

# research update

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

## Smoake is dangerous to ye Lungs

A new study of smokers with preserved pulmonary function finds that a lot of them have lung symptoms. And even if they don't fulfil the criteria for chronic obstructive pulmonary disease, they still experience the familiar pattern of exacerbations and limitation of activity and end up using the same drugs as people with COPD. Nothing has changed in the 412 years since King James I of England declared smoking to be "A custome lothsome to the eye, hatefull to the Nose, harmefull to the braine, dangerous to the Lungs, and in the blacke stinking fume thereof, neerest resembling the horrible Stigian smoke of the pit that is bottomelesse."

• *N Engl J Med* 2016, doi:10.1056/NEJMoa1505971

## Door knobs, toilet seats, and MRSA

In my childhood, antibiotics were new, and germs were still greatly feared. They were divided into family germs, which were harmless and could be shared by eating the same bit of cake, versus other people's germs, which were disgusting and could kill you if you weren't careful with door knobs, toilet seats, or even public library books. Obviously "good homes" would be less of a risk than places frequented by the lower classes.

I'm reminded of this by a study from Columbia University Medical Center, which sought to determine the role of household contamination in recurrent community acquired methicillin resistant *Staphylococcus aureus* (MRSA) infection. All household members from the dwellings of 82 index patients were swabbed and so were door knobs, the television remote control, the living room light switch, toys, the couch, the computer or radio, the house telephone or index cellular phone, the bathroom sink, the toilet seat, the kitchen towel, and kitchen appliance handles. Thirteen out of 35 patients with recurrent MRSA infection came from the 20 households found to be "dirty," as opposed to the 62 that were "clean." You can never be too careful.

• *JAMA Intern Med* 2016, doi:10.1001/jamainternmed.2016.1500



## Apple juice to keep the doctor away

Here's a randomised, single blind non inferiority trial conducted between the months of October and April during the years 2010 to 2015 in a tertiary care paediatric emergency department in Toronto, Ontario, Canada. Study participants were children aged 6 to 60 months with gastroenteritis and minimal dehydration. These little ones with mild diarrhoea and vomiting were randomised either to an electrolyte replacement mix or to dilute apple juice. They tended to prefer the latter, and thanks to this teaching hospital trial we can rest content in the knowledge we already had—that kids in rich countries with mild diarrhoea and vomiting get better whatever they are given or choose to drink.

• *JAMA* 2016, doi:10.1001/jama.2016.5352

## Caregivers of critically ill patients, a year later

Here's a nice example of research based on the "subjective" experiences of real people, which is published in the *New England Journal of Medicine*, because it hides its qualitative heart beneath a cloak of conventional sampling methods and statistics. The people described are caregivers (60% spouses, 70% women) of patients who had received seven or more days of mechanical ventilation in intensive

care units in 10 Canadian hospitals. Anyone who has been in this situation will know how stressful it can be, and the net effect of prolonged severe stress in most people is what we label as depression. The bottom line of this study is that 67% of caregivers had high levels of depressive symptoms one week after patients were discharged from the intensive care unit, and 43% still had these at one year. These are useful figures, signifying a massive and enduring burden to thousands of people.

• *N Engl J Med* 2016, doi:10.1056/NEJMoa1511160

## Human but acellular dialysis access

I normally avoid *Lancet* articles that hype bionic advances, but I do sympathise with renal doctors who have to find new modes of access to be able to perform haemodialysis in very sick patients. A novel bioengineered human acellular vessel implanted into the arm seems to hold promise, and for once I won't moan about a phase II trial appearing in this august journal, as precursor to a full trial.

• *Lancet* 2016, doi:10.1016/S0140-6736(16)00557-2

## Hysteroscopic fertility

I don't know how common it is for fertility clinics to carry out routine hysteroscopy before in vitro fertilisation, but judging from a pair of trials on the *Lancet* website it is time they stopped. The Dutch inSIGHT trial shows that routine hysteroscopy does not improve livebirth rates in infertile women with normal transvaginal ultrasound findings of the uterine cavity scheduled for a first IVF treatment. A cross European trial called TROPHY shows that outpatient hysteroscopy before IVF in women with normal ultrasound findings of the uterine cavity and a history of unsuccessful IVF treatment cycles does not improve the livebirth rate. So this procedure should go on the Choosing Wisely bin-list for national health service gynaecology.

