

LETTERS

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DIET AND CARDIOVASCULAR RISK

Why did the *BMJ* publish such a biased article?

I don't understand why the *BMJ* published such a biased article—I identified 10 biases.¹

- Methodological bias: the authors sent a questionnaire in 1992 and patients were followed up 15 years later without new questionnaires or requests for information about their habits. The conclusions are based on biased and misleading arguments.
- Selection bias: at least one out of two patients declined to be included in the study.
- Measurement bias: authors knew nothing about the life habits of patients.
- Follow-up bias: only one questionnaire is not appropriate follow-up.
- Expectation bias: the absence of masking or blinding may mean that the data err towards the expected outcome.
- Lack of sensitivity: the measurement tool used in this study is not sensitive enough to detect important differences in the variable of interest.
- Compliance bias: adherence to the reported diet habits was not measured.
- Misclassification bias: it is impossible to know if patients were classified correctly (low carbohydrate v high carbohydrate diet).
- Confounding bias: no more than 51% of potential patients were included.
- Non-response bias (49% of potential patients): limits generalisability, not validity.

According to Stephen Lock (ex-editor of the *BMJ*): “Medical journals will soon be wrapping up next week's fish and chips.”

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Competing interests: None declared.

- 1 Lagiou P, Sandin S, Lof M, Trichopoulos D, Adami H-O, Weiderpass E. Low carbohydrate-high protein diet and incidence of cardiovascular diseases in Swedish women: prospective cohort study. *BMJ* 2012;344:e4026. (26 June.)

Cite this as: *BMJ* 2012;345:e5104

Advice to avoid low carbohydrate-high protein diets is not evidence based

Lagiou and colleagues' paper bases all of its 15 years' worth of conclusions on a single, solitary, and clearly inaccurate, baseline food frequency questionnaire; it didn't control for clearly known dietary confounders; it found a minuscule absolute increase in risk; and the diet it reported on can't even be fairly described as a low carbohydrate diet.¹

Useful? Conclusive? Press worthy? It gets worse.

An accompanying editorial by Floegel and Pischon gave this very clear, yet completely non-evidence based, advice: “Despite the popularity of these diets, clinicians should probably advise against their use for long term control of body weight.”²

The paper and editorial were unforgivably, irresponsibly, and shamefully misinformative—something our already nutritionally confused world really didn't need.

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Competing interests: YF is author of a book on fallacies of modern day dieting slated to be published in spring 2013 by Simon and Schuster.

- 1 Lagiou P, Sandin S, Lof M, Trichopoulos D, Adami H-O, Weiderpass E. Low carbohydrate-high protein diet and incidence of cardiovascular diseases in Swedish women: prospective cohort study. *BMJ* 2012;344:e4026. (26 June.)
- 2 Floegel A, Pischon T. Low carbohydrate-high protein diets. *BMJ* 2012;344:e3801. (19 June.)

Cite this as: *BMJ* 2012;345:e5106

Research authors' reply

Campillo-Soto repeatedly mentions “biases” but uses this epidemiological term loosely and unconventionally. Selection bias is not really a concern in a cohort study and neither is measurement bias—assessment of exposures cannot be differentially affected by the outcome if it is not known when the exposure is reported. In his reference to “compliance bias” and “expectation bias,” again interesting terminology, Campillo-Soto

confuses interventional and observational epidemiological study designs. As for follow-up bias, it is relevant when participants are lost to follow-up, but this was not the case in our study—linkage to registries allowed us almost complete follow-up of all subjects.

One of Freedhoff's criticisms was something that we had already stated in our manuscript: that our study population's diets were less extreme in their low carbohydrate content than advertised dietary regimens. The associations we detected, however, are monotonic, so that the risk would be expected to be higher for more extreme low carbohydrate-high protein regimens. We disagree that the study is misinformative—all aspects were clearly presented—and, more importantly, we disagree that the increase in risk is minuscule.

Both Campillo-Soto and Freedhoff criticise our use of a food frequency questionnaire, even though, despite their limitations, such questionnaires are standard tools in large nutritional epidemiological cohort studies. Both our critics also point out that dietary assessment only at recruitment generated misclassification. We agree, but in a cohort study this misclassification is non-differential and, thus, much more likely to attenuate an existing association rather than generate it. Pagona Lagiou professor, Department of Hygiene and Epidemiology, University of Athens Medical School, Goudi, GR-115 27, Athens, Greece plagiou@med.uoa.gr
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Editorial authors' reply

Freedhoff's claim that our recommendation for clinicians to advise against the long term use of low carbohydrate-high protein diets because of higher morbidity and mortality from cardiovascular diseases is not evidence based is not correct.

