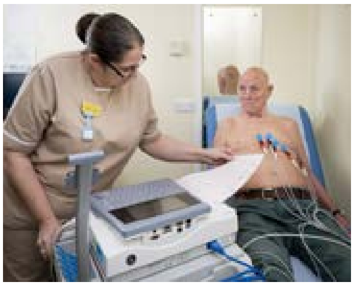
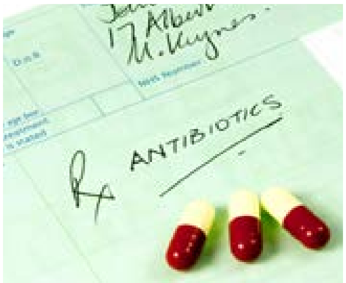
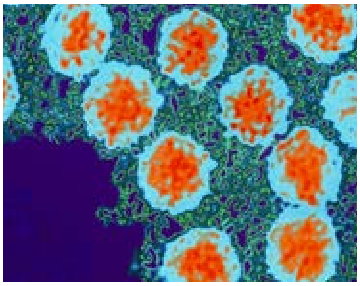
research



Outlook after new diagnosis of heart failure remains poor p 269



Electronic intervention could reduce antibiotic prescribing for RTIs p 270



Enterovirus in childhood might predict development of coeliac disease p 272

ORIGINAL RESEARCH Population based cohort study

Trends in survival after a diagnosis of heart failure in the UK 2000-17

Taylor CJ, Ordóñez-Mena JM, Roalfe AK, et al

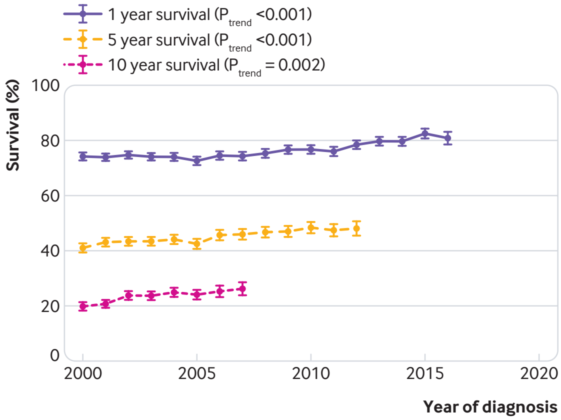
Cite this as: *BMJ* 2019;364:l223
Find this at: http://dx.doi.org/10.1136/bmj.l223

Study question Has the short term and long term survival of people with heart failure improved over time by year of diagnosis, hospital admission at the time of diagnosis, and socioeconomic group?

Methods This population based cohort study used UK primary care data (Clinical Practice Research Datalink) from 1 January 2000 to 31 December 2017 that were linked to inpatient Hospital Episode Statistics and Office for National Statistics mortality data. The cohort consisted of 55 959 patients aged 45 and older with a new diagnosis of heart failure and 278 679 age and sex matched controls. The main outcome measures were survival rates at 1, 5, and 10 years and cause of death for people with and without heart failure; and temporal trends in survival by year of diagnosis, hospital admission, and socioeconomic group.

Study answer and limitations Overall, 1, 5, and 10 year survival rates increased by 6.6% (from 74.2% in 2000 to 80.8% in 2016), 7.2% (from 41.0% in 2000 to 48.2% in 2012), and 6.4% (from 19.8% in 2000 to 26.2% in 2007), respectively. There were 30 906 deaths in the heart failure group over the study period. Heart failure was listed on the death certificate in 13 093 (42.4%) of these patients, and in 2237 (7.2%) it was the primary cause of death. Improvement in survival was greater for patients not requiring admission to hospital around the time of diagnosis (median difference 2.4 years; 5.3 *v* 2.9 years, P<0.001). There was a deprivation gap in median survival of 2.4 years between people who were least deprived and those who were most deprived (11.1 *v* 8.7 years, P<0.001). The main limitations of this study were that the type of heart failure (reduced or preserved ejection fraction) was not identified, and that some of the routinely collected data may be incomplete or subject to misclassification bias.

What this study adds Survival after a diagnosis of heart failure has shown only modest improvement in the 21st century and lags behind other serious conditions, such as cancer. New strategies to achieve timely diagnosis and treatment initiation in primary care for all socioeconomic groups should be a priority for future research and policy.



Survival rates at 1, 5, and 10 years for people with heart failure by year of diagnosis

Funding, competing interests, and data sharing
Full details of funding, competing interests, and data sharing are available on bmj.com.

Improving outpatient antibiotic prescribing

ORIGINAL RESEARCH REDUCE cluster randomised trial

Effectiveness and safety of electronically delivered prescribing feedback and decision support on antibiotic use for respiratory illness in primary care

Gulliford MC, Prevost AT, Charlton J, et al

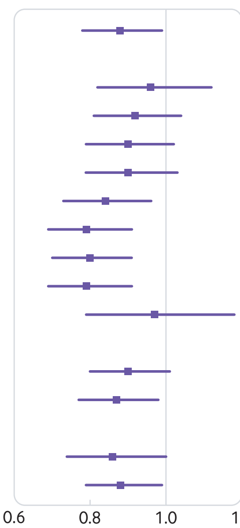
Cite this as: *BMJ* 2019;364:l236

Find this at: http://dx.doi.org/10.1136/bmj.l236

Study question Can electronic delivery of prescribing feedback and decision support interventions reduce antibiotic prescribing for self limiting respiratory tract infections (RTI) in primary care?

Methods In a trial of UK general practices contributing to the Clinical Practice Research Datalink, 79 practices were randomised (1:1) to antimicrobial stewardship (AMS) intervention or usual care. The AMS intervention included a brief training webinar, automated monthly feedback reports of antibiotic prescribing, and electronic decision support tools to inform appropriate prescribing over