• *Lancet* 2016, doi:10.1016/S0140-6736(16)00231-2; doi:10.1016/S0140-6736(16)00557-2

## Deaths, late deaths, and role of infecting dose in Ebola virus disease in Sierra Leone

Bower H, Smout E, Bangura MS, et al

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Find this at: <http://dx.doi.org/10.1136/bmj.i2403>

### Study question

How frequent is fatal recrudescence with Ebola virus disease after discharge from treatment, and does the infecting dose affect case fatality rates?

### Methods

A retrospective cohort study included all 151 survivors of Ebola virus disease treated at the Kerry Town Treatment Centre, Sierra Leone. They underwent vital status checks at four to nine months after discharge, and again six to 13 months after discharge. Verbal autopsies were conducted for survivors who had died since discharge. We interviewed survivors still living in Western Area and their household members to establish exposure levels to Ebola as a proxy of infecting dose, including for those who died. All living participating household members gave individual, written informed consent (parents or guardians gave consent for those aged under 18 years).

### Study answer and limitations

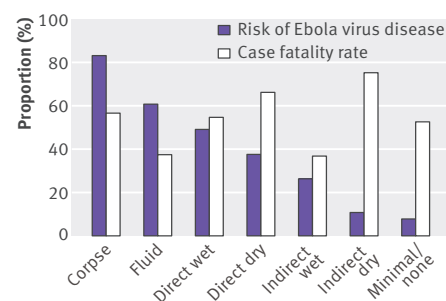
Four survivors died after discharge, all within six weeks of discharge (two probably due to late complications, one to previous tuberculosis, and only one after apparent full

recovery from Ebola virus disease), giving a maximum estimate of recrudescence leading to death of 0.7%. 395 people in these households were reported to have had Ebola virus disease, of whom 227 died; a further 53 people fulfilled the case definition for probable disease, of whom 11 died. Case fatality rates were higher in children aged under 2 years and adults older than 30 years, in larger households, and in infections occurring earlier in the epidemic in Sierra Leone. There was no consistent trend of case fatality rate with exposure level, although increasing exposure increased the risk of Ebola virus disease. The study was limited to survivors' households, so probably underestimated the true case fatality rate.

### What this study adds

Recrudescence of severe Ebola virus disease appears to be rare up to 10 months after discharge. Infecting dose, as measured by extent of exposure to body fluids, correlated with risk of developing Ebola virus disease, but there was no consistent trend with case fatality rate.

Funding, competing interests, and data sharing Save the Children internal funds and the Wellcome Trust's Enhancing Research Activity in Epidemic Situations programme (grant no ER1502). No competing interests declared. A full dataset will be available with restrictions to ensure confidentiality and prevent deductive disclosure in the London School of Hygiene and Tropical Medicine's data repository, DataCompass. Consent mentioned publication but did not explicitly mention data sharing; the presented data are anonymised and risk of identification is low.



Relation of exposure level with risk of Ebola virus disease and with case fatality rate. To assess risk of disease by exposure level, primary cases in each household were excluded. Probable Ebola virus disease and deaths are included. Corpse=direct contact with body of a person who died of Ebola virus disease; fluid=direct contact with body fluids of patient with wet symptoms; direct wet=direct contact with patient with wet symptoms; direct dry=direct contact with patient with dry symptoms; indirect wet=indirect contact with patient with wet symptoms; indirect dry=indirect contact with patient with dry symptoms; minimal/none=minimal or no known contact



Details of deaths after discharge for four survivors of Ebola virus disease. All other 147 survivors from the Kerry Town Ebola treatment centre were alive at follow-up (six to 13 months after discharge)

Patient	Age (years)	Sex	Timing of death (no of days after discharge)	Full recovery	PCR result at death	Likely diagnosis
A	25	Female	15	No	Negative	Ebola related pancreatitis
B	32	Female	1	No	Negative	Ebola related stroke
C	17	Male	35	Yes	Negative	Chest infection or recrudescence of Ebola?
D	6	Male	7	No	Weak positive	Tuberculosis

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# Coding errors and the apparent “weekend effect”



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## Biases in detection of apparent “weekend effect” on outcome with administrative coding data

Li L, Rothwell PM; on behalf of the Oxford Vascular Study

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### Study question

What impact do errors in routine administrative diagnostic coding of acute hospital admissions have on the apparent “weekend effect”?

