## RESEARCH

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### THIS WEEK'S RESEARCH QUESTIONS

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- 19 Is a surgeon's length of experience associated with rates of permanent complications after thyroidectomy?

### Surgical experience and complication rates

At which point on a surgeon's learning curve are complications least likely to occur? Antoine Duclos and colleagues' regression analysis looked at the association between length of experience and the reporting of major complications after thyroidectomy in France during 2008 and 2009 (p 19). Complication rates were well below 3%, overall, for the 3500-odd operations done by 28 surgeons in five high volume centres. But complications did vary with years of experience and age, with surgeons aged 35-50 having the safest outcomes.

Allowing for the learning curve is just one of the many things that make surgical research tricky. The whole range of challenges is currently being examined by the IDEAL Collaboration, a group of surgeons, methodologists, and editors working on better methods for studying and reporting surgical and other operator dependent interventions and innovations (http://bit.ly/vzmHkc and http://bit.ly/weH85Z).

Endocrine surgeon Andrew J McIrvine suggests a more prosaic explanation for Duclos and colleagues' findings (http:// bit.ly/wcOQcO). In his rapid response



he ponders why "the complication that increases with age of surgeon is hypocalcaemia due to inadvertent removal of parathyroids. Strangely, the other measured complication—damage to the recurrent laryngeal nerve—was not increased." Mr McIrvine wondered "if this is because colour perception deteriorates with age of natural lens. The distinction between parathyroid tissue and other structures is often due to a subtle colour difference. Having had a new plastic lens inserted for a cataract my colour perception is better through the 'new' eye."

### Antihypertensive drugs and risk of gout

Hypertension is one of the most common comorbidities of gout and is independently associated with incident gout. Unfortunately, some antihypertensive drugs can themselves increase levels of serum uric acid and thus contribute to the risk of gout. Intriguingly, however, calcium channel blockers and losartan have been found to lower serum uric acid levels, and so possibly lower the risk of gout.

To investigate the potential relation between various antihypertensive drugs and risk of gout, Hyon Choi and colleagues (p 18) conducted a nested case-control study of almost 25 000 incident cases of gout and 50 000 matched controls using data from a UK general practice database. They found that use of calcium channel blockers and losartan was associated with a moderately lower risk of incident gout among patients with hypertension. These associations were independent of other risk factors for gout and were stronger with longer duration and higher dose of use. By contrast, diuretics,  $\beta$ blockers, angiotensin converting enzyme inhibitors, and non-losartan

angiotensin II receptor blockers were associated with a significantly increased risk of incident gout.

The authors conclude that their findings may be useful in choosing the most appropriate antihypertensive drug for patients with hypertension, and the linked editorial by Luis Ruilope (p 9) and rapid responses on bmj.



### RESEARCH ONLINE: For these and other new research articles see www.bmj.com/research

**Understanding recent trends in incidence of invasive breast cancer in Norway** Harald Weedon-Fekjær and colleagues' study indicates that changes in the incidence of invasive breast cancer since the early 1990s—increasing, levelling off, and then falling—may be fully attributed to mammography screening and hormone treatment, with each factor contributing a similar amount (doi:10.1136/bmj.e299).

**Efficacy and safety of enoxaparin versus unfractionated heparin during percutaneous coronary intervention** Enoxaparin seems to be better than unfractionated heparin at reducing mortality and bleeding during percutaneous coronary intervention, particularly in patients undergoing primary percutaneous coronary intervention for ST elevation myocardial infarction, according to a systematic review and meta-analysis by Johanne Silvain and colleagues (doi:10.1136/bmj.e553).

**Effect of n-3 long chain polyunsaturated fatty acid supplementation in pregnancy on infants' allergies in first year of life** An Australian trial by D J Palmer and colleagues showed that taking these supplements in pregnancy did not reduce the overall incidence of immunoglobulin E associated allergies in early life for infants at high hereditary risk, although atopic eczema and egg sensitisation were lower (doi:10.1136/bmj.e184).

