research update

FROM THE JOURNALS Edited highlights of Richard Lehman's blog on http://bmj.co/Lehman

How global is your BMI?

I guess how you read a paper like this depends on where you are, how old you are, and how overweight you are. You'll skip the text and try to find yourself on one of the figures matching your body mass index with your mortality risk. The take home message for me is that the older you are, the less it matters whether you are overweight. This is what I want to hear. It's quite another matter for the under 40s. Much as it pains an antipuritan such as me to admit it, obesity really is a massive population health problem for developed countries. It was quite different when I grew up in England. Food was generally so horrible that you ate as little of it as you could. Now that it is nice, I eat as much of it as possible. It's a race between the menu and the funeral. The strength of this new survey is that it draws data from the group you probably belong to, limiting confounding and reverse causality by restricting analyses to never smokers and excluding pre-existing disease and the first five years of follow-up. It's a wonderful example of the classic *Lancet* global health article, based on studies of more than 10 million people across four continents. What it really cries out for though is a link to some interactive infographics to play with à la David Spiegelhalter or Hans Rosling.

Lancet 2016, doi:10.1016/S0140-6736(16)30175-1

Olanzapine stops chemo vomiting

For about 5000 years doctors sought out plants that would make their patients vomit, believing that this would expel noxious humours. In this week's *New England Journal of Medicine* there's a good example of this in an interesting short piece about early clinical trials (doi:10.1056/NEJMp1605900) featuring Adrien Helvétius (1662–1727) who introduced ground ipecacuanha root (ipecac) from Brazil. It was still given to children who had received unintentional overdoses when I was a junior doctor. But the true benefactors of humankind today are those who discover powerful antiemetics to help patients receiving cancer chemotherapy. Many antiemetics have been discovered by chance, and the latest of them is olanzapine. We're used to seeing it used as an antipsychotic, which causes somnolence, weight gain, and type 2 diabetes. But over the past two or three years it's been increasingly used short term as an antiemetic for patients with cancer. This trial shows that it is highly effective even at the extreme end of the vomiting spectrum. It was compared with placebo in combination with dexamethasone, aprepitant or fosaprepitant, and a 5-hydroxytryptamine type 3 receptor antagonist, in patients with no history of chemotherapy who were receiving cisplatin (≥70 mg/m2 of body surface area) or cyclophosphamide–doxorubicin. I think I shall start taking olanzapine half an hour before switching on the news. It might prevent that strange feeling of nausea and being about to go mad.

N Engl J Med 2016, doi:10.1056/NEJMoa1515725

@POTUS and affordable care

He hasn't gone yet, but for me Barack Obama already inspires a kind of nostalgia. He has goodness. This was thwarted by malign opposition at every point of his presidency, but by some miracle the Affordable Care Act made it onto the statute book. Obama takes pages in *JAMA* to describe its achievements. It is not a single payer, universal system—it is full of misaligned incentives; and the United States continues to have the world's least cost effective healthcare delivery system. But for Americans, the ACA represents a step forward. "As this progress with health care reform in the United States demonstrates, faith in responsibility, belief in opportunity, and ability to unite around common values are what makes this nation great." Please let the US continue this way under its next president. These are the values of the world and not of any one nation, and if we do not unite around them we are stuffed.

JAMA 2016, doi:10.1001/jama.2016.9797

Quetiapine for sleep

Over the past 10 years of my time as a GP partner, we came under increasing pressure to cut down on prescribing benzodiazepines to help people sleep. Observational evidence (since contested) blamed them for falls in elderly patients. Their prescription still awakens moral displeasure. Consequently, elderly people are given other drugs with really serious adverse effects: tricyclic antidepressants and trazodone, which commonly cause serotoninergic poisoning when combined with selective serotonin reuptake inhibitors or tramadol, or both, and antipsychotics such as risperidone and quetiapine, which cause daytime somnolence, parkinsonism, diabetes, and weight gain. A survey of admissions to a clinical teaching unit in Canada confirms the popularity of quetiapine in particular (it's the sound of its name I suppose). About 45% of the admitted patients aged 65 or over were taking 10 or more drugs, and about 12.5% were receiving quetiapine. Many others were given it for sleep during admission. This misuse of quetiapine is quite disquieting I opine.

JAMA 2016, doi:10.1001/jamainternmed.2016.3309

Arthroscopic surgery for knee pain


LIVING ART ENTERPRISES/SPL

ORIGINAL RESEARCH Randomised controlled trial with two year follow-up

Exercise therapy versus arthroscopic partial meniscectomy for degenerative meniscal tear in middle aged patients

Kise NJ, Risberg MA, Stensrud S, Ranstam J, Engebretsen L, Roos EM

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Find this at: http://dx.doi.org/10.1136/bmj.i3740

Study question Is exercise therapy superior to arthroscopic surgery for knee function in middle aged patients with degenerative meniscal tears verified by magnetic resonance imaging?

