research

Early antibiotics for UTI in older people is recommended to prevent serious complications
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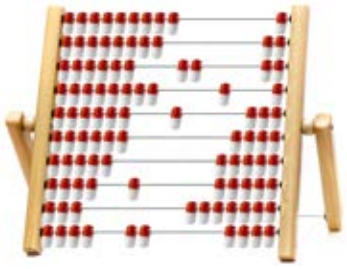

Antibiotics are prescribed for longer than recommended for many common conditions
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Optimal airway management for out of hospital cardiac arrest depends on ECG rhythm
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COMMENTARY

Antibiotics: when to prescribe, and for how long

Primary care is responsible for around 80% of all antibiotic prescribing in the NHS,[1] with rates likely to be similar worldwide. The two studies on the following pages add to the growing evidence base informing policy on antimicrobial stewardship, which has helped primary care clinicians reduce prescribing by 13% in the past five years[1] without increasing serious complications, including sepsis.[2]

These studies also highlight the daily challenge of ensuring that patients who are unlikely to benefit are not treated, whereas those who require antibiotics receive the right class, at the right time, at the right dose, and for the right duration. This task is made considerably more difficult by the absence of real-time microbiology in primary care.

Treating UTI

The first study, by Gharbi and colleagues, explores the effect on bloodstream infections of different antibiotic prescribing strategies for urinary tract infections (UTI) in older people.[3] This study is one of a growing number investigating the relation between prescribing in primary care and serious infections,[4] and it is timely because rates of bloodstream infection (and mortality) are increasing, particularly in this age group.[1] The government has committed to halving bloodstream infections by 2021,[5] and this study provides evidence that UTI treatment delays could be causing harm.[3]

They analysed 312 896 uncomplicated lower UTI episodes among patients aged 65 years and older. Antibiotics were prescribed to 87% of patients on the same day (immediate prescribing). The remainder either had no record of a prescription within seven days (7%) or had one issued within seven days (deferred prescribing, in 6%). Bloodstream infections and mortality rates were significantly higher in the groups with no or deferred prescriptions.

The relation might not be causal, however, and the implications are likely to be more nuanced than doctors risking the health of older adults to meet targets for antimicrobial stewardship. First, evidence shows doctors are cautious when managing infections in vulnerable groups.[6 7] Second, deferred prescribing in this study is probably different from delayed prescribing. Most clinicians issue a prescription on the day of presentation, with verbal advice to delay treatment, rather than waiting for a patient to return or issuing a post-dated prescription. The group given immediate antibiotics in the study probably contained some patients managed in this way.

Third, a deferred prescription may indicate diagnostic uncertainty. Perhaps a urine sample was sent (something the authors acknowledge they were unable to measure) and the laboratory result prompted treatment a few days later. Fourth, "no prescription" could be a marker for same day admission, possibly with a bloodstream infection.

It is also worth remembering that although bloodstream infections associated with the urinary tract are an important and increasing problem, the annual incidence of *Escherichia coli* related bloodstream

Primary care is responsible for around 80% of all antibiotic prescribing in the NHS

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Adhering to NICE guidelines would result in 65m fewer antibiotic days each year in the UK

infection (the most common) is 37/100 000,[9] and only half of affected patients present first to primary care. Thus, a practice of 10 000 patients will see one or two patients each year with this infection, compared to around 1800 UTI episodes.[10]

What are the implications for practice? Prompt treatment should be offered to older patients, men (who are at higher risk than women), and those living in areas of deprivation who are at the highest risk of bloodstream infections. More research is needed to establish if treatment should be initiated with a broad or a narrow spectrum antibiotic and to identify those in whom delaying treatment (for investigation) is safe.