## Effectiveness of agricultural interventions that aim to improve nutritional status of children: systematic review

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### CEDITORIAL by Dorward and Dangour

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**Cite this as:** *BMJ* **2012;344:d8222** doi: 10.1136/bmj.d8222

This is a summary of a paper that was published on bmj.com as *BMJ* 2012;344:d8222

**STUDY QUESTION** What is the effect of agricultural interventions that aim to improve the nutritional status of children in developing countries?

SUMMARY ANSWER Some evidence suggests that food based agricultural interventions change the diet of poor households in a positive way and increase the absorption of vitamin A; however, the overall amount and quality of the evidence available are insufficient to provide an answer at a reasonable level of confidence. WHAT IS KNOWN AND WHAT THIS PAPER ADDS Very little is known about the effectiveness of food based agricultural interventions in reducing under-nutrition. The available evidence shows no effects of these interventions on the nutritional status of children, but the studies reviewed are affected by several methodological weaknesses.

### Selection criteria for studies

We included only agricultural interventions with the explicit goal of improving the nutritional status of children: bio-fortification, home gardening, aquaculture, small scale fisheries, poultry development, animal husbandry, and dairy development. We included studies from the published (Econlit, IBSS, PubMed, Web of Science) and unpublished literature (Agris, Eldis, IDEAS, IFPRI, Jolis, World Bank) that were produced after 1990, were written in English, were conducted in a middle or low income country, reported effect on at least one of the selected outcome indicators, and used a credible counterfactual method. We selected 23 studies for the review.

### Primary outcome(s)

We investigated effects along all main steps of the causal chain running from the agricultural intervention to the final goal of reducing under-nutrition: participation in the programme by poor people, household income, composition of the diet, iron and vitamin A intake, and prevalence of stunting, wasting, and underweight.

### Main results and role of chance

The studies reported no information on participation rates or characteristics of programme participants. The interventions reviewed had a positive effect on production and consumption of the agricultural goods promoted, but we found no evidence of a change in total household income and little evidence of a change in the overall diet of poor people. We found no evidence of an effect on iron intake but some evidence of a positive effect on the absorption of vitamin A. Very little evidence existed of an effect on the prevalence of under-nutrition. Of eight studies reporting undernutrition rates, only one found a statistically significant effect on prevalence of stunting, whereas three studies found a positive effect on wasting.

### Bias, confounding, and other reasons for caution

Many of the studies reviewed had methodological weaknesses. Post hoc power calculations showed that most studies were unlikely to find an effect on undernutrition rates if present, because of the small sample sizes used. Under-nutrition is a complex phenomenon determined by multiple causes. Factors such as the health environment and cultural practices may have affected the impact of the agricultural interventions reviewed independently of their efficacy.

### Study funding/potential competing interests

This study was fully funded by the UK Department for International Development as part of a programme promoting systematic reviews of the effectiveness of development programmes in developing countries.

Effect of food based agricultural interventions					
Outcome indicator	Evidence of effect	Description			
Participation by poor people in programme	None	Information on participation rates and characteristics of participants not reported			
Household income	Poor	Five studies reported effect on household income, but without statistical tests of significance in four cases			
Composition of diet	Some	19/23 studies reported statistically significant effects on consumption of food promoted by intervention, but effect on overall composition of diet was rarely reported			
Intake of micronutrients	Some	Two studies assessed effect on iron intake and found none; four studies reported positive effect on serum retinol concentration			
Children's nutritional status	Very poor	Of eight studies reviewed, one found effect on stunting, three on underweight, and two on wasting			

## Effectiveness of multifaceted educational programme to reduce antibiotic dispensing in primary care: practice based randomised controlled trial

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Cite this as: BMJ 2012;344:d8173 doi: 10.1136/bmj.d8173

This is a summary of a paper that was published on bmj.com as *BMJ* 2012;344:d8173

**STUDY QUESTION** Can a multifaceted flexible educational programme help to reduce all cause antibiotic dispensing at the practice level in primary care?

