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White rice and risk of type 2 diabetes

New study highlights old challenges of nutritional epidemiology

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A marked rise in the incidence of type 2 diabetes is a characteristic feature of populations that have undergone nutritional transition.[1] First seen in the developed Western world, the same pattern is now being replicated in low income and middle income countries, where most new cases of diabetes now occur.[2] The role of poor diet in the diabetes epidemic is undisputed, but the details have long been debated.[3] Although overconsumption of energy and accumulation of excess body fat is a common cause of type 2 diabetes,[4] diet almost certainly has other unknown effects, and specific foods with particular adverse effects may have a direct role in the development of type 2 diabetes.

In nutritional epidemiology, interpretation of the observed association and, in particular, determination of the likelihood of causality are problematic

The linked paper by Hu and colleagues sheds new light on the relation between diet and diabetes, and the authors bring a new level of rigour to efforts to answer the question of the possible effect of higher consumption of white rice.[5] They systematically searched for prospective studies of the effect of consumption of white rice on the risk of diabetes and quantitatively summarise the findings of individual studies. The study includes a large number of incident cases of diabetes recorded over a long follow-up period and reports a dose-response association between white rice consumption and risk of diabetes. However, as is common in nutritional epidemiology,[6] interpretation of the observed association and, in particular, determination of the likelihood of causality are problematic.[7]

It is often difficult to quantify consumption of the dietary component of interest and collect adequate information about factors that might confound the association. Large scale studies must rely on inexact tools to measure dietary factors, and errors in measuring individual levels of consumption can be large.[7] Broadly, imprecise measurement of the exposure of interest (in this case rice consumption) will usually produce an underestimate of the true strength of the association with the outcome (diabetes). The same cannot be said for imprecise or incomplete measurement of potential confounding factors. Inadequate adjustment of the model for potential confounding factors may deliver results that are wrong in terms of the strength of the association and also in the direction of the effect identified. The confounders adjusted for varied between studies,[5] and the impact of each on the final estimate of effect cannot be determined from the data presented. A meta-analysis based on the individual participant records from the included studies, rather than the published summary estimates, would enable a much deeper exploration of the associations and greater insight into the adequacy of the adjustments made.

Hu and colleagues calculated risk ratios for each included study by comparing the rates of diabetes in the group with the highest consumption of white rice with those in the group with the lowest consumption. However, the highest and lowest levels of rice consumption varied greatly between studies. For example, in the primary analysis, a difference in consumption of 33 g/day (56 g/day *v* 23 g/day) is plotted on the same scale as a difference in consumption of 250 g/day (750 g/day *v* 500 g/day). Such massive differences in consumption are unlikely to produce the same effects on the risk of diabetes. Although these discrepancies may explain some of the heterogeneity in the size of the effect estimates obtained, what is really needed is a more sophisticated analysis based on primary rather than summary data.

Although the findings of the current study are interesting they have few immediate implications for doctors, patients, or public health services and cannot support large scale action. Further research is needed to develop and substantiate the research hypothesis. Ideally, incident diabetes should be investigated in participants of an adequately powered randomised controlled trial in which white rice consumption is substantially modified in an intervention group.[8] Such a study would need to be large and would be a challenge to complete, but it would not be impossible to conduct in the right setting with moderate resources.

The real problem for the field of nutritional research is one of attracting the kind of resources that are available for the development of a promising drug treatment. Diet related ill health is now widely believed to be the leading cause of chronic disease around the world,[9] but definitive research that precisely and reliably defines the effects of plausible, scalable, and affordable interventions is almost completely absent. Public health nutrition awaits the discovery of the model that will secure the investment needed to answer questions about the role of nutrition in health using large randomised studies. Until then, the effect of the consumption of white rice on the development of type 2 diabetes will remain unclear.