Currently, no randomised controlled trials (RCTs) or meta-analyses of RCTs have investigated the association between low carbohydrate-high protein diets and hard clinical endpoints of cardiovascular disease. Because of this lack of level 1 evidence, we looked at level 2 evidence—which includes that from prospective cohort studies—and found several original studies. In most such studies, including that by Lagiou and colleagues, lower carbohydrate and higher protein intake was associated with a higher risk of cardiovascular disease and increased mortality. In a recent analysis of the high quality Nurses' Health study and the Health Professionals Follow-Up study this association was particularly strong for protein from animal sources.¹ We based our conclusions on these results from European and US cohorts, which represent the highest level of evidence available.

In addition, RCTs may be best for evaluating treatment effects in a clinical setting and for drug trials, but their experimental study design may not be appropriate for lifestyle interventions because general behaviour is a matter of personal choice.² Although observational studies may be susceptible to measurement error and bias, in the context of lifestyle interventions they may offer several advantages over RCTs (they may better reflect a real life situation; at the population level they may provide higher external validity; and they are feasible to conduct). This is one of the reasons why international organisations such as the World Health Organization consider results from prospective cohort studies as the highest level of evidence for recommendations on nutrition and chronic disease risk.³

Therefore, more high quality prospective cohort studies, such as Lagiou and colleagues' study, are needed to enhance the level of evidence. In the meantime, available evidence from existing observational studies should not be ignored.

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Competing interests: None declared.

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CHEST PAIN AND ST ELEVATION

Sudden death in young men from South East Asia and Pacific rim

In their case report of a 57 year old Vietnamese man, with an electrocardiogram indicating a Brugada phenotype, Page and colleagues omitted an important message about sudden unexpected death in men from South East Asia.¹

This phenomenon has been described in many of these countries, including Thailand (Lai-Tai syndrome), Laos, Vietnam, and Kampuchea, in addition to countries on the Pacific rim, including the Philippines (Bangungot syndrome), Korea, Japan (Pokkuri disease), and Singapore.² The phenomenon is seen in indigenous populations and in migrants from these countries, and it is almost exclusive to men aged 20-49 years, with most dying suddenly and unexpectedly in their sleep.

In many cases, survivors have been shown to have a Brugada-type electrocardiogram. It seems to be most prevalent in north eastern Thailand and among members of the Hmong tribe, which extends into Laos, China, and Vietnam.³

Doctors sitting postgraduate exams should be aware of this geographical association of sudden death in young men in and from South East Asia.

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Competing interests: None declared.

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TRUSTS AND PFI DEALS

Reduce repayment rates to 0.5%

Monitor anticipated the Peterborough and Stamford debacle.¹ Why did Monitor not raise similar concerns in south east London before the financially disastrous merger of three hospitals?¹ Hospital consultants warned of the problem on the basis of an analysis by the finance directors, which stated unequivocally that private finance initiative (PFI) payments for the merged trust could not be met by income from payment by results.²

Who should shoulder the blame? The trusts' leaders? South Thames strategic



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health authority, which ignored the risk? The investigative team sent in by the authority, which did the same? Monitor? The Department of Health? The then government?

Government suggests that PFI is a small part of the hospital's financial crisis. Rubbish. PFI interest rates should be renegotiated.² Greece's debt has been written down by telling banks to allow default on loans. When the baseline interest rate is 0.5% it is obscene to allow rates of 6-20%. An investigation by Shaoul of Manchester Business School, which was based on accounts filed at Companies House, showed that the rate of return for PFI companies on 12 large PFI hospitals was 58%.³

If PFI repayments for South London Healthcare Trust are 6%, reducing the rate to 0.5% would save around £12m (€15m; \$18.5m) annually and the £65m deficit would be cleared in seven years (or two years if they are 20%).

In 2007 the Department of Health told the BBC, "PFI is only ever used if it is affordable to the NHS, meets patient needs, and offers value for money."⁴ Rubbish again.

The press is full of trusts in trouble—struggling, merging, closing bits but not reducing deficits. There is an economic crisis. Why are we waiting?