**SUMMARY ANSWER** The STAR educational programme led to practice-wide reductions in dispensing of oral antibiotics for all causes over the subsequent year with no significant change in admissions to hospital, reconsultations, or antibiotic costs.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS Antibiotics continue to be overprescribed in primary care. A flexible blended learning and skill acquisition programme led to reductions in antibiotic dispensing throughout individual practices in the subsequent year.

### Design

In this randomised controlled trial, general practices were the unit of randomisation and analysis. Clinicians and researchers were blinded to group allocation until after randomisation. Intervention practices followed an educational programme (Stemming the Tide of Antibiotic Resistance (STAR), www.stemmingthetide.org), which included a practice based seminar reflecting on the practices' own dispensing and resistance data, online training, and practising consulting skills in routine care. Control practices did not.

### **Participants and setting**

A total of 68 general practices in Wales participated, with about 480 000 patients. Of these, 34 practices were randomised to receive the educational programme, with 34 as controls. Before randomisation, 139 clinicians from intervention practices and 124 from control practices had agreed to participate. We analysed practice level dispensing data for all clinicians in the 68 practices.

### **Primary outcome**

Our primary outcome was the total number of oral antibiotic items dispensed for all causes per 1000 patients in the practice in the year after intervention, adjusted for the previous year's dispensing.

### Main results and the role of chance

The rate of oral antibiotic dispensing (items per 1000 registered patients) decreased by 14.1 in the intervention group but increased by 12.1 in the control group, a net difference of 26.1. After adjustment for baseline dispensing rate, this amounted to a 4.2% (95% confidence interval 0.6% to 7.7%) reduction in total oral antibiotic dispensing for the year in the intervention group relative to the control group (P=0.02). Reductions were found for all classes of antibiotics other than penicillinase-resistant penicillins but were largest and significant for phenoxymethylpenicillins (penicillin V) (7.3%,

### Percentage reduction in dispensed oral antibiotic items in intervention practices undergoing educational programme aimed at reducing antibiotic prescribing in primary care, relative to control practices

% reduction in intervention group relative to control group (95% CI)	Pvalue
4.2 (0.6 to 7.7)	0.02
4.7 (-1.6 to 10.7)	0.14
7.3 (0.4 to 13.7)	0.04
2.3 (-8.0 to 11.6)	0.65
7.7 (1.1 to 13.8)	0.02
8.3 (-2.9 to 18.5)	0.14
-3.4 (-12.3 to 4.8)	0.43
3.3 (-2.4 to 8.9)	0.24
4.7 (-1.5 to 10.6)	0.22
	group relative to control group (95% Cl)           4.2 (0.6 to 7.7)           4.7 (-1.6 to 10.7)           7.3 (0.4 to 13.7)           2.3 (-8.0 to 11.6)           7.7 (1.1 to 13.8)           8.3 (-2.9 to 18.5)           -3.4 (-12.3 to 4.8)           3.3 (-2.4 to 8.9)

\*Annual number of dispensed units for oral antibiotics per 1000 registered patients.

0.4% to 13.7%) and macrolides (7.7%, 1.1% to 13.8%). The mean cost of the programme was £2923 (€3491, \$4572) per practice (SD £1187). There was a 5.5% reduction in the cost of dispensed antibiotics in the intervention group compared with the control group (-0.4% to 11.4%), equivalent to a reduction of about £830 a year for an average intervention practice. There were no significant harms.

### Bias, confounding, and other reasons for caution

We do not know which practitioners responded most to the intervention or for which patients and diagnoses the greatest reductions were achieved. Lack of diagnostic data associated with each dispensed antibiotic item means that we were unable to consider the effect on inappropriate antibiotic prescribing. We do not know if hospital admissions were increased among those who might otherwise have been prescribed antibiotics and were unable to compare effects on length of consultations.

### Generalisability to other populations

Our inclusion of practices in which not all clinicians participated enhances generalisability, as not all clinicians are likely to participate should the intervention be rolled out. Studies that analyse data only from participating clinicians and individually recruited patients are likely to overestimate potential practice effects.