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RESEARCH, p 15

Vaccine protection against disease can endure beyond the management of HPV related disease in women already vaccinated

Effect of quadrivalent HPV vaccination on HPV related disease in women treated for cervical or vulvar/vaginal disease

Subsequent disease is reduced in women who undergo treatment post-vaccination

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The two most carcinogenic types of human papillomavirus (HPV) types 16 and 18, are responsible for around 70% of cervical cancers, 85% of anal cancers, and a smaller proportion of other anogenital and oral cancers.[1] Vaccines that target these two sexually transmitted HPV types have consistently shown high efficacy in preventing disease related to those specific HPV types in people who have not yet been exposed.[2-6] In the linked study, which is a post hoc analysis of the main efficacy trials (FUTURE I and FUTURE II) of the quadrivalent HPV vaccine that also targets non-carcinogenic HPV types 6 and 11 (responsible for most genital warts),[2 3] Joura and colleagues show a reduction in subsequent HPV related disease in vaccinated women who received treatment for cervical, vulvar, or vaginal disease (including genital warts) during the course of the trial.[7] This protection extended to disease associated with not only the four HPV types targeted by the vaccine but also 10 other HPV types that cause cancer.

The study's findings—including reductions in any HPV related disease (irrespective of causal HPV type) of 46.2% after cervical surgery and 35.2% after diagnosis of vulvar or vaginal disease—are welcome, but some important caveats deserve consideration.

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Firstly, the authors classified "new" disease as disease detected more than 60 days after surgery or diagnosis on the basis of data from the FUTURE I study, in which 82% of those diagnosed with vulvar or vaginal disease received treatment within 60 days. This 60 day threshold was used to minimise the risk of capturing residual (not new) disease while maximising follow-up time, which was less than four years in both trials. In the subgroup analysis of women in the placebo group who developed cervical disease related to HPV types 6, 11, 16, or 18 after cervical surgery, the authors report that six of nine women had different HPV types from those detected in their surgical specimen, which supports the notion that cases detected after 60 days were indeed "new." However, if the remaining three women had residual disease, the efficacy against subsequent cervical disease would decrease to about 60%, with even wider confidence intervals suggesting substantial uncertainty. The study investigators found similar results when they extended the time interval to 90 days, by which time 91% of women had received treatment in FUTURE I; however, without conclusive diagnosis of new disease, uncertainty in the reported estimates remains appreciable.

Secondly, understanding the subgroup of women being studied—namely, those in the vaccine arm who developed HPV related disease after being vaccinated—is a key factor in putting the study's results into context. Joura and colleagues maintain that cases of disease in the vaccine arm did not result from vaccine failure. Furthermore, all but five women in the study received the full three dose vaccine series as per protocol. Therefore, vaccinated women who developed vaccine type (HPV types 6, 11, 16, and 18) disease during the trial presumably had been exposed to HPV infection(s) of the same type at the time of vaccination. The authors provide an example of two vaccinated women who underwent cervical surgery and then subsequently developed cervical disease; in both of these women the HPV types associated with disease were indeed concordant with those detected at day 1 of vaccination. A closer look at all 26 vaccinated women who developed disease related to HPV types 6, 11, 16, or 18 could further inform the level of concordance between HPV infection(s) at the time of vaccination and in subsequent disease, but this information is not provided. Nonetheless, it can be deduced that any disease that was prevented was associated with HPV infections that were not present at the time of vaccination, which simply reinforces what we already know—that women can benefit from HPV vaccination against unexposed types even if they are exposed to one or more other vaccine types. On one hand, as the authors note, the study corroborates previous findings that the benefits of vaccination are not limited to the primary target group of young sexually naive girls; but on the other hand, the current study's findings further highlight the importance of vaccinating at an early age, when exposure to HPV is minimal, to maximise protection against all HPV types targeted by the vaccine.

Thirdly, and most importantly, this study examines a unique subgroup of women who were vaccinated before the first treatment for HPV related disease. The findings cannot be generalised beyond this group, specifically to women who are considering HPV vaccination after treatment for HPV related disease, contrary to the authors' suggestion that the women in the current study can serve as a surrogate. Without fully understanding individual characteristics and heterogeneities in these different populations, any inference or extrapolation of the current study's findings is premature. Because previous cervical disease was an exclusion criterion for enrolment in the vaccine trials, only surveillance of vaccinated populations in the real world can provide clear evidence of the effectiveness of the vaccine in women who have been treated before vaccination. As we await this information, it is important to emphasise to providers and decision makers that little, if any, generalisation of study findings can be made.

