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Quitting smoking and gaining weight: the odd couple

We need observational data to settle this question

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Smoking and obesity or overweight are risk factors for many diseases, making them among the world's greatest health problems. Tobacco is the main cause of premature death worldwide, being responsible for 5.1 million deaths each year.[1] Obesity, together with overweight, causes 2.8 million deaths.[1] Smoking and obesity are moving in opposite directions, with the prevalence of smoking declining and that of obesity increasing in lower middle income countries and deprived population groups in high income countries.[2] It has long been known that smokers weigh less than former smokers or people who have never smoked.[2] Weight gain is a widely anticipated consequence of quitting, and many smokers—particularly women[3]—avoid quitting for fear of gaining weight.[4] A common question that many smokers ask is not, "Will I gain weight after quitting?" but "How much will I gain after stopping?"

In the linked paper, Aubin and colleagues present a meta-analysis of 62 clinical trials that measured weight gain after smoking cessation.[5] Independent of the type of treatment used (including unassisted cessation), average weight was 4-5 kg higher one year after quitting, with 13% of people gaining more than 10 kg and 16% losing some weight. These data are an important contribution to the evidence base on weight gain and smoking cessation and will probably be translated into headlines shouting that the jury is now in: quitting smoking causes weight gain. This could result in many people delaying cessation, perhaps indefinitely.

It may be unwise to incorporate this message into clinical or public health practice. The data were extracted from clinical trials, not from "real world" population based studies of cessation. Those who enrol in trials are known to differ in important respects from non-participants.[6] Smokers who take part in trials and attend cessation clinics are a self selecting minority of smokers who may differ in important respects from those who quit without professional assistance.[7] Those who decide they need help to stop smoking tend to lack self efficacy. They might have similar problems with the dietary and physical activity behaviours important in weight control. So these results may not be generalisable to all smokers who quit because two thirds to three quarters of ex-smokers stop smoking without professional help or interventions.[8]

Cohort studies have shown that many smokers gain weight after quitting in the short term but not in the long term. Smokers who quit tend to gain weight as they grow older at a similar rate to those who have never smoked

Cohort studies have shown that many smokers gain weight after quitting in the short term but not in the long term.[9] Smokers who quit tend to gain weight as they grow older at a similar rate to those who have never smoked. The size of the gain may depend on the years of follow-up after quitting and other personal characteristics, such as sex, age, ethnicity and, importantly, baseline body mass index at the time they quit.[10] A meta-analysis of prospective population based cohort studies of weight changes after cessation is needed. One that could analyse the data by specific subgroups and control for potential confounders such as baseline weight, glycaemic index, and comorbidities would provide useful data to complete the overall picture on quitting smoking and weight gain.

Finally, the relative long term health effects of weight gain and smoking cessation also need to be considered with respect to the ultimate public health message that we should derive from this and future studies. Although obesity is positively associated with an increased risk of all cause mortality,[11] cohort studies indicate that modest weight gain does not increase the risk of death[12]; smoking does.

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RESEARCH, p 14

Is it right on the basis of this study to recommend that patients should put up with their resistant cough because it could reduce their risk of pneumonia? This would run counter to current evidence based guidelines