### Study funding/potential competing interests

This study was funded by the UK Medical Research Council (G0500956). The South East Wales Trials Unit is funded by the National Institute for Health and Social care Research, which also provide service support costs.

Trial registration number ISRCT No 63355948.

### Antihypertensive drugs and risk of incident gout among patients with hypertension: population based case-control study

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#### CEDITORIAL by Ruilope

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**Cite this as:** *BMJ* **2012;344:d8190** doi: 10.1136/bmj.d8190

This is a summary of a paper that was published on bmj.com as *BMJ* 2012;344:d8190

**STUDY QUESTION** What are the independent associations of antihypertensive drugs with the risk of incident gout among people with hypertension? **SUMMARY ANSWER** Compatible with their urate lowering properties, calcium channel blockers and losartan are associated with a lower risk of incident gout among people with hypertension. By contrast, diuretics, β blockers, angiotensin converting enzyme inhibitors, and non-losartan angiotensin II receptor blockers are associated with an increased risk of gout.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Hypertension is a common comorbidity of gout, affecting up to 74% of patients with gout. This study provides large scale evidence for the independent differential effect of antihypertensive drugs for and against the risk of gout.

### **Participants and setting**

All incident cases of gout (n=24768) among adults aged 20-79 and a random sample of 50 000 matched controls from a UK general practice database, 2000-7.

### Design, size, and duration

Nested case-control study. The final cohort encompassed 1775 505 people followed for an average of 5.2 years.

#### Primary outcomes, risks, exposures

Relative risk of incident gout associated with use of antihypertensive drugs.

### Main results and the role of chance

The table shows the relative risks of incident gout associated with current use of antihypertensive drugs among those with hypertension (n=29 128) after adjusting for age, sex, body mass index, general practitioner visits, alcohol intake, pertinent drugs, and comorbidities. These results were similar in the group without hypertension. The multivariate relative risks for <1, 1-1.9, and  $\geq 2$  years' duration of use among those with hypertension were

## Multivariate relative risks of incident gout associated with current use (<31 days) of antihypertensive drugs among those with hypertension

Antihypertensives	Adjusted relative risk (95% CI)
Diuretics	2.36 (2.21 to 2.52)
βblockers	1.48 (1.40 to 1.57)
Calcium channel blockers	0.87 (0.82 to 0.93)
Angiotensin converting enzyme inhibitors	1.24 (1.17 to 1.32)
Losartan	0.81 (0.70 to 0.94)
Non-losartan angiotensin II receptor blockers	1.29 (1.16 to 1.43)

1.02, 0.88, and 0.75 for calcium channel blockers and 0.98, 0.87, and 0.71 for losartan (both P<0.05 for trend).

#### Bias, confounding, and other reasons for caution

Despite the large size of the study cohort, the number of participants in certain subgroups was relatively small, which limited our ability to obtain robust estimates.

### Generalisability to other populations

This study was carried out using a large UK general practice database; therefore, findings are likely to be applicable to the general population.

### Study funding/potential competing interests

This work was supported in part by grants from the National Institutes of Health (AR056291 and P60AR047785). The Spanish Centre for Pharmacoepidemiological Research has received an unrestricted research grant from Novartis to work on other projects related to gout. HKC has received research funding for other projects from Takeda Pharmaceuticals and has served on advisory boards for Takeda Pharmaceuticals, Savient Pharmaceuticals, and URL Pharma; the authors have no relationship with companies that might have an interest in the submitted work in the previous three years; they have no non-financial interests that may be relevant to the submitted work.

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# Influence of experience on performance of individual surgeons in thyroid surgery: prospective cross sectional multicentre study

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Cite this as: *BMJ* 2011;343:d8041 doi: 10.1136/bmj.d8041

This is a summary of a paper that was published on bmj.com as *BMJ* 2011;343:d8041

**STUDY QUESTION** Is a surgeon's length of experience associated with rates of permanent complications after thyroidectomy?