Half a million new cases of cervical cancer are estimated to occur each year, mostly in resource constrained settings, and HPV vaccination offers a tremendous opportunity for cancer prevention. Worldwide, decision makers who are increasingly considering adopting HPV vaccination programmes need information on the total potential health gains and the priority target groups for vaccination. The current study moves us closer to understanding the full scope of benefits from HPV vaccination by showing for the first time that vaccine protection against disease can endure beyond the management of HPV related disease in women already vaccinated. As evidence of both the efficacy and effectiveness of vaccination continues to emerge, responsible communication of the remarkable yet complex properties of HPV vaccines—specifically information about where the evidence is clear and where it remains uncertain—is crucial.

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RESEARCH, p 16

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Do you take blood pressure in both arms?
http://bit.ly/z9nKlc

Differences in blood pressure between arms

May be diagnostically useful but needs further evaluation as a prognostic marker

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A difference in blood pressure readings between arms can be seen in congenital heart disease, aortic dissection, peripheral vascular disease, and unilateral neuromuscular abnormalities. In the absence of these conditions, any discrepancy is small (mean difference: 5 mm Hg and 4 mm Hg for systolic and diastolic blood pressure, respectively).[1] About 20% of patients in primary care or secondary care have a between arm blood pressure difference of 10 mm Hg or more and 4% have a difference of 20 mm Hg or more.[2] Although such a difference in blood pressure is thought to be a marker of atherosclerosis,[3] its clinical significance is not fully understood. In a linked research study,[4] and in a recent meta-analysis,[5] Clark and colleagues provide additional evidence on the diagnostic and prognostic relevance of this phenomenon.

In their meta-analysis of cross sectional studies,[5] Clark and colleagues reported that a between arm blood pressure difference of 15 mm Hg or more was associated with peripheral vascular disease (sensitivity 15% and specificity 96%) and with cerebrovascular disease (sensitivity 8% and specificity 93%), but not with coronary artery disease. A difference of 10 mm Hg or more was associated only with peripheral vascular disease (sensitivity 32% and specificity 91%).[5] The overall low sensitivity and high specificity suggest that the measurement of blood pressure in both arms is not a good screening test for asymptomatic peripheral vascular disease.

On the basis of these prevalence data, it might seem sensible to examine whether, as a marker of asymptomatic peripheral vascular disease of the upper extremities, a difference in blood pressure between arms predicts future cardiovascular events and mortality. Although extensive data show an association between peripheral vascular disease of the lower extremities and both all cause mortality and mortality from cardiovascular disease,[6] little evidence exists for the prognostic value of between arm blood pressure differences.[4 7] The authors of a prospective study of 1872 community dwelling adults and patients evaluated for peripheral vascular disease of the lower extremities in the United States found that a between arm systolic blood pressure difference of 15 mm Hg or more might be associated with a modest increase in all cause mortality and mortality from cardiovascular disease, but the findings were of borderline statistical significance.[7] The linked study, however, reports that a difference of 15 mm Hg or more was significantly associated with all cause mortality and mortality from cardiovascular disease in 230 adults with hypertension in a primary care setting in the United Kingdom over a median follow-up of 9.8 years.[4] In the authors' meta-analysis, the pooled hazard ratios were 1.6 (95% confidence interval 1.1 to 2.3) for all cause mortality and 1.7 (1.1 to 2.5) for mortality from cardiovascular disease.[5]

Subsequent blood pressure monitoring should be performed in the arm with the higher readings