Pneumonia and ACE inhibitors—and cough

Too early to use ACE inhibitors to prevent pneumonia

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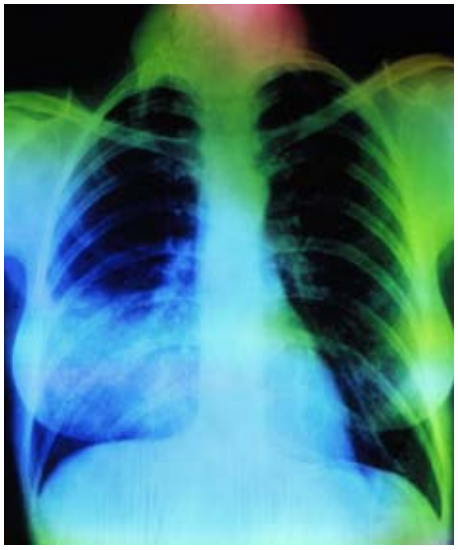
Angiotensin converting enzyme (ACE) inhibitors are widely used to treat heart failure and hypertension. They act through blocking the conversion of angiotensin I to angiotensin II; this inhibits the breakdown of bradykinin, which in turn lowers arteriole resistance and increases venous return. Many patients taking ACE inhibitors experience a persistent dry cough, which is thought to be caused by increased concentrations of bradykinin; the cough is triggered by the endothelial effects of bradykinin and other peptides. Refractory cough is the most common reason for switching from ACE inhibitors to angiotensin II receptor blockers (ARBs), which do not inhibit the breakdown of kinins and are less likely to cause troublesome coughing. In the linked study, Caldeira and colleagues examined the risk of pneumonia with both classes of drug, hypothesising that the cough associated with ACE inhibitors might be protective against pneumonia.[1]

Coughing is one of the most common reasons that patients consult a primary care doctor, and it has a substantial effect on quality of life. It also has a large economic impact—annual expenditure on cough treatments is unknown because many are over the counter preparations, but it is estimated to run into millions of pounds in the United Kingdom. In patients taking ACE inhibitors the chronic cough is associated with throat irritation, and the only wholly effective way to prevent it is to stop taking the drug.[2] However, coughing helps protect the respiratory tree from aspiration of pharyngeal contents and increases clearance of inhaled organisms. It therefore follows that ACE inhibitors, but not ARBs, could protect against lower respiratory tract infection, and this has been suggested by some earlier trials.

Caldeira and colleagues studied this question by performing a systematic review and meta-analysis of trials and studies of ACE inhibitors and ARBs.[1] Their review seems to support the pharmacological and pathological hypothesis and suggests a protective role for ACE inhibitors in reducing the incidence of (and possibly mortality from) pneumonia.



SPL

Pneumonia may be reduced in users of ACEIs

The authors undoubtedly made stringent attempts to pool all available data and undertook a thorough search of clinical studies of ACE inhibitors and ARBs with few eligibility restrictions. The review was not restricted to prospective randomised controlled trials and included both retrospective and prospective observational cohort and case-control studies. Most data came from unpublished studies identified from a search of regulatory documents placed on the Food and Drug Administration website.

Respiratory infection was not a primary outcome in most of these studies, and data were collected predominantly from reporting of adverse events (in randomised controlled trials) or from database coding for pneumonia or lower respiratory tract infection (in observational studies). Pneumonia and lower respiratory tract infections represent a heterogeneous group of overlapping disorders with multiple causes and several different ICD9/10 (international classification of diseases, 9th/10th revision) and other codes.

Meta-analysis is a useful tool if the quality and evidence base of the contributing studies is satisfactory. In this study, the quality of reporting was assessed using several different tools, and the results suggest a high risk of reporting bias, together with substantial heterogeneity. This is explained by the variety of study designs included, and it probably excludes further quantitative and subgroup analysis.[3] The efficacy findings should therefore be interpreted with caution.

It is unclear why, in the overall comparison of ACE inhibitors and ARBs in preventing pneumonia, the effect was noted only in the cohort and nested case-control studies and not in the randomised trials. The analysis of randomised controlled trials is probably more robust owing to the inherent bias in the design of observational studies.

This does not mean an effect was not present, but it is difficult to agree with the authors that "best evidence" points to ACE inhibitors protecting against pneumonia. Is it right on the basis of this study to recommend that patients should put up with their resistant cough because it could reduce their risk of pneumonia? This is an important clinical question, but to agree would run counter to current evidence based guidelines that recommend discontinuation.[2] Extrapolation of results could lead to serious misconceptions: could a smoker's cough ever be considered to confer a health benefit? Further studies are needed and should include full health economic analyses and investigation of alternative hypotheses. Immunomodulatory effects and a reduction in systemic cytokine responses have been noted with ACE inhibitors,[4] and improvements in respiratory function with increases in exercise tolerance, perfusion, and gas transfer have been reported.[5] The ACE inhibitor cough has been associated with a genetic variant of the bradykinin B2 receptor promoter,[6] and linkage to other genes that influence susceptibility to infection is a possibility. A better understanding of the pharmacological properties and effects of these widely prescribed drugs is needed before we advise patients to put up with their cough because it may prevent them from getting pneumonia.