Short course

The second study, by Pouwels and colleagues, builds on good evidence that "short" antibiotic courses are as effective as "long" courses for most infections treated in primary care.[11 12] The authors show convincingly that adhering to guidance on treatment length would result in 14 fewer days of antibiotic use for every 10 prescriptions issued, or to around 65 million fewer antibiotic days each year for the UK.[12] This is double the number of antibiotic days that would be saved if the UK were to hit its 2016 target of halving unnecessary antibiotic prescriptions by 2020.[13]

We prescribers can now familiarise ourselves with NICE guidance and optimise practice from here on.[14] Both clinicians and patients may need convincing to abandon longer courses, and campaigns by Public Health England to "Keep Antibiotics Working" could emphasise that shorter courses will kill bacteria and are less harmful than longer courses. Also, that some symptoms can persist beyond the end of the course, in some cases for up to four weeks.[15 16]

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Antibiotic prescribing in primary care

ORIGINAL RESEARCH Population based cohort study

Antibiotic management of urinary tract infection in elderly patients in primary care and its association with bloodstream infections and all cause mortality

Gharbi M, Drysdale JH, Lishman H, et al

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Study question Is the timing of antibiotic prescribing for adults aged 65 years or older with a lower urinary tract infection (UTI) associated with adverse outcomes?

Methods This retrospective population based cohort study used primary care consultation records linked to hospital episode statistics and death records in England. The study included patients aged 65 years or older presenting to their general practitioner with suspected or confirmed lower UTI from November 2007 to May 2015 and compared outcomes for those prescribed antibiotics on the day of consultation (immediate antibiotics group) with those where antibiotics were deferred by up to seven days, or not prescribed (no antibiotics

ORIGINAL RESEARCH
Cross sectional analysis and comparison with guidelines

Duration of antibiotic treatment for common infections in English primary care

Pouwels KB, Hopkins S, Llewelyn MJ, Walker AS, McNulty CAM, Robotham JV

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Find this at: http://dx.doi.org/10.1136/bmj.l440

Study question Are general practitioners prescribing antibiotic courses for longer than recommended in guidelines?

Methods The authors extracted data on antibiotic prescribing and consultations from The Health Improvement Network (THIN) primary care database, 2013-15. The duration of antibiotic prescriptions for 13 indications was evaluated: acute sinusitis, acute sore throat, acute cough and bronchitis, pneumonia, acute exacerbation of chronic obstructive pulmonary disease, acute otitis media, acute cystitis, acute prostatitis, pyelonephritis, cellulitis, impetigo, scarlet fever, and gastroenteritis. The main outcomes were the percentage of antibiotic prescriptions with a duration exceeding the guideline recommendation and the total number of days beyond the recommended duration for each indication.

Study answer and limitations The most common reasons for antibiotics being prescribed were acute bronchitis and cough (386 972, 41.6% of the included consultations), acute sore throat (239 231, 25.7%), acute otitis media (83 054, 8.9%), and acute sinusitis (76 683, 8.2%).

Actual versus recommended antibiotic treatment durations for respiratory tract indications*

Indication	No with indication	Antibiotic prescriptions with duration exceeding recommendation (5 days)		Excess days (% of total days)
		No	% (95% CI)	
Acute cough and bronchitis	386 972	331 257	85.6 (85.5 to 85.7)	805 051 (29.5)
Acute otitis media	83 054	71 750	86.4 (86.1 to 86.6)	193 262 (31.9)
Acute COPD exacerbation	12 067	10 742	89.0 (88.4 to 89.6)	26 732 (30.8)

COPD=chronic obstructive pulmonary disease.
*Only including respiratory conditions for which most recent guideline recommendations are the same as the guideline recommendations during the study period (2013-15).

group). The main outcomes were bloodstream infection, hospital admission, and all cause mortality within 60 days.

Study answer and limitations Overall, 312 896 UTI episodes (157 264 unique patients) were examined. After confounders had been adjusted for, the participants in the deferred antibiotics and no antibiotics groups were significantly more likely to experience a bloodstream infection compared with those in the immediate antibiotics group (adjusted odds ratio 7.12, 95% confidence interval 6.22 to 8.14 and 8.08, 7.12 to 9.16, respectively). The risk of all cause mortality was significantly higher with deferred antibiotics and no antibiotics than with immediate antibiotics during the 60 day follow-up (adjusted hazard ratio 1.16, 95% confidence interval 1.06 to 1.27 and 2.18, 2.04 to 2.33, respectively). The main limitations of the study are common to observational studies using routine electronic health record data, and include unmeasured and residual confounders, missing data, misclassification biases, and inconsistencies in coding within and between practices and over time.

