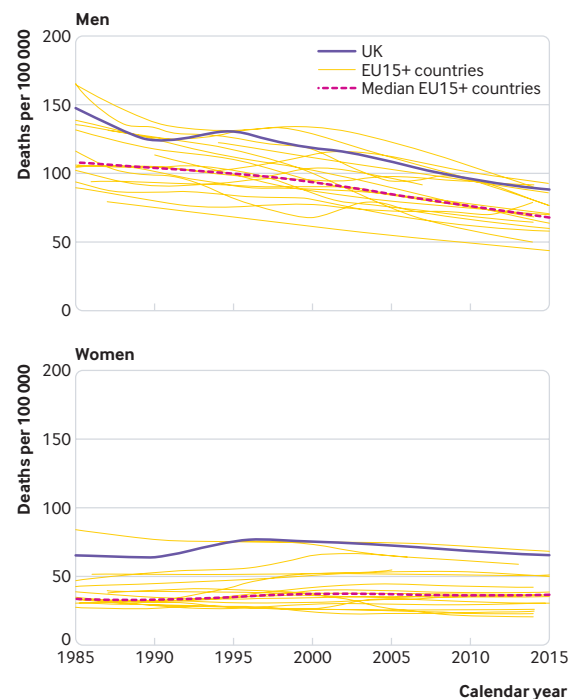
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**Study question** What are the trends in mortality from respiratory disease in the UK compared with European Union (EU) 15+ countries?

**Methods** This study was an observational analysis of death rates from primary respiratory diseases in EU15+ countries between 1985 and 2015 using data from the World Health Organization mortality database. EU15+ countries comprise the UK, Austria, Belgium, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxembourg, Netherlands, Portugal, Spain, Sweden, Australia, Canada, the United States, and Norway. Age standardised death rates per 100 000 population were calculated. Overall trends in respiratory disease mortality in the UK were compared with EU15+ countries by using locally weighted scatterplot smoother modelling.

**Study answer and limitations** Between 1985 and 2015, age standardised death rates in the UK for overall respiratory disease fell from 151 to 89 per 100 000 for men and changed from 67 to 68 per 100 000 for women. In the EU15+ countries, the corresponding changes were from 108 to 69 per 100 000 for men and from 35 to 37 per 100 000 for women. There was higher mortality in the UK than in most EU15+ countries for subcategories of respiratory disease in both men and women. Weaknesses of the study are that the data do not provide causal explanations and that reasons for the observed differences cannot be characterised.



Trend in age standardised death rates per 100 000 population

**What this study adds** This study confirms that overall mortality from respiratory disease is decreasing over time, both in the UK and in EU15+ countries. The UK has higher mortality from overall respiratory disease and subcategories of respiratory disease (obstructive, infectious, and interstitial respiratory disease) than most EU15+ countries.

**Funding, competing interests, and data sharing** This study was not externally funded. The authors have no competing interests. No additional data are available.

# Use of tests in UK primary care

## ORIGINAL RESEARCH Retrospective analysis of 250 million tests

### Temporal trends in use of tests in UK primary care, 2000-15

O'Sullivan JW, Stevens S, Hobbs FDR, et al

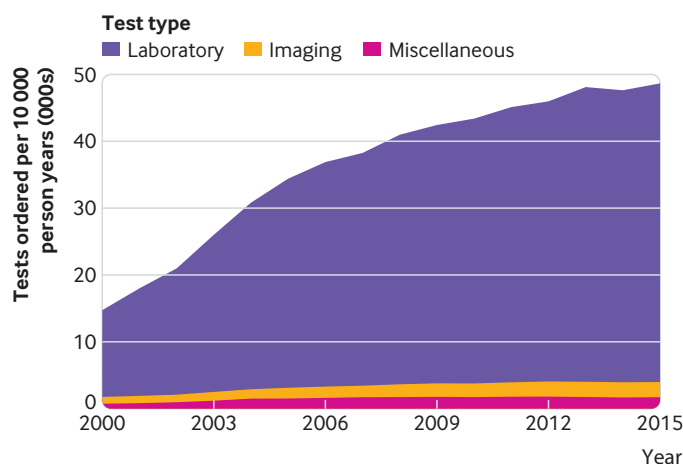
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Find this at: <http://dx.doi.org/10.1136/bmj.k4666>

**Study question** Has there been an increase in test use in UK general practice, and, if so, to what degree and which tests showed the largest increase?

**Methods** The authors used data from the UK Clinical Practice Research Datalink to retrospectively analyse temporal trends in the use of tests from general practices from 2000/1 to 2015/16. They calculated crude and age and sex standardised rates of total test use and of 44 specific tests.