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Accurate diagnosis of the communication disorder is important, at the very least to be able to explain to patients and friends what the problem is and what strategies might be used to aid communication

Is early speech and language therapy after stroke a waste?

Perhaps, but some intervention to promote communication is better than none

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Research into rehabilitation is a relatively young discipline and there are still few centres of academic excellence in stroke rehabilitation. Randomised trials are difficult to conduct in this area. Large variations in patients and disease characteristics make designing trials tricky; blinding may be difficult; and identifying appropriate control interventions and ensuring that interventions are standardised, especially in multi-site studies, is challenging. However, such problems are not unique to rehabilitation research and can be overcome using complex intervention evaluation methods, as has been shown in other areas of stroke care.[1] In a linked research paper, Bowen and colleagues report the findings of the ACT NoW (Assessing Communication Therapy in the North West) study, which is a large scale multicentre randomised controlled trial of speech and language therapy in the rehabilitation of patients after stroke.[2] This study is welcome because, as with other treatment interventions, it is essential that rehabilitation is subjected to rigorous scrutiny.

Single case studies, observational studies, and small single centre randomised trials provide weak evidence for guiding clinicians and planners of care, and they cannot answer fundamental questions about how and what services should be delivered. The direct cost of stroke care, including rehabilitation, in England and Wales is estimated to be £3bn (€3.8bn; $4.7bn) a year.[3] The yearly cost of providing occupational therapy and physiotherapy, speech, and language therapy services alone in one 30 bed stroke unit in London, for example, is more than a third of a million pounds. Rehabilitation treatments cannot be assumed to be benign and evidence of their cost effectiveness is needed.

The ACT NoW trial examined outcomes for patients with aphasia or dysarthria in the first four months after stroke. Treatment by a speech and language therapist up to three times a week (using techniques agreed by the speech and language therapy community as being best practice) was compared with a control that comprised similarly resourced social contact (without communication therapy) from employed visitors.

HATTIE YOUNG/SPL

Any strategy to aid communication is good

No differences were seen between groups in terms of functional communication at six months as assessed by a blinded independent therapist. Professional speech and language therapy is currently widely provided in stroke rehabilitation services, which makes the findings of the trial highly controversial. They should stimulate an important debate on the way that speech therapy is delivered in the early stages after stroke. It is important to understand the design and conduct of this trial when interpreting its findings and implications for future research and clinical practice. Recruitment to the study was slow and selective, with only 21% of patients with suspected acute onset communication problems being recruited and only 44% of patients who were identified as eligible finally giving consent. There were some protocol violations, particularly in the control group, and more patients without follow-up in the control group. However, the final sample did seem to be representative of the pool of patients presenting to the stroke services. Despite these caveats, for a pragmatic trial of a complex intervention, it was performed well.

The findings do however raise the question of what role, if any, speech and language therapy services should play in early rehabilitation after stroke. About a third of people who have a stroke are likely to be aphasic, and aphasia can have a serious impact on all aspects of patients' lives and on their carers. Aphasia often negatively affects mood, self image, wellbeing, relationships, employment, and recreational opportunities. Therefore the research question examined by the ACT NoW trial investigators of whether enhanced communication rehabilitation improves speech outcomes if delivered in the first four months after stroke is clearly an important one.

A recent update of the Cochrane review for aphasia after stroke,[4] which includes the ACT NoW study, has been published. Most of the studies undertaken thus far, including ACT NoW, have focused on specific interventions aimed at improving deficits in language rather than tackling functional communication through, for example, non-verbal strategies. The Cochrane meta-analysis shows that some form of intervention is better than none, but that no particular intervention is better than another. Accurate diagnosis of the communication disorder is important, at the very least to be able to explain to patients and friends what the problem is and what strategies might be used to aid communication. In specific instances the opinion of an expert in communication disorders will be needed—for example, to help with decisions regarding questions of mental capacity. However, routinely reassessing performance in the early months does not seem to be of benefit. Patients should be encouraged to communicate as much as possible, whether with a therapist or a communication partner. Technologies such as computer programs may be useful.