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EFFECT OF TELEHEALTH

Trial policy, politics, and publication ethics

Limitations listed for the Whole System Demonstrator trial of telehealth did not include close involvement of the funder in its design and execution. Under "Finances," the authors state:

“The Department of Health reviewed the protocol . . . and provided project manager support.”¹

The Department of Health makes greater claims for its involvement in the trial. In January 2012 it signed a “concordat” with the technology industry, which referred to “a randomised controlled trial funded and run by the Department of Health.”²

The authors have not commented formally on the substantial mismatch between their findings and conclusions (which were measured and cautious³) and those used by the Department of Health to inform policy (which were one sided and sensationalist^{2,3}), although individual Whole System Demonstrator researchers have expressed misgivings in scientific meetings.

Randomised trials, which control for context, have limited purchase for evaluating politically driven eHealth programmes.⁴ The Department of Health’s cherry picking of unanalysed data to put on its website before the trial had finished recruiting was scientifically inappropriate but politically expedient.⁵

The *BMJ* has led the field in exposing how the drug industry’s conflicts of interest distort research. In failing to require these authors to consider conflicts of interest by the state (whose intention to implement telehealth was enshrined in policy before the trial’s results were analysed), and in privileging randomised trials over study designs that allow analysis of political influences, the *BMJ* has let itself be used as a pawn by an increasingly powerful industrial-political complex.

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Competing interests: None declared.

- 1 Steventon A, Bardsley M, Billings J, Dixon J, Doll H, Hirani S, et al. Effect of telehealth on use of secondary care and mortality: findings from the Whole System Demonstrator cluster randomised trial. *BMJ* 2012;344:e3874. (21 June.)
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Authors’ reply

We agree with Greenhalgh about the importance of non-randomised studies.¹ Yet many commentators agree that randomised trials also have an important role to play, and we hope that this trial will provide valuable information about telehealth.

Our analysis was conducted and written up in line with published recommendations and our original protocol.² Dissemination policies were governed by the standard contractual terms for projects funded by the Department of Health Policy Research Programme.³ The terms specified that permission to submit findings for publication cannot be withheld. Draft copies of proposed publications were sent to the Department of Health in advance of submission for publication and clearance was given in line with the contract. We favoured publication of the articles in the peer reviewed press, so that the draft articles could be extensively examined.

As Greenhalgh notes, the Department of Health published several documents during the peer review process.⁴ The research team was not involved in these interpretations of the findings and the resulting documents. Our role has been to design and conduct a relevant and high quality evaluation and to report the findings clearly and transparently. We believe we have done this with the peer reviewed material.

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REPORTING SUSPECTED CHILD ABUSE

The GMC’s paradoxical behaviour

Advice from the General Medical Council (GMC) on “Protecting children and young people” is at variance with its conduct, and

the response of the medical establishment is muddled.¹ The GMC destroyed the careers of paediatricians who exposed child abuse, but it allowed about 100 doctors who were convicted of accessing child pornography on the internet to remain on the medical register. The GMC allowed one gynaecologist to continue in practice after being placed on the Sex Offenders Register for that offence, but his trust restricted his clinical activities. Eighteen months later he received a silver clinical excellence award (CEA). He must have been nominated by his trust and the Advisory Committee for Clinical Excellence Awards must have checked whether the GMC had concerns about his character. How can such a doctor be awarded a national CEA?

The GMC provides advice about research misconduct but allows professors who falsify clinical research to get off without meaningful punishment. Those professors invariably retain the national CEAs that they obtain by falsifying research.

The GMC’s advice on whistleblowing resonates with its advice on reporting suspected child abuse, but the GMC and medical establishment have destroyed the careers of whistleblowers. Yet when a GMC member had concealed from the GMC and from the police fraud committed by another doctor, the GMC ignored its own advice on reporting misconduct and the legal advice from its solicitors. It refused to act against the GMC member and allowed him to continue sitting on the panel that hears cases of alleged misconduct by other doctors.²

I have reported concerns to the GMC for 30 years. Some cases are current. I discern no change in the “club culture,” with the GMC “looking after its own” as Janet Smith reported.³

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Competing interests: PTW has a silver clinical excellence award.

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Cite this as: *BMJ* 2012;345:e5191

SANCTITY OF LIFE LAW

A step too far

I agree that the sanctity of life law has gone too far.¹ Unless this judgment is modified, it could “gradually and detrimentally distort healthcare provision, healthcare values, and common sense.”¹ Why? Because although the judgment was specific to patients in a minimally conscious state, logically all decisions about withholding or withdrawing clinically



assisted nutrition and hydration for patients lacking capacity will need to go to the Court of Protection unless a legally valid advance directive to refuse treatment exists.