Summary of participants' characteristics and outcomes related to episodes of urinary tract infection (UTI). Values are numbers (percentages) unless stated otherwise

Variables	Total UTI cases (n=312 896)	Immediate antibiotics (n=271 070)	Deferred antibiotics (n=19 292)	No antibiotics (n=22 534)	P value
Mean (SD) age (years)	76.7 (9.2)	76.3 (9.1)	79.1 (9.2)	79.3 (9.5)	
Age group (years):					
65-74	136 175 (43.5)	122 458 (45.2)	6402 (33.2)	7315 (32.5)	
75-84	107 485 (34.35)	92 856 (34.3)	6881 (35.7)	7748 (34.4)	
≥85	69 236 (22.1)	55 756 (20.6)	6009 (31.15)	7471 (33.15)	
Women	246 630 (79.8)	217 843 (80.4)	13 657 (70.8)	15 130 (67.1)	
Bloodstream infection <60 days:					
No (%)	1539 (0.5)	479 (0.2)	413 (2.15)	647 (2.9)	<0.001
Adjusted odds ratio (95% CI)*		Reference	7.12 (6.22 to 8.14)	8.08 (7.12 to 9.16)	<0.001
Death <60 days:					
	6193 (2.0)	4431 (1.6)	545 (2.8)	1217 (5.4)	<0.001
Adjusted hazard ratio (95% CI)†	-	Reference	1.16 (1.06 to 1.27)	2.18 (2.04 to 2.33)	<0.001

*Multivariable logistic regression.
†Multivariable Cox regression.

What this study adds This study suggests a significantly higher risk of bloodstream infection and all cause mortality associated with deferred antibiotics or no antibiotics given to older adults (≥65 years) with symptoms of UTI. The authors advocate early initiation of antibiotics for UTI in older adults.

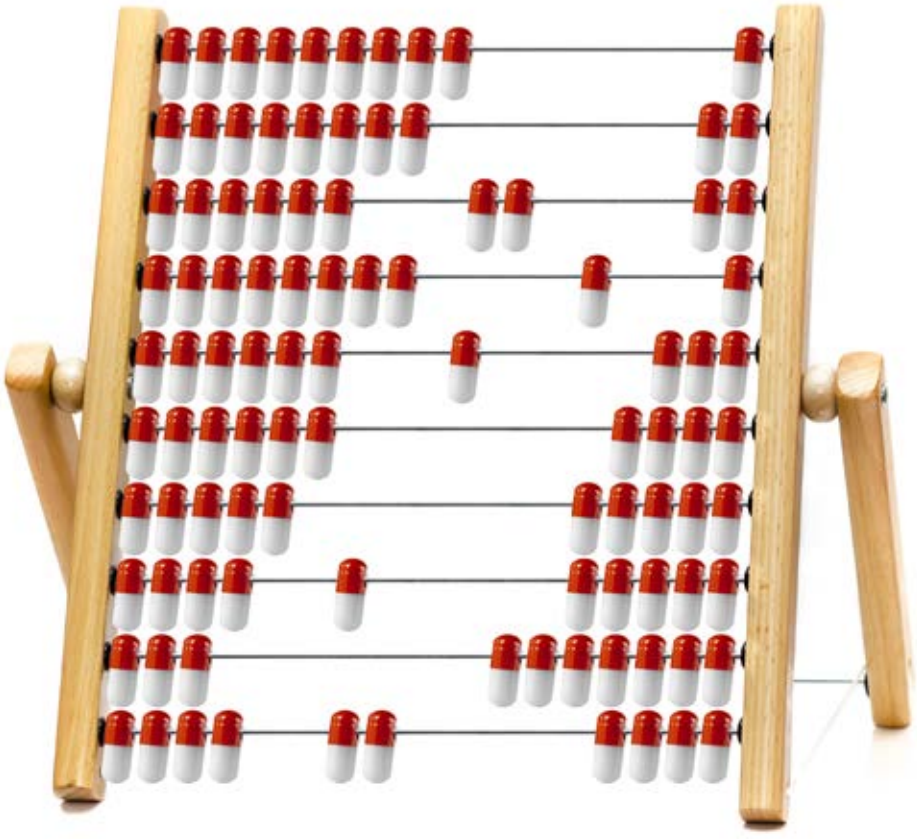
Funding, competing interests, and data sharing See the full paper on bmj.com for details of funding and competing interests. Data are obtainable from Clinical Practice Research Datalink under standard conditions.