Recovery of speech after stroke may be prolonged, and communication may still be improving many months and even years after the event. Speech therapy might be more effective if given later. If this is the case, it would be better to reallocate resources away from delivering communication therapy in the acute phase in hospital and sometimes early after discharge to providing more intensive therapy beyond four months.

The ACT NoW trial provides no solutions on how to manage aphasia effectively early after stroke. More focus on the early phase mechanisms that underpin the speech deficit may be needed before further pragmatic trials are undertaken. Although the results do highlight that scarce professional speech and language therapy resources may be inappropriately allocated at present, they do not spell the end of such therapy in the acute phase of stroke rehabilitation.

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RESEARCH, p 16

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- Editorial: Tackling the problems of seriously challenged NHS providers (*BMJ* 2012;344:e4422)
- News: South London Healthcare is "the first of many" NHS trusts to face administration (*BMJ* 2012;344:e4456)
- News: Up to two thirds of the 100 trusts yet to reach foundation status will not make it (*BMJ* 2012;345:e4532)

PFI hospitals bear the cost of Libor manipulation

A public inquiry is needed to determine the extent of the problem

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The fraudulent manipulation by Barclays Capital of the interbank lending rate (Libor) has real consequences for cash strapped NHS hospitals facing merger and service closure as a result of private finance initiative (PFI) debt repayments.[1] Libor, which is used by banks to set interest rates,[1] is linked to financial products known as derivatives that are widely used in PFI deals. By manipulating the Libor rate up or down banks can, at the expense of their clients, protect the profits they make from the trading of derivatives and mislead the market about the true cost of bank borrowing. South London Healthcare NHS Trust is in special administration, effectively bankrupt, because trust income is falling but PFI costs are rising,[2] partly because of reliance on derivative arrangements of the type marketed by Barclays Capital. The government has yet to examine PFI deals for fraud, although in the United States hospitals and local councils are considering suing banks for compensation, according to a BBC report.[3]

The derivatives industry, in which Barclays Capital is a major player, is fundamental to PFI. Derivatives are tradeable financial instruments used to protect lenders of long term debt from the risk of credit default (the risk that a loan is not repaid). According to the US regulator, the Commodity Futures Trading Commission, Barclays Capital traders manipulated the Libor rate by making "false, misleading or knowingly inaccurate [interest rate] submissions" to "benefit Barclays' derivatives trading positions."[4] Several other banks are being investigated by the European Union, including the Royal Bank of Scotland (RBS), which also has extensive PFI interests.

Derivatives are central to PFI because of the peculiar nature of this type of lending. In PFI deals, loans are secured not against assets but against hospitals' future revenue streams. Investment banks such as Barclays Capital that lend to PFI projects on this basis use derivatives known as "swaps" to protect the future revenue from which their loan is repaid. A swap is a derivative instrument used to insure (or hedge) against payment default in the event of adverse movements

GETTY

Inflation swaps…have helped NHS trusts overcome initial affordability problems but created problems for the future

in interest or inflation rates. The Princess Royal University Hospital PFI in Bromley, which is a major contributor to the South London Healthcare NHS Trust deficit, was drawn up to include interest rate and inflation rate swaps. Interest rate swaps allow the PFI company to fix interest rates that would otherwise fluctuate in the money markets, locking the public sector into high interest rates when the cost of government borrowing is at a historic low. Inflation rate swaps involve passing the risks of inflation back to the public sector by indexing PFI payments to inflation even where PFI industry costs are not affected by inflation and interest rates already include a premium for anticipated inflation.[5] In Bromley, and many other NHS PFI schemes, the whole PFI debt repayment rises annually with the retail price index or a multiple of it.[5]