The strengths of the study include its prospective design, generalisability, and long term follow-up. However, there are some limitations to consider when interpreting the findings. Because true within person variations in blood pressure exist and measurement errors occur,[8] repeated simultaneous blood pressure measurements are needed for accurate measurement of differences between arms.[1] Clark and colleagues used the average of a single set of sequential readings taken over three visits for their estimate of the difference between arms, so that people with highly variable blood pressure could have been misclassified as having a large difference.[4] Evidence suggests that people with such variability have an increased risk of cardiovascular events.[9] The Framingham risk score was computed using crude categories for risk factors (for example, current smoking instead of pack years), and this may have allowed residual confounding.[10] In addition, unmeasured confounding as a result of the use of antiplatelet agents, antihypertensives, and lipid lowering drugs might have led to overestimation of the association. Furthermore, given the modest sample size, some changes in the associations after adjusting for pre-existing cardiovascular disease may reflect unstable estimation from sparse strata, rather than true adjustment for confounding (for example, only one of 47 patients with pre-existing cardiovascular disease had a between arm difference of 15 mm Hg or more).[4] These limitations mean that the study cannot be considered to be definitive, and the prognostic value of blood pressure differences between arms remains to be replicated in future studies.

How should clinicians use measurements of bilateral arm blood pressure in their practice? As recommended by current hypertension guidelines, including the new update from the National Institute for Health and Clinical Excellence,[11] bilateral blood pressure measurements should be done routinely to avoid delayed diagnosis or undertreatment of hypertension in those with a 10 mm Hg difference between arms (20% of primary and secondary care patients). What about measurement technique? On the basis of available evidence and practicality,[1 12] a sequential measurement, followed by confirmation with at least two simultaneous measurements using two automatic devices, seems to be a reasonable approach. The optimal number of repeated measurements and monitoring intervals are unknown.

If the difference is 10 mm Hg or more on repeated simultaneous measurements, the positive predictive value for peripheral vascular disease of the upper extremities is high and further diagnostic evaluation is warranted, especially in people with risk factors for cardiovascular disease. Subsequent blood pressure monitoring should be performed in the arm with the higher readings. In the absence of obstructive peripheral vascular disease, there is insufficient evidence for evaluating prognosis or guiding treatment with antiplatelet drugs or statins on the basis of between arm differences in blood pressure. More work is needed to examine how well between arm difference in blood pressure compares with other markers of subclinical atherosclerosis, biomarkers, and clinical predictors as a predictor of mortality from cardiovascular disease.

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RESEARCH, p 19

Although the early assignment of patients to subspecialist care achieves better patient outcomes for specific conditions, data on this approach for older adults are much less convincing

Is it time for a new kind of hospital physician?

The changing demography requires current models of inpatient care to evolve

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Today's consultant physician manages inpatients who are older and have more comorbidities and a greater complexity of acute illness than in the past. Since 1948, life expectancy in the United Kingdom has increased by 18% and 16.7% for men and women, respectively.[1] Half of those aged over 60 years have at least one chronic illness, and this proportion will increase over the next 20 years as the population aged over 85 doubles.[2] These demographic shifts place increasing strain on a service that is required to deliver £20bn (€24bn; $32bn) of efficiency savings by 2014.

MARK THOMAS/SPL

In a linked article, Wachter and Bell describe the transformation of the organisation of hospital care in the United States and UK over the past 15 years.[3] Although changes in US and UK hospital care have been shaped by the structure and culture of the respective healthcare systems, common drivers of change include increasing costs, a need to provide quality care, and restricted resident (US) and junior doctor (UK) hours. The result in both systems is strikingly similar; a new cadre of generalist physicians equipped to meet the complex needs and changing demographics of patients has emerged. Wachter and Bell draw attention to the emerging body of research showing that care delivered by hospitalists in the US reduces length of stay and costs, with a variable impact on quality of care,[4] while in the UK, delivery of care by acute medical units has been associated with reduced mortality and duration of hospital stay.[5]