Methods Middle aged patients (mean age 49.5 years, range 35.7-59.9) with degenerative meniscal tears were randomly allocated to treatment with exercise therapy alone or arthroscopic partial meniscectomy alone. The two primary endpoints were patient reported knee function at two years and thigh muscle strength at three months. The primary patient reported endpoint was change in $KOOS_4$ (knee injury and osteoarthritis outcome score), defined as the average score for four of the five KOOS subscale scores covering pain, other symptoms, function in sport and recreation, and knee related quality of life from baseline to two years. The muscle strength outcomes were peak torque and total work for both knee extension and knee flexion at 60 degrees per second.

Study answer and limitations No clinically relevant difference was found between the two groups in change in $KOOS_4$ at two years. At three months, muscle strength was more improved in the exercise therapy group. The study did not include a sham surgery group, which would have helped to clarify non-specific or placebo effects.

What this study adds This study suggests that exercise therapy alone and arthroscopic partial meniscectomy alone were similarly effective for pain relief and functional improvement in a younger and more active population with a lower body mass index (26.2) than previously studied. Exercise therapy resulted in better thigh muscle strength compared with surgery.

Funding, competing interests, data sharing This trial was funded by Sophies Minde Ortopedi AS, the Swedish Rheumatism Association, the Swedish Scientific Council, the Region of Southern Denmark, the Danish Rheumatism Association, and the Health Region of South-East Norway. The researchers were independent from the funders and there were no relevant competing interests. Anonymised data will be shared on reasonable request.

Study registration www.clinicaltrials.gov (NCT01002794).

COMMENTARY A highly questionable practice without supporting evidence of even moderate quality

Arthroscopic partial meniscectomy—keyhole surgery for middle aged to older adults with knee pain to trim a torn meniscus—is one of the most common surgical procedures in the US and UK. Remarkably, there is no good evidence that the procedure is beneficial.

Over the past decade a series of rigorous trials, summarised in two recent systematic reviews and meta-analyses, have provided compelling evidence that arthroscopic knee surgery offers little benefit for most patients with knee pain.[4 5] The latest nail into this coffin appears in a linked paper by Kise and colleagues[6]: a rigorous comparison between exercise therapy alone and arthroscopic partial meniscectomy alone in adults with a degenerative meniscal tear. The authors found no between group difference in patient reported knee function at the two year follow-up, but greater muscle strength in the exercise group at three months.

How did this procedure become so widespread without supporting evidence of even moderate quality? Orthopaedic surgeons used to treat young people presenting after an injury with a "locked knee" by trimming the torn meniscus in open surgery. Once arthroscopy became technically possible, the indication crept from locked knees in young patients to all patients of all ages with knee pain and meniscus tears of any sort; tears which, on magnetic resonance imaging, have proved poorly associated with symptoms.[7]

There are many possible reasons for reluctance to change practice, including perverse financial incentives

Good evidence has been widely ignored, and arthroscopic surgery for knee pain continues unabated.[8 9] There are many possible reasons for reluctance to change practice, including perverse financial incentives and an understandable difficulty in relinquishing long held beliefs. Orthopaedic surgeons prefer to argue instead that the available trials do not reflect the real world, and if they did, results would be different.[12-19]

We are at the point where any careful scrutiny would conclude that the estimated two million arthroscopic partial meniscectomies undertaken globally each year at a cost of several billion US dollars is potentially just medical waste. System level measures leading to more appropriate use of scarce medical resources are urgently required.

If we were to generously give advocates of arthroscopic partial meniscectomy the benefit of the doubt we might allow that under such high stakes circumstances, acting to severely limit these procedures could be considered precipitous and premature. If so, we would undertake the practical, real world trials embedded in the flow of practice that could satisfy orthopaedic surgeons' concerns about current evidence.

Which of these two options (or perhaps, to some degree, both) we should take is a matter requiring urgent societal debate and rapid resolution. What we should not do is allow the orthopaedic community, healthcare providers, and funders to ignore the results of rigorous trials and continue widespread use of procedures for which there has never been compelling evidence.