**Study answer and limitations** 262 974 099 tests were analysed over 71 436 331 person years. Age and sex adjusted use increased by 8.5% annually (95% confidence interval 7.6% to 9.4%); from 14 869 tests per 10 000 person years in 2000/1 to 49 267 in 2015/16, a 3.3-fold



Temporal trends in total test use by test type

increase. Patients in 2015/16 had on average five tests per year, compared with 1.5 in 2000/1. Test use also increased across all age

## COMMENTARY Large increases suggest it's time for a rethink

Above O'Sullivan and colleagues investigate temporal trends in the use of tests in UK primary care over a 15 year period (2000-15).<sup>2</sup> Test use is an integral part of clinical decision making and this large scale study examined more than 260 million tests for more than 11 million patients in primary care. Use of tests increased significantly across all age groups, in both sexes, for all test types, and for 40 of the 44 tests specifically studied, showing a substantial increase in test use over time.

Why is this happening? This study was unable to examine the purpose of tests ordered (diagnosis or disease monitoring, for example) or if tests were clinically indicated. However, the exponential increase in certain blood tests, such as for vitamin D,

ferritin, and iron, often ordered for patients presenting with non-specific symptoms, could indicate over-testing.

Over-testing has many drivers—these include health system factors where, in fee-for-service health systems, financial or other incentives might inadvertently promote increased testing.<sup>3,4</sup> Expanded disease definitions identify more previously healthy people as being unwell; a review of US clinical guidelines reported that for 10 of 16 guidelines studied, disease definitions had been widened.<sup>3,5</sup>

An example is the publication of new diagnostic criteria for chronic kidney disease on the basis of largely laboratory measurements of kidney function and damage.<sup>6</sup> These new variables result in more than 1 in 8 US adults

### Reducing over-testing represents an evidence based approach to decreasing costs without compromising health

(14%) having a diagnosis of chronic kidney disease. The combination of this high rate of diagnosis with the low rate of total kidney failure suggests that many of those with a diagnosis of chronic kidney disease will never progress to symptomatic kidney disease.<sup>6</sup>

#### Overmedicalisation

Policy drivers such as the UK's system of pay for performance for general practices (Quality and Outcomes Framework) might also influence test rates. Thyroid function tests, included as part of the QOF, saw a 7.1% average annual increase over the study period.<sup>2</sup> A proportion of people tested will receive a diagnosis of subclinical hypothyroidism,<sup>7</sup> which is often treated with thyroid hormones, especially when it co-occurs with symptoms

potentially attributable to hypothyroidism, such as fatigue and weight gain.<sup>8</sup> A recent systematic review and meta-analysis of 21 randomised controlled trials, however, reported that thyroid hormone treatment was not statistically significantly associated with improvements in quality of life or thyroid related symptoms for people with subclinical hypothyroidism.<sup>7</sup> This is an example of overmedicalisation, where a patient might be treated for a laboratory abnormality without clinical benefit but with attendant risks of side effects as well as the practical inconvenience.

Clinicians might also order unnecessary tests from fear of missing a diagnosis or defensive medicine, caused by escalating litigation rates.<sup>3,9</sup> Many primary care patients

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groups, in both sexes, across all test types (laboratory, imaging, and miscellaneous), and for 40 of the 44 tests that were studied specifically. Renal function tests were the most commonly ordered test for most of the study period (2002/3 to 2015/16). Full blood count was used most often in 2000/1 and 2001/2 and was then the second most frequently ordered test during the rest of the study (2002/3 to 2015/16). Liver function tests were the third most commonly ordered test from 2001/2 to 2015/16, with urine dipstick testing third in 2000/1. Knee magnetic resonance imaging (MRI) had the highest average annual increase in use (69%, 95% confidence interval 3% to 107%), followed by vitamin D tests (54%, 50% to 57%) and brain MRI (47%, 40% to 56%).

**What this study adds** Total test use has increased markedly over time, in both sexes, and across all age groups, test types (laboratory, imaging, and miscellaneous) and for 40 of 44 tests specifically studied. Of the patients who underwent at least one test annually, the proportion who had more than one test increased significantly over time.

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present with non-specific symptoms, and trying to differentiate those with serious underlying disease is a real challenge. A systematic review and meta-analysis investigating the effect of diagnostic tests for patients with a low pretest probability of serious illness (presenting with symptoms such as fatigue and low back pain) reported that testing did little to reassure patients, decrease their anxiety, or resolve their symptoms, although tests did reduce further visits to primary care.<sup>10</sup>

### Cultural beliefs

Patients might seek tests for reassurance without understanding the limitations of the tests. Cultural and societal beliefs dictate that “prevention is better than cure” and that being proactive about health can only bring positive effects.<sup>3</sup> Patient expectations are shaped

by many factors but are influenced by misinformation about the accuracy of tests and the role of screening in healthy people.

The promotion of screening by private enterprises and industry with vested interests exacerbates this problem.

With escalating healthcare expenditure internationally, reducing over-testing represents an evidence based approach to decreasing costs without compromising health.<sup>4</sup>

O’Sullivan and colleagues have shown that test use in UK general practice has increased exponentially. Future research should focus on why, in terms both of clinical indication and reasoning and of patient beliefs and expectations about the purpose and accuracy of tests.