Fundamental differences and questions remain, however. The US hospitalist provides continuity of care throughout the admission, whereas acute physicians in the UK provide care up to the first 48-72 hours, after which patients who are still in hospital are handed over to another doctor. Furthermore, unlike in the US, the UK model encompasses two kinds of hospital based generalist: doctors who provide general internal medicine alongside their subspecialty and geriatricians who specialise in the care of older people. These geriatricians represent the largest single cohort of medical consultants in the UK—1201 in 2010.[6] Although subspecialty physicians make an important contribution to generalist service provision, general internal medicine as a career path is declining in popularity in the UK. In 2010, 60.5% of doctors from the six major medical subspecialties practised general internal medicine, down from 76.1% in 2002.[6] Currently 3838 (54.4%) medical registrars are registered for dual accreditation in general internal medicine and a subspecialty, but of these only 1597 would wish to practise general internal medicine on becoming a consultant.[7] The unpopularity of consultant general internal medicine practice has been attributed to increasing service requirements and out of hours care.[7] Other factors probably include an unselected workload, lack of specialist prestige, the breadth of medical knowledge that is needed, and disproportionate depletion of the ward team owing to on-call duties and training accreditation based on the acute medical unit. The main concerns reported by general internal medicine trainees about their training are inflexible training posts, burgeoning workload and rising levels of sickness in junior doctors.[7] The on-call general internal medicine registrar is widely viewed as being overburdened by duties that include managing acutely ill patients both throughout the hospital and on the acute medical unit, and 80% of recently qualified doctors report this workload to be "unmanageable" or "very unmanageable."[8]

Health services that have championed medical specialism must now meet the care requirements of older patients, which increasingly fail to align to a single system specialty when patients present with an acute illness. In the context of the recent reports of undignified and inhumane standards of care in hospital, the question of how well equipped the NHS is to care for older patients has never been more relevant.[9] Does the US model, whereby generalist hospitalists deliver continuity of care throughout a patient's admission, offer particular benefits for acutely ill older patients? Geriatricians in the UK have the right set of skills to care routinely for complex older patients—from admission to the acute medical unit through to discharge—but their number is insufficient to meet the needs. Rather than the expertise of a geriatrician being available only if there is sufficient capacity on a specialist ward, it would make sense to embed a geriatrician on the acute medical unit alongside geriatric services to improve delivery of existing geriatric expertise to patients. Moreover, extending acute physician care beyond the acute medical unit to medical and surgical wards may improve patient outcomes and reduce length of stay, as it has done on the acute medical unit.

In the UK and in Europe,[10] doctors trained in general internal medicine are most similar to the US hospitalist model because they provide continuing care to inpatients who are not managed by subspecialty care. Although the early assignment of patients to subspecialist care achieves better patient outcomes for specific conditions, data on this approach for older adults are much less convincing.[11] Most patients admitted as a medical emergency in the UK may now benefit from continuing care from a generalist, with subspecialists taking a consulting and interventional role. In such a scenario, subspecialties would retain specialty registrar trainees but release other trainees to generalist teams. This would amount to a redeployment of trainee doctors, and, with a renewed emphasis on acquisition of the skills necessary to manage the changing demography of patients within a ward based team, may help re-enthuse trainees and consultants.[12]

The evidence base for best practice in organising acute care pathways is limited, which has prompted the Royal College of Physicians, London, to launch a commission on the "future hospital," which is due to report in spring 2013. Ongoing evaluation of services and research is crucial to determining the nature of working patterns, skills, and expertise of doctors that would have the greatest impact on patient outcomes. We all have an interest in ensuring that the next generation of doctors is equipped and organised to meet the requirements of older patients.

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ANALYSIS, p 25

Response on bmj.com **"We recognise the 'implementation challenge' highlighted by the authors, and agree that reliable and consistent measurement of patient experience is a critical factor in driving improvements"**
Gillian Leng (left), NICE Deputy Chief Executive, Professor Mark Baker, London
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doc2doc Discuss this paper in BMJ Group's diabetes forum: http://bit.ly/HjiyRH)

Putting patients first

NICE guidance on the patient experience is a welcome small step on a long journey

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The recent publication of National Institute for Health and Clinical Excellence (NICE) guidance and quality standards on patient experience,[1 2] which are summarised in a linked article,[3] provides some statutory weight to complement recent important recommendations on dignity in care from the NHS Confederation, the Local Government Association, and Age UK.[4] The aims of the guidance, to create "sustainable change that will result in an 'NHS cultural shift' towards a truly patient-centred service" are laudable, and it is good to see that the principle that high quality patient experience should be at the heart of good clinical care is being upheld. Where implemented, NICE's recommendations will lead to feasible and effective improvements in care. However, much of the guidance states the obvious, and many challenges remain to providing a health service that systematically, reliably, and demonstrably puts patients first.