### Methods

In a population based study of 92 728 residents of Oxfordshire, UK, in 2002-14 (Oxford Vascular Study), all patients with clinically confirmed acute stroke were prospectively identified with multiple overlapping methods of ascertainment. These ideal standard clinical data were compared with routine hospital administrative diagnostic codes for acute stroke during the same period. The impact of inaccurate coding, and other potential biases, on apparent 30 day case fatality of acute stroke for weekday compared with weekend admissions was determined. The

authors also carried out a scoping review of previous studies of weekend effects in stroke.

### Study answer and limitations

Among 1292 admissions for acute stroke, 319 (24.7%) were missed by administrative coding. Of 1693 apparent admissions for acute stroke identified by coding, 638 (37.7%) patients were admitted for conditions other than acute stroke. Such “false positive” cases accounted for a higher proportion of all admissions coded as acute stroke on weekdays than at the weekend (41.0% v 26.5%;  $P < 0.001$ ). The most common false positive coding was of pre-planned elective admissions for follow-up investigation, procedure, or rehabilitation after previous stroke. The 30 day case fatality after these elective admissions was lower than the fatality after confirmed admissions for acute stroke (3.8% v 22.1%;  $P < 0.001$ ). Consequently, inclusion of low risk false positive coding cases lowered the 30 day case fatality of weekday admissions from 22.9%, when based on true acute stroke admissions, to 17.5% when based on all coded stroke admissions ( $P = 0.001$ ), giving the illusion of a weekend effect. Generalisability of

these findings to other countries where coding practice is different is uncertain. Other potential biases in detection of apparent weekend effects on stroke outcome in this study included patients with minor stroke being less likely to present at weekends. In the scoping review of previous studies, no overall weekend effect for stroke outcome was apparent in cohorts of patients with clinically confirmed strokes, particularly in studies in which there was no imbalance in baseline characteristics and severity of stroke on admission between weekday and weekend admissions.

**What this study adds** Use of retrospective administrative hospital coding data to determine weekend effects on outcome in acute medical conditions, such as stroke, can be undermined by inaccurate coding, which can introduce biases that cannot be reliably dealt with by adjustment for case mix.

**Funding, competing interests, data sharing** OXVASC has been funded by Wellcome Trust, Wolfson Foundation, UK Stroke Association, British Heart Foundation, Dunhill Medical Trust, and the NIHR Oxford Biomedical Research Centre. PMR is in receipt of an NIHR senior investigator award and a Wellcome Trust senior investigator award. The authors declare no competing interests and have no additional data to share.

See EDITORIAL, p 303; FEATURE, p 305

	Total	No (%) of deaths at 30 days	No (%) of admissions		P value
			Weekdays	Weekend	
<b>Correctly identified episodes by coding (true positive)</b>					
No of patients	1055	233 (22.1)	772	283	0.44
<b>Incorrectly identified episodes by coding (false positive)</b>					
No of patients	638	66 (10.3)	536	102	<0.001
Cancelled admission	15	0 (0)	15 (2.8)	0 (0)	0.09
Elective admission*	293	11 (3.8)	267 (49.8)	26 (25.5)	<0.001
Non-stroke diagnoses*	226	29 (12.8)	183 (34.1)	43 (42.2)	0.12
Admission date wrong*	72	23 (31.9)	46 (8.6)	26 (25.5)	<0.001
General practitioner information wrong	20	0 (0)	16 (3.0)	4 (3.9)	0.62
Unknown	12	3 (25.0)	9 (1.7)	3 (2.9)	0.39

\*Detailed subcategories are reported in full paper.