The judge reputedly stated that, in the absence of an advance directive, little weight should be attached to a person's previously expressed values, wishes, and views.¹ We seem to be trapped on a slippery slope of an increasingly restrictive legal "stranglehold." The judgment could affect patients in chronic persistent coma, those with end stage dementia, and people with terminal cancer or end stage organ failure, and it would intrude alarmingly on palliative care. I am sure that the judge did not intend this, but slippery slopes are, by definition, slippery.

Health professionals, the legal profession, and parliament must continue to accept that life sustaining treatment (including nutrition and hydration) is often futile, even counterproductive, and that when death is inevitable we should move from life sustaining (death prolonging) treatments to more appropriate comfort care. Doctors have neither a duty nor the right to prescribe a lingering death.

Perhaps two traditional dictums can still help doctors maintain an appropriate, ethical, moral, and common sense balance in decision making: "First do no harm" and "Thou shalt not strive officiously to keep alive."

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Competing interests: None declared.

1 Gillon R. Sanctity of life law has gone too far. *BMJ* 2012;345:e4637. (12 July.)

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IN PRAISE OF YOUNG DOCTORS

Box ticking is a waste of time

I agree with Heath that something has gone very wrong with medical training.¹ After six years at medical school I am sure I have had to tick (literally) more boxes than any previous generation.

I spent a huge amount of time desperately trying to get clinical evaluation exercise (CEX) forms signed, loitering in the emergency department for a DOPS (direct observation of procedural skills) opportunity, or pursuing the foundation year 2 doctor for a case based discussion (CBD) form. I doubt whether these work based assessments (or supervised learning events, as my new e-learning portfolio jubilantly announces they are called) really improve clinical skills. Most doctors sign assessment forms with little interest, and the

forms simply detract from the teaching itself. Time spent trying to get forms signed reduces time spent with patients.

Regular appraisal of medical students and junior doctors is necessary, but box ticking is not the best way to go about it. What about things that can't be quantified this way? Clinical thinking, complex decision making, and professional judgment are skills that are hard to measure and take years of experience to gain.

I am glad that Heath acknowledges the commitment and dedication of most junior doctors. However, our conscientious nature makes clambering through these endless hoops burdensome and demoralising. Add to this the huge debt we face after six years at university and it is easy to see why some feel despondent at the start of their careers.

Unfortunately, I suspect it won't be long before we have our commitment and dedication "snuffed out."¹ If Heath wants a doctor who thinks and questions,¹ she and the royal colleges urgently need to act to change clinical education.

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1 Heath I. In praise of young doctors. *BMJ* 2012;345:e4549. (11 July.)

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What are we being trained for?

As people about to cross the student-doctor boundary we echo Heath's sentiments.¹ During the past five years, our performance has been determined by exercises and assignments that reduced us to tick boxes.

We were given formulas to perform examinations, take histories, and break bad news. We were even assessed on our abilities to reflect, and there was a formula for that too. As we start working on the wards for the first time we anticipate discovering a strategy for success in that environment. To one of the authors' chagrin, when a junior doctor asked a consultant during a ward round about a patient's management, the consultant retorted, "You're not here to think, boy."

The graduation address to Harvard Medical School's class of 2012 reminded the graduates of how the wonders of modern medicine may be futile in the face of social inequality and that they could change the healthcare system.² We understand the burden on medical schools and training programmes to produce competent doctors, but this should not amount to creating mere minions. They must not strip individuals of their identities. The consequences may be



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that doctors at the end of the production line are too detached from the society they serve to cater for patients' needs appropriately.

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MANAGEMENT OF CHRONIC EPILEPSY

Fluoroquinolones can also lower the seizure threshold

Fluoroquinolones should be added to the list of drugs that can lower the seizure threshold,¹ especially because they are commonly used by clinicians who may not be aware of this fact. They are thought to increase the risk of seizure by inhibiting the GABA receptor complex.² Fluoroquinolones are more likely to have central nervous side effects in older patients, when patients are also taking non-steroidal anti-inflammatory drugs,³ when there are electrolyte imbalances, and when patients fail to adjust to a "renal" dose. This side effect is also more likely when fluoroquinolones are prescribed with other agents that reduce the seizure threshold,⁴ such as theophylline, which is another commonly used drug that was not mentioned but is worth remembering.

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Competing interests: None declared.

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