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Surgeon specialisation and operative mortality in the United States

Sahni NR, Dalton M, Cutler DM, Birkmeyer JD, Chandra A

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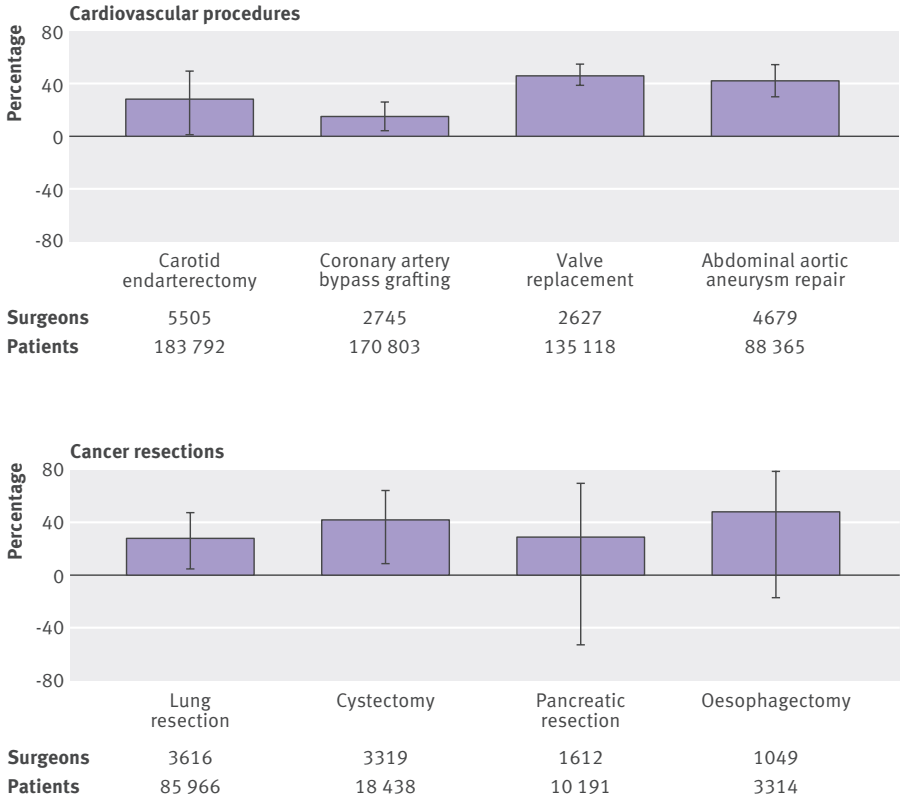
Find this at: http://dx.doi.org/10.1136/bmj.i3571

Study question Does an association exist between a surgeon's degree of specialisation in a specific procedure and patients' mortality?

Methods US Medicare data from 2008-13 on 695 987 patients aged 66 or older who underwent one of eight procedures (originally researched by Birkmeyer et al to examine the volume-outcomes relation) were analysed. Surgeon specialisation was defined as the number of times surgeons (n=25 152) performed the specific procedure divided by their total operative volume across all procedures. A multilevel mixed logit model was used to estimate the association between surgeon specialisation and operative mortality independent of surgeons' volume for the specific procedure, with control for patients' characteristics and unobserved physician specific and hospital specific factors. The primary outcome measure was relative risk reduction in risk adjusted and volume adjusted 30 day operative mortality between surgeons in the bottom and top quarter of surgeon specialisation.

PHANIE/ALAMY



Relative risk reduction (with 95% CI) in risk adjusted and volume adjusted operative mortality rate between bottom and top quarter of surgeon specialisation

Study answer and limitations For all four cardiovascular procedures and two out of four cancer resections, a surgeon's degree of specialisation was a significant predictor of operative mortality independent of the number of times he or she performed that procedure. For five procedures (carotid endarterectomy, valve replacement, lung resection, cystectomy, and oesophagectomy), the relative risk reduction from surgeon specialisation was greater than that from surgeon volume in that specific procedure. Furthermore, surgeon specialisation accounted for 9% (coronary artery bypass grafting) to 100% (cystectomy) of the relative risk reduction otherwise attributable to volume in that specific procedure. No mechanism was identified for this relation, and the study was limited by potential unobserved choices and characteristics of surgeons.

What this study adds For several common procedures, surgeon specialisation is an important predictor of operative mortality independent of volume in that specific procedure.

Funding, competing interests, data sharing This report represents independent research funded in part by the National Institute on Aging for JDB, DMC, and AC. No additional data available.

ORIGINAL RESEARCH Population based retrospective cohort study evaluating death and recurrence

Use of imaging tests after primary treatment of thyroid cancer in the United States

Banerjee M, Wiebel JL, Guo C, Gay B, Haymart MR

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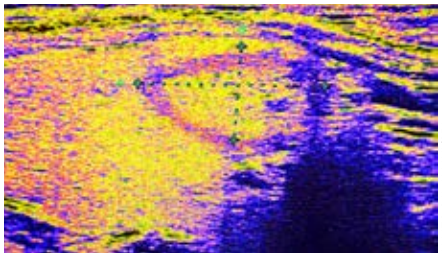
Find this at: http://dx.doi.org/10.1136/bmj.i3839

Study question Is imaging after primary treatment for thyroid cancer associated with treatment for recurrence and disease specific survival?