# Potato intake and incidence of hypertension

**ORIGINAL RESEARCH** Results from three prospective US cohort studies

## Potato intake and incidence of hypertension

Borgi L, Rimm EB, Willett WC, Forman JP

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**Study question** Is higher intake of baked, boiled, or mashed potatoes, French fries/chips, or potato crisps associated with incidence of hypertension?

**Methods** Non-hypertensive participants of three prospective longitudinal US cohort studies were included in the analyses (62 175 women in the Nurses' Health Study, 88 475 women in the Nurses' Health Study II, and 36 803 men in the Health Professionals Follow-up Study). Prospective, independent associations of baked, boiled, or mashed potatoes, French fries, and crisps with the

risk of developing new onset hypertension were determined after adjustment for multiple potential confounders.

**Study answer and limitations** Compared with consumption of less than one serving a month, the random effects pooled hazard ratios for four or more servings a week were 1.11 (95% confidence interval 0.96 to 1.28; P for trend=0.05) for baked, boiled, or mashed potatoes, 1.17 (1.07 to 1.27; P for trend=0.001) for French fries, and 0.97 (0.87 to 1.08; P for trend= 0.98) for crisps. In substitution analyses, replacing one serving a day of baked, boiled, or mashed potatoes with one serving a day of non-starchy

vegetables was associated with decreased risk of hypertension (hazard ratio 0.93, 0.89 to 0.96). As with any observational study, the findings could be explained by residual confounding.

**What this study adds** The findings of this study suggest that eating four or more servings of boiled, baked, or mashed potatoes or French fries a week increases the risk of incident hypertension.



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## COMMENTARY Dietary patterns matter more than isolated food items

We seem to be constantly assailed by conflicting recommendations about the risk posed by specific dietary foods. This is a major challenge for clinicians, not only in responding to patients' questions but also in giving advice about what diet to follow to lower the risk of disease.

The linked study by Borgi and colleagues reports associations between potato consumption and hypertension in three large cohorts of women and men in the United States.<sup>1</sup> Although the authors found an association between consumption of baked, boiled, or mashed potato and hypertension in women, this association was not found among men. A higher consumption of French fries was associated with hypertension in both men and women. However, consumption of potato crisps was not associated with hypertension in women and was actually associated with a lower risk of hypertension in men.

As with much of nutritional epidemiology, it is always possible that uncontrolled confounders contributed to the observed associations. Food frequency questionnaires cannot collect detailed

### We seem to be constantly assailed by conflicting recommendations about the risk posed by specific dietary foods

information on cooking methods. The consumption of French fries may be a proxy for a dietary pattern higher in sodium and saturated fat not fully captured in the food frequency questionnaire and not adequately controlled for in the analysis. The inconsistent findings in the male cohort and with potato crisps may have been because sodium intake was poorly assessed—high variances of urinary sodium and potassium have been reported from food frequency questionnaires, especially in men, who may be less aware of how their food was prepared.<sup>2</sup>

### Glycaemic load

The authors suggest that the glycaemic load of potato could help to explain their findings. This is plausible and consistent with other research.<sup>3,4</sup> However, the glycaemic load of the whole meal is influenced by a range of factors including the protein and fibre content of the meal and the glycaemic index of any other carbohydrate containing foods consumed.<sup>6</sup>

There is a broader problem with ignoring overall dietary patterns. The US National Institutes of Health recommend the DASH diet (dietary approaches to stop hypertension) as a strategy for reducing hypertension. This diet is rich in fruit, vegetables, and whole grains and low fat dairy foods, and it includes meat, fish, poultry, nuts, and beans. It is limited in sugar sweetened foods and drinks, red meat, and added fats. The DASH diet includes potatoes and evidence from the DASH trials suggests that this overall dietary pattern is effective in preventing and controlling hypertension.<sup>7</sup>

Prevention and early management of hypertension is a major priority of governments and international organisations in their attempts to reverse the rising prevalence of chronic disease. Diet has an important part to play. However, dietary behaviour and patterns of consumption are complex and difficult to measure. We will continue to rely on prospective cohort studies, but those that examine associations between various dietary patterns and risk of disease provide more useful insights for both policy makers and practitioners than does a focus on individual foods or nutrients.<sup>9</sup>

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