It is a sad indictment of modern healthcare that we need such guidance in the first place. Restaurants and retailers may need to prompt new employees to offer good customer service, but most people would expect that delivering good service would be second nature for staff from the "the caring professions." Sadly, evidence suggests that this is not the case.[5] The reality is that people who work in healthcare often seem to be immune to anxiety, excessive waiting, and impersonal and unnecessarily distressing experiences, and almost every day they walk past or participate in care that isn't delivering a good experience.

How, then, can desirable standards be implemented? Improvements will not be seen unless we understand and improve the attitudes and behaviours of healthcare professionals as well as systems and structures of care. Key to this will be reliable and consistent measurement of patient experience, at a level of sophistication way beyond the hospital-wide annual patient surveys or the ward based experience metrics currently used. The detailed quality measures included in the quality standards document are a good place to start.[1] Ideally, these markers should be measured at the level of the clinical team and results systematically fed back to provide insight and drive change. Improvement of biomedical care processes and outcomes has progressed enormously through the provision of comparative peer outcomes data to clinicians. Now provision of comparative peer outcomes data for patient experience should become a priority.

The definition of patient experience used in the recently published NICE guidance is, unfortunately, limited by an inability to see beyond hospitals and general practices into the lives of those cared for by health services. Arguably the most important challenges faced by the NHS, and most other health systems, are long term conditions, an ageing population, and multimorbidity. A much broader definition of "patient experience" to include the experience people have of living with conditions day to day, and not just of the healthcare they receive, will be needed for these challenges to be successfully met. The guidance offers only a cursory nod towards this with reference to patient education courses and information, but health systems will need to go much further. In truth, self management already is default care for people who live with long term conditions. If the experience of patients who self manage is to be improved, they must be recognised as active co-producers of their own health and supported to develop the knowledge and skills needed to become confident self managers of their conditions.

A compelling body of evidence makes it clear that well designed and well delivered interventions to support self management—particularly proactive behaviourally focused interventions designed to build self efficacy—have a positive effect on clinical symptoms and outcomes, attitudes and behaviours, quality of life, and use of healthcare resources.[6 7] Two UK national demonstration programmes, Co-creating Health and Year of Care, have successfully drawn on this strong evidence base and shown that it is possible to deliver such interventions routinely in day to day care within the NHS.[8 9] That such approaches are not the norm is one of the greatest failings of modern medicine, particularly as people with long term conditions consume around 70% of health and social care resources in the United Kingdom, and there is a national imperative to embed self management support into the UK's health service.

The English Department of Health and NICE should consider the broader context of the patient experience and develop as a matter of urgency further separate guidance and standards on supporting the self management of health conditions. NICE must show an understanding that support for self management has a distinctive theoretical basis within health psychology, which profoundly distinguishes it from more didactic patient education and information provision, and that this is consistent with international best practice. The provision of guidance on a suitable standard of self management support would lay a firm foundation on which future clinical guidelines and standards relating to long term conditions could build, and it would endorse self management support as the organising principle for the care of long term conditions. This would have the effect of ensuring consistency of care across clinical pathways and between different clinical disciplines, which many patients with multimorbidities often find lacking.

NICE guidelines too often reinforce the myth of a "right way" to deliver care, at the risk of ignoring principles of shared decision making. Future guidance should strive to promote the right of patients to understand the options available and to be supported to make the decisions that are right for them.

To make a real difference more is needed than just writing things down. If those who deliver healthcare assume that these standards are already met we will fail our patients and ourselves. Patient experience needs to be measured, evaluated, and improved upon. The current guidance is a small, albeit important, step in a much longer journey towards improved patient experience.