**SUMMARY ANSWER** Patients were at increased risk of permanent complications after thyroidectomy performed by less experienced surgeons and by those in practice for 20 years or more, suggesting that surgeons aged 35 to 50 years provided the safest care.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS Although complication rates can vary greatly during a surgeon's career, the potential for a decline in performance among very experienced surgeons remains unclear. This study suggests that the optimum performance of surgeons in thyroid surgery cannot be achieved or maintained by merely accumulating experience, and factors contributing to poor performance in very experienced surgeons should be explored further.

### Participants and setting

We considered all patients who underwent a thyroidectomy by every surgeon in five high volume referral centres in France (Lille, Lyon, Marseille, Paris, and Poitiers).

### Design

We conducted a prospective cross sectional multicentre study from April 2008 to December 2009. Characteristics of patients, surgeons, and centres were considered simultaneously in a final multilevel analysis. We used mixed effects logistic regression to determine the association between the length of surgeon's experience and the occurrence of postoperative complications. Surgeons' performance over the course of their careers was plotted as a function of age or the number of years spent in practice since graduation.

#### **Primary outcomes**

Presence of two permanent major complications (recurrent laryngeal nerve palsy or hypoparathyroidism), six months after thyroid surgery.

#### Main results and the role of chance

Of 3679 eligible procedures, 3574 (97%) were completed by 28 surgeons during a one year period. Overall rates of recurrent laryngeal nerve palsy and hypoparathyroidism were 2.08% (95% confidence interval 1.53% to 2.67%) and 2.69% (2.10% to 3.31%), respectively. Twenty years or more of practice was associated with increased probability of both recurrent laryngeal nerve palsy (odds ratio 3.06(1.07 to 8.80), P=0.04; table) and hypoparathyroidism (7.56 (1.79 to 31.99), P=0.01). Surgeons' performance had a concave association with length of experience (P=0.036) and age (P=0.035); surgeons aged 35 to 50 years had better outcomes than their younger and older colleagues.

#### Bias, confounding, and other reasons for caution

The large effect sizes recorded might raise important issues about patient safety and surgeons' experience, but those findings should be interpreted cautiously in the light of wide confidence intervals. Results validity also depends on how surgeons' experience was measured and whether the risk adjusted rates of complications showed surgical outcomes adequately. A recommended design would be to follow a particular cohort of surgeons over time to explore changes in performance during their careers.

### Generalisability to other populations

Our study sample had few middle aged surgeons with an intermediate length of experience, and might not have been representative of the average population of surgeons. Future studies should investigate larger populations of surgeons in various settings and other surgical specialties.

### Study funding/potential competing interests

This study was funded by the French Ministry of Health and the Hospices Civils de Lyon. The funding sources did not have any role in study design, execution, or publication. We have no competing interests.

	Adjusted odds ratio (95% CI)			
Independent variable	Recurrent nerve palsy	Hypoparathyroidism		
Length of surgeon experience (5-19 years)				
<2 years	2.41 (0.69 to 8.36)	5.93 (1.28 to 27.39)		
2-4 years	1.77 (0.55 to 5.69)	5.80 (1.34 to 25.10)		
≥20 years	3.06 (1.07 to 8.80)	7.56 (1.79 to 31.99)		
No of surgical procedures undertaken on the same	day (<3 procedures)			
3-4 procedures	0.90 (0.46 to 1.79)	0.84 (0.49 to 1.46)		
≥5 procedures	1.15 (0.42 to 3.20)	0.73 (0.26 to 2.05)		
Complex case (routine case)	1.56 (0.80 to 3.07)	1.51 (0.89 to 2.55)		
Female patient (male patient)	2.74 (1.08 to 6.97)	1.98 (0.96 to 4.06)		
Patient age (by 10 year increase)	1.02 (0.83 to 1.25)	0.84 (0.71 to 0.99)		
Patient body mass index (by 5 point increase)	1.21 (0.93 to 1.57)	1.06 (0.84 to 1.33)		
Weight of thyroid specimen (by 100 g increase)	1.23 (0.71 to 2.15)	1.34 (0.83 to 2.14)		