Antibiotic treatments for upper respiratory tract indications and acute cough and bronchitis accounted for more than two thirds of the total prescriptions considered, and for most of these indications 80% or more of the treatment courses exceeded guideline recommendations. Although the study accounted for the presence of comorbidities and excluded complicated, recurrent infections that might require longer treatment, it was unable to account fully for patient factors that might underlie decisions to prolong treatment.

What this study adds For many common infections treated in primary care, a substantial proportion of antibiotic prescriptions have durations that exceed those recommended in guidelines.

Funding, competing interests, and data sharing
Authors of this study were supported by the National Institute for Health Research (NIHR) Health Protection Research Unit in Healthcare Associated Infections and Antimicrobial Resistance at the University of Oxford in partnership with Public Health England (HPRU-2012-10041) and the NIHR Oxford Biomedical Research Centre.

No competing interests. THIN data were analysed under licence and are not available for sharing.



Pre-hospital advanced airway management for adults with out-of-hospital cardiac arrest

Izawa J, Komukai S, Gibo K, et al

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Find this at: http://dx.doi.org/10.1136/bmj.l430

Study question Is advanced airway management (AAM) for out-of-hospital cardiac arrest in adults associated with survival compared with no AAM?

Methods This cohort study was conducted between January 2014 and December 2016 using a nationwide, population based registry in Japan (All-Japan Utstein Registry) and including consecutive cases of out-of-hospital cardiac arrest in adults. The patients were separated into two subcohorts by their first documented electrocardiographic rhythm: shockable (ventricular fibrillation or pulseless ventricular tachycardia) or non-shockable (pulseless electrical activity or asystole). Patients who received AAM (supraglottic airway placement and endotracheal intubation) during cardiopulmonary resuscitation were sequentially matched with patients at risk of AAM within the same minute on the basis of time dependent propensity scores. The primary outcome was survival at one month or at hospital discharge within one month.

Study answer and limitations Among 310 620 adults with out-of-hospital cardiac arrest, results differed according to each patient's first documented electrocardiographic rhythm. Advanced airway management was not associated with survival in the shockable cohort (1546/8057 (19.2%) in the AAM group *v* 1500/8057 (18.6%) in the no AAM group; adjusted risk ratio 1.00, 95% confidence interval 0.93 to 1.07), but it was associated with better survival in the non-shockable cohort (2696/118 021 (2.3%) *v* 2127/118 021 (1.8%); adjusted risk ratio 1.27, 1.20 to 1.35). However, the absolute favourable effect in the non-shockable cohort was very small.

What this study adds These findings suggest that different airway management strategies should be emphasised on the basis of the initial electrocardiographic rhythm: shockable or non-shockable.

Funding, competing interests, and data sharing
This study was supported by the Clinical Investigator's Research Project at Osaka University Graduate School of Medicine and the Ministry of Education, Culture, Sports, Science and Technology of Japan.

Outcomes in time dependent propensity score sequentially matched cohort

Outcomes*	No (%) of patients with outcome/total patients		Unadjusted risk ratio (95% CI)	Adjusted risk ratio† (95% CI)
	No AAM	AAM		
Shockable rhythm:				
Survival	1500/8057 (18.6)	1546/8057 (19.2)	1.09 (1.02 to 1.17)	1.00 (0.93 to 1.07)
Favourable functional survival	865/8057 (10.7)	776/8057 (9.6)	0.97 (0.88 to 1.07)	0.87 (0.79 to 0.96)
Non-shockable rhythm:				
Survival	2127/118 021 (1.8)	2696/118 021 (2.3)	1.26 (1.19 to 1.34)	1.27 (1.20 to 1.35)
Favourable functional survival	489/118 021 (0.4)	499/118 021 (0.4)	1.10 (0.96 to 1.26)	1.11 (0.97 to 1.26)

AAM=advanced airway management.

*At one month or at hospital discharge within one month.

†Each risk ratio was adjusted for prefecture preference categories for performing supraglottic airway placement and endotracheal intubation, year, season, day, time, age, sex, cause of cardiac arrest, witness category, basic life support by bystander with or without dispatcher instruction, use of public access defibrillator, pre-hospital involvement of clinician, time from call to cardiopulmonary resuscitation by emergency medical services staff, defibrillation before matching, and administration of adrenaline before matching.