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PRACTICE, p 41

Efforts to study the effect of low dose aspirin on cancer occurrence should include the application of appropriate causal modelling to observational data

Aspirin and cancer prevention

More evidence, but still not enough to support an aspirin a day for all adults

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When Eichengrün and colleagues at dye manufacturer Friedrich Bayer & Co synthesised acetylsalicylic acid in 1897 the success story of aspirin began,[1] and its potential applications are still being revealed. It is well established that aspirin reduces pain, limits the inflammatory response, and reduces cardiovascular disease but that it can lead to major bleeding events and gastrointestinal upset. For several years increasing numbers of studies have suggested a benefit of aspirin on the occurrence of polyps and colorectal cancer.[2 3] Potential beneficial effects on other common cancer types have also been reported.[4] Two recently published large scale studies have provided additional evidence that low dose aspirin reduces the incidence of cancer, death from cancer, and cancer metastasis.[5 6]

The first, an analysis of the short term effects of daily aspirin (<300 mg) use on various cancer related outcomes in 51 randomised controlled trials,[5] found that allocation to aspirin reduced deaths from cancer (odds ratio 0.85, 95% confidence interval 0.76 to 0.96), particularly from five years of daily use onwards, resulting in fewer deaths from non-vascular disease. In addition, aspirin significantly reduced the risk of incident cancer in women and men by about 25%. Furthermore, the effect of low dose aspirin on incident cancer increased with longer follow-up, whereas its effects on major cardiovascular disease and extracranial bleeds decreased.

The second study summarised the effects of aspirin on cancer metastasis in five large scale randomised trials.[6] In this study, allocation to aspirin reduced the risk of cancer with distant metastasis. The hazard ratio was 0.64 (0.48 to 0.84) for all cancers, 0.54 (0.38 to 0.77) for adenocarcinoma, and 0.82 (0.53 to 1.28) for other solid cancers. The study's findings suggest that low dose aspirin should be considered in the treatment of some patients with cancer.

The findings of the two recent studies are compelling and strongly suggest that, at least for specific subgroups, daily low dose aspirin could reduce cancer related outcomes. However, can we now argue that everyone should take a daily aspirin? Should we conclude that because daily aspirin has confirmed benefits on cardiovascular disease and now seems to be effective in preventing cancer, two of the major contributors to mortality and morbidity in the general population, we should be more proactive in getting people to take daily aspirin?

Despite clear results from the two recent analyses, the topic is still complex and many uncertainties remain.[7] The two studies include evidence from randomised controlled trials. Although well conducted randomised trials are considered to provide strong clinical evidence, trial participants are a highly selected group, recruited according to clear inclusion and exclusion criteria, and evidence from trials cannot always be extrapolated and applied to the general population. Although these recent results are supported by some observational studies,[3 7] the scientific question of whether we should recommend low dose aspirin for everyone could be answered only by using a distinct causal modelling approach. Such an approach is complex and has rarely been used to analyse observational data.[8] If low dose aspirin has a causal effect in cancer prevention, then this effect must be present across different study designs. However, large scale primary prevention trials in men and women have failed to show an effect of low dose aspirin on colorectal cancer, total cancer, or cancer mortality.[9 10]

There is little doubt that low dose aspirin has beneficial effects on cardiovascular events. But even in this area, which has a large body of evidence, it is unclear which patients should be given aspirin because the benefits are not constant across groups with different risk factor profiles. For cancer prevention, where far less published evidence is available, the uncertainty is even greater. For example, what should a doctor recommend to a patient with Barrett's oesophagus, who is considered to be at higher risk of developing cancer, but who may not tolerate the gastric side effects of aspirin? What about patients with asthma? How should a doctor advise the patient with a family history of cancer but a propensity to bleed in whom there is a small chance that aspirin may induce a major bleeding event? Results of one of the recent studies suggest that an increased risk of bleeding is only apparent in the short term,[5] but should we take the risk of prescribing aspirin in the hope that the patient gets through that short time window of increased bleeding risk without an adverse event?

Too many questions remain unanswered to warrant a recommendation to treat all adults with low dose aspirin to prevent cancer. However, the increasing evidence that aspirin may interfere with the pathogenesis of at least some cancers is compelling and should motivate further targeted research at the population level. Efforts to study the effect of low dose aspirin on cancer occurrence should include the application of appropriate causal modelling to observational data, in addition to the identification of subgroups of patients who would benefit most and those in whom adverse effects of aspirin are most likely to occur. Research should focus on plausible interactions of specific biological mechanisms, including biomarkers and genetic information. Until then, doctors should continue to make decisions on long term treatment with low dose aspirin in individual patients by carefully balancing risks and benefits.

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