Derivatives' fees and profits are high. In the US industry it is estimated that fees for derivative arrangers, which in PFI deals are usually the lending banks themselves, account for 7-10% of total investment costs.[6] Profits from derivatives (known as the swap margin) are tied to Libor and, in the case of inflation swaps, are relatively unregulated and set by a small number of firms such as Barclays Capital. Inflation swaps and indexation, which are used to defer debt repayment, have such major cost implications that PFI has been described as a "pay for two get one hospital" policy.[7]

Treasury guidance acknowledges that inflation swaps are unlikely to offer value for money and advises against their use.[5] Nonetheless, swaps have been adopted in a succession of NHS hospital schemes and signed off by government because banks have consented to hospitals making lower PFI payments at the beginning of a contract secure in the knowledge that index linked payments will rise in the future. The arrangement has helped NHS trusts overcome initial affordability problems but created problems for the future.

In 2010, after the financial crash, Treasury guidance warned that the cost of derivatives had increased substantially,[8] but hospitals and local communities were left to bear the financial pain and service losses that inflated costs lead to. A public register of contracts and a major public inquiry are needed to determine the full extent to which the high interest rates, swap mechanisms, and swap margins fuelling the latest round of hospital and service closures are products of Libor manipulation and fraud.

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Using prostate specific antigen testing alone to select men for biopsy has led to an epidemic of low risk prostate cancer

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Treating prostate cancer

No benefit from radical prostatectomy for men with low risk disease

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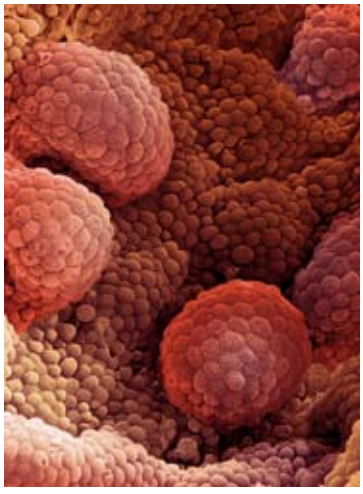
More than 40 000 men in the United Kingdom are diagnosed as having prostate cancer each year and the incidence has tripled since the 1970s,[1] largely because of efforts to promote early detection using prostate specific antigen tests. Men with localised prostate cancer face a bewildering array of treatment options, including watchful waiting, active surveillance, external beam radiotherapy, brachytherapy, cryotherapy, high intensity focused ultrasound, and radical prostatectomy. Until now men have had to make their choice without the help of evidence from good quality randomised controlled trials. The results of the recently published Prostate cancer Intervention Versus Observation Trial (PIVOT) are welcome,[2] but how will they help men diagnosed today as having localised prostate cancer to make a choice about treatment?

PIVOT recruited 731 North American men with localised prostate cancer between 1994 and 2002 and randomised them to radical prostatectomy or watchful waiting. At the time of recruitment, testing for prostate specific antigen was the norm, and the case mix reflects that, with its preponderance of low risk cases. More than half the patients had died at the time of analysis. Randomisation to surgery was associated with a non-significant 2.9% absolute reduction at 12 years in the primary outcome—overall mortality (hazard ratio 0.88, 95% confidence interval 0.71 to 1.08). A subgroup analysis showed that radical prostatectomy was associated with a trend towards decreased overall mortality in men with intermediate risk (0.69, 0.49 to 0.98) or high risk (0.74, 0.49 to 1.13) disease. The absolute reduction in mortality from prostate cancer was 12.6% and 6.7% for intermediate risk and high risk disease, respectively. This is probably sufficient evidence to continue to regard radical prostatectomy as a standard of care for younger and fitter men with intermediate risk and high risk disease, who would benefit in terms of overall mortality. Compliance with randomised allocation was not perfect—15% of men randomised to surgery did not undergo surgery and 20% of those randomised to watchful waiting received radical treatment. This would have resulted in differences between the trial arms being underestimated.