Methods This study included 28 220 patients in the Surveillance Epidemiology and End Results-Medicare database in the United States, diagnosed with differentiated thyroid cancer between 1998 and 2011. Propensity score analyses assessed the relation between imaging and treatment for recurrence (logistic model) and disease specific survival (Cox proportional hazards model).

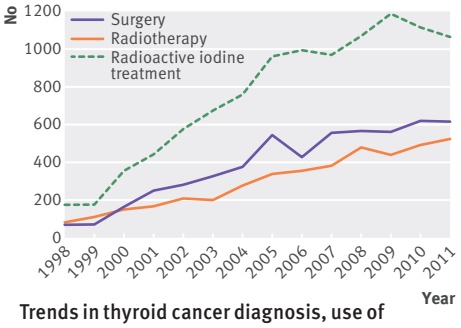


JAMES CAVALLINI/SPL

A nodular tumour in the thyroid gland

Study answer and limitations Over time, there was a substantial rise in incident cancers, imaging after primary treatment, and treatment for recurrence. No significant change was seen in death rate. There was a significant relation between use of ultrasound and additional surgery and radioactive iodine as treatment for recurrence. Radioiodine scans and positron emission tomography (PET) scans were associated with use of additional surgery, additional radioactive iodine, and radiation as treatment for recurrence. However, only radioiodine scans were associated with an improved disease specific survival (hazard ratio 0.70, 95% confidence interval 0.60 to 0.82). Limitations included lack of information on the indications for imaging and treatment and lack of detail on the role of the patient and physician in decision making.

What this study adds The marked rise in imaging after primary treatment for differentiated thyroid cancer was associated with increased treatment for recurrence; however, apart from the use of radioiodine scans in presumed iodine avid disease, there was no clear improvement in disease specific survival. These findings emphasise the importance of better characterising unnecessary imaging and tailoring imaging after primary treatment to patient risk.



Trends in thyroid cancer diagnosis, use of imaging, treatment for recurrence, and death from thyroid cancer. Imaging includes neck ultrasounds, radioiodine and PET scans. Treatments for recurrence include additional neck surgery, additional radioactive iodine treatment, and radiotherapy

Funding, competing interests, data sharing MRH is supported by NIH grant 1K07CA154595-02; MB is partly supported by grant 5 P30 CA 046592 from the National Cancer Institute. Support was provided by the Punya Foundation for Thyroid Cancer Research. No competing interests declared. Statistical code available from the first author at mousumib@umich.edu; dataset available from SEER-Medicare at http://appliedresearch.cancer.gov/seermedicare/.

RESEARCH METHODS AND REPORTING Consensus and checklist

When and how to update systematic reviews

Garner P, Hopewell S, Chandler J, et al; panel for updating guidance for systematic reviews (PUGs)

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Updating systematic reviews is, in general, more efficient than starting afresh when new evidence emerges. The panel for updating guidance for systematic reviews (comprising review authors, editors, statisticians, information specialists, related methodologists, and guideline developers) met to develop guidance for people considering updating systematic reviews. The panel proposed the following:

1. Decisions about whether and when to update a systematic review are judgments made for individual reviews at a particular time. These decisions can be made by agencies responsible for systematic review portfolios, journal editors with systematic review update services, or author teams considering embarking on an update of a review.

2. The decision needs to take into account whether the review addresses a current question, uses valid methods, and is well conducted; and whether there are new relevant methods, new studies, or new information on existing included studies. Given this information, the agency, editors, or authors need to judge whether the update will influence the review findings or credibility sufficiently to justify the effort in updating it.

3. Review authors and commissioners can use a decision framework and checklist to navigate and report these decisions with "update status" and rationale for this status. The panel noted that the incorporation of new synthesis methods (such as Grading of Recommendations Assessment, Development and Evaluation (GRADE)) is also often likely to improve the quality of the analysis and the clarity of the findings.

4. Given a decision to update, the process needs to start with an appraisal and revision of the background, question, inclusion criteria, and methods of the existing review.

5. Search strategies should be refined, taking into account changes in the question or inclusion criteria. An analysis of yield from the previous edition, in relation to databases searched, terms, and languages can make searches more specific and efficient.

6. In many instances, an update represents a new edition of the review, and authorship of the new version needs to follow criteria of the International Committee of Medical Journal Editors. New approaches to publishing licences could help new authors build on and re-use the previous edition while giving appropriate credit to the previous authors.

The panel also reflected on this guidance in the context of emerging technological advances in software, information retrieval, and electronic linkage and mining. With good synthesis and technology partnerships, these advances could revolutionise the efficiency of updating in the coming years.