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TEK IMAGE/SPL

## Impact of patient and public involvement on enrolment and retention in clinical trials

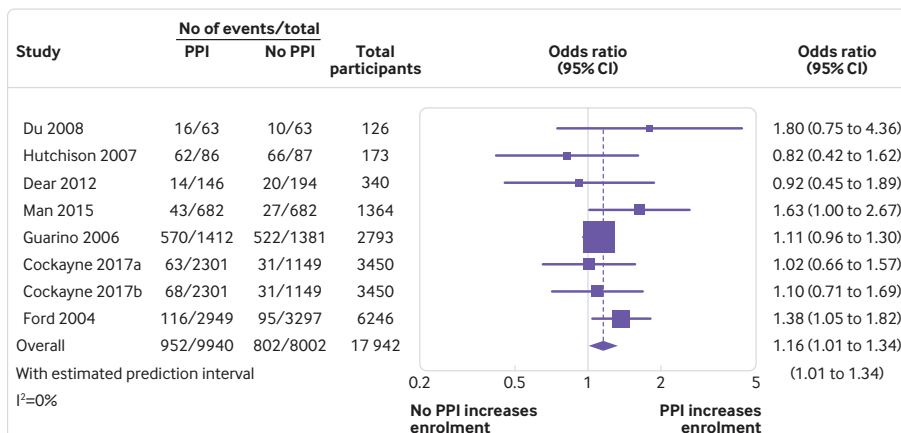
Crocker JC, Ricci-Cabello I, Parker A, et al

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**Study question** What is the impact of patient and public involvement (PPI) on rates of and retention in clinical trials?

**Methods** 10 electronic databases were searched for studies quantitatively evaluating the impact of a PPI intervention (any form of active patient or lay involvement in the trial process, such as membership of a trial advisory group, user testing, or peer recruitment), compared with no intervention or non-PPI intervention(s), on rates of enrolment, retention, or both of participants in a clinical trial or trials. PPI interventions could include additional non-PPI components inseparable from the PPI (such as other stakeholder involvement). Random effects meta-analyses were used to determine the average effect of PPI interventions on enrolment and retention in clinical trials, with the main analysis including randomised studies only and a secondary analysis adding non-randomised studies.



Odds ratios for patient enrolment in clinical trial with versus without patient and public involvement (PPI) intervention (randomised studies only)

**Study answer and limitations** The review included 26 studies; 19 were eligible for enrolment meta-analysis and five for retention meta-analysis. On average, PPI interventions modestly but significantly increased the odds of participant enrolment in the main analysis (odds ratio 1.16, 95% confidence and prediction interval 1.01 to 1.34). Non-PPI components of interventions may have contributed to this effect. The findings for retention were inconclusive owing to the paucity of eligible studies (odds ratio 1.16, 0.33 to 4.14, for main analysis).

**What this study adds** These findings add weight to the case for PPI in clinical trials by indicating that it is likely to improve participant enrolment rates. Further research is needed on the impact of PPI on retention rates.

**Funding, competing interests, and data sharing** This research was supported by the National Institute for Health Research Oxford Biomedical Research Centre and the University of Oxford Returning Carers Fund. The dataset is available on request.

Study registration PROSPERO CRD42016043808.

## AUTHOR'S PERSPECTIVE Joanna Crocker

### Time to embrace patient involvement in clinical trials?

This review paper is a significant step in a long and bumpy journey. For several years, the NIHR has mandated researchers to involve patients or members of the public in research as partners or advisers. I was tasked with measuring the effect of PPI, which had barely been attempted before—in part as there is disagreement about the rationale for PPI and its framing as a methodological intervention, and in part because the complexity and diversity of PPI make this a hugely challenging endeavour. I was, however, fortunate to be supported by a committed advisory group of patients, PPI practitioners, and academic experts.

We took the consequentialist rationale for PPI—that it improves research—and aimed to measure its effect on one important element of research quality and efficiency: recruitment and retention of participants in clinical trials.

We hoped that this review would shed light on the extent to which PPI does (or does not)

affect recruitment and retention rates, and on factors which might influence this. The first of many challenges we faced was defining and identifying PPI, as there is no universal definition and it is poorly reported in the literature. In the end, we opted for a relatively broad definition, carrying out subgroup analyses to distinguish between different types of PPI.

We discovered that while not all PPI interventions significantly improved recruitment, on average they did. This effect seemed to be magnified when people with lived experience of the condition under study were involved. Some authors thought these findings merely proved what was already obvious, while others were genuinely surprised. I was disappointed we weren't able to draw conclusions about the effect of PPI on retention because of the dearth of studies evaluating this, but at least it highlighted a research gap.

Whatever your beliefs about PPI, our findings do indicate one likely and important

benefit to clinical trials. They are limited by the particulars of the PPI interventions included (some were not pure PPI; none was introduced early enough to influence the research question or whole trial design). And they tell us nothing about when, why, and how PPI has this effect—which we are exploring in a follow-on realist analysis of the included studies. Our findings have already informed a related study that aims to develop a PPI intervention to enhance recruitment and retention in surgical trials. I hope they will be useful to others planning and designing clinical trials too: if you hadn't thought about involving patients before, or were sceptical about the benefits, perhaps it's time to think again?

Joanna Crocker is a research fellow at the Nuffield department of primary care health sciences

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