Where the findings of this study really seem to challenge current practice is in the management of low risk prostate cancer. In the subgroup of 296 men with low risk disease, the risk of death from prostate cancer was less than 3% at 12 years, with no significant benefit from surgery. Indeed, the trend in terms of prostate cancer specific mortality (1.48, 0.42 to 5.24) and overall mortality (1.15, 0.80 to 1.66) favoured watchful waiting rather than surgery. These data are consistent with previous reports on the natural course of low risk prostate cancer. An analysis of Medicare data from more than 14 000 men with localised prostate cancer managed by watchful waiting reported a 2% 10 year prostate cancer specific mortality in men with T1, Gleason score 5-7 disease.[3] However, data from the CAPSURE database suggest that nine out of 10 men with low risk prostate cancer in the United States receive immediate treatment.[4] In the UK that figure is six out of 10, according to the British Association of Urological Surgeons registry.[5] Thus, the current practice of treating low risk disease with radical prostatectomy is at odds with the best available evidence now provided by PIVOT—that surgery for low risk prostate cancer is not effective.



STEVE GSCHMEISSNER/SPL

Watchful waiting should be standard for low risk cases

A further observation is worthy of note. Transrectal ultrasound guided biopsy of six to 12 cores would typically have been used for diagnosis in patients enrolled in PIVOT. We now know that, if low risk patients (Gleason score of 6) in this trial had gone on to have the more comprehensive template mapping biopsies, around 25% of them would have been found to harbour Gleason 7 disease.[6] The risk of upgrading is far higher than the 3% risk of death from prostate cancer at 12 years on watchful waiting.[2] It follows that most men with low risk (Gleason score 6) disease on transrectal ultrasound biopsy who are upgraded to Gleason 7 on template mapping biopsy have indolent disease that will not harm them, at least in the medium term. This has major implications for the way in which active surveillance is conducted. Current guidelines restrict active surveillance to men with a Gleason score of 6 and regard the subsequent detection of Gleason 7 disease as an indication for radical treatment.[7] The results of PIVOT imply that this will lead to overtreatment for many men.

The PIVOT trial suggests surgery is of value in patients with high risk prostate cancer and that patients with low risk cancer have an excellent prognosis even without surgery. The standard of care for low risk prostate cancer should be watchful waiting, which raises an important question: if low risk prostate cancer does not need treatment, then does it need to be diagnosed at all? In future we need to focus on avoiding not just the treatment, but also the diagnosis, of low risk disease. Using prostate specific antigen testing alone to select men for biopsy has led to an epidemic of low risk prostate cancer. Patient selection for biopsy using a risk calculator to estimate individual risk of serious cancer reduces unnecessary biopsies and the detection of low risk disease.[8] Many new biomarkers, such as germline polymorphisms and functional magnetic resonance imaging,[9 10] show promise as markers of risk for more serious prostate cancer. When the value of these markers has been defined, they could improve the ability of risk calculators to diagnose only those prostate cancers that will benefit from treatment. If shown to be successful, such an approach could cut the annual incidence of prostate cancer in the UK by more than 10 000 and save time, costs, and the emotional distress associated with deciding how to treat low risk disease.

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ALISON WRIGHT/CORBIS

The clinical and health services research enterprise is not well aligned with the evidence needs of healthcare decision makers

Improving comparative effectiveness research

New methodological standards focus on quality and relevance of research to patients

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In June 2012, just before the Supreme Court of the United States narrowly affirmed the constitutionality of the Affordable Care Act, the Patient Centered Outcomes Research Institute (PCORI) issued a mandated draft report that provides an initial methodological blueprint for the conduct of research into comparative effectiveness.[1] PCORI was established in 2010 as part of the act, which was inspired by the view that reliable evidence about which health services work best for which patients is needed to inform clinical decisions and health policy decisions.

The PCORI report offers a concise and coherent set of observations about the flaws in the current US health research enterprise and it discusses how PCORI aims to remedy this. It shows that the institute is thinking seriously about how to put into practice the concept of "patient centredness" in research, taking a term that was originally generated for political reasons and translating it into an executable approach to evidence development. The report offers a framework for thinking about the process of determining which methods would be most appropriate for tackling specific research questions. It also compiles an initial set of standards and best practices for several research methods that will probably be widely used in comparative effectiveness and patient centred outcomes research.

The report's introduction acknowledges that, "when it comes to health and healthcare choices, despite the best intentions of the research community far too often the information available isn't good enough."[1] As highlighted throughout the report and in the background papers commissioned to inform it, an essential aspect of dealing with this problem is to engage healthcare decision makers (patients, caregivers, practising clinicians, healthcare administrators, healthcare purchasers, payers, and policy makers) in a meaningful way at all phases of the research process. The clinical and health services research enterprise is not well aligned with the evidence needs of healthcare decision makers. This major new research funding institute takes a step forward in focusing on this misalignment as the guiding premise for its work.[2-4]

Most of the PCORI report focuses on standards or "best practices" for the conduct of patient centered outcomes research, consistent with the legislative language that established the main functions of the institute's methodology committee.[5] A highly informative series of background papers on best practices in research was commissioned to support this work. These dealt with general research topics (such as standards for priority setting, patient centredness, patient engagement, causal inference, heterogeneity of treatment effects) and best practices for the use of specific research methods (including registries, adaptive and Bayesian clinical trials, and studies of diagnostic tests).[6]

Several aspects of the PCORI methods standards distinguish them from a rapidly growing body of work that shares the overall aim of increasing the quality, consistency, and relevance of research by providing methodological standards. The standards in the initial report focus mainly on the design of primary research, rather than methods for the review of completed studies. The Agency for Healthcare Research and Quality has produced an extensive library of methodological guides that are targeted at those who conduct systematic literature reviews, with the aim of improving their transparency, consistency, and scientific rigour.[7] Similarly, the European Union Network of Health Technology Assessment has recently issued draft guidelines for those who conduct relative efficacy assessments of drugs, which cover topics such as choice of comparators, composite endpoints, and applicability.[8] Although such recommendations offer indirect guidance to academics and product developers designing primary clinical research studies, their utility for this secondary purpose is uncertain.

Other organisations have also published best practice guidance for the design of primary research.[9] The PCORI standards, because of their direct link to the funding decisions to be made by that organisation, have greater potential to influence research practices, however. The PCORI report notes that because the draft standards had not yet benefited from public input, funding applications will not be scored on the basis of adherence. This implies that PCORI intends that future proposals will be evaluated in light of revised standards. The degree to which these standards influence researchers' behaviour will depend on whether PCORI can persuade its scientific review panels to accord adequate weight to adherence to these standards when rating submitted proposals. Alternatively, PCORI itself could hold researchers accountable to these standards.

Almost all of the standards proposed in the draft report are general in nature. For example, the standard on patient outcomes recommends that researchers "measure outcomes that people in the population of interest notice and care about." Individual researchers are then advised to seek input from patients in selecting these outcomes for the topic they intend to study. It will ultimately be more efficient and effective for PCORI to produce or support the development of condition specific standards on major elements of study design, rather than depending on individual researchers to do this work independently. An example of what such guidance might look like is reported in a recent publication that describes a structured multi-stakeholder deliberative process that recommended a core set of 14 patient reported outcomes for inclusion in trials of cancer drugs, including a list of validated instruments, as well as a data collection schedule and procedures.[10] Related multi-stakeholder efforts to develop condition specific standards for study design are also now under way internationally, with an initial focus on drugs for Alzheimer's disease (www.greenparkcollaborative.org). Broad adherence to such condition specific standards, incentivised through links to research funding or product reimbursement decisions, could greatly improve the quality and relevance of future research and should also result in more consistent design across studies, thereby enhancing the value of information available from the synthesis of multiple studies within that domain.

The report's most important contribution may be that it illustrates the potentially far reaching benefits of establishing an organisation with the remit to develop and enforce standards for research that reflect the type of evidence that would be most useful for patients, caregivers, clinicians, payers, and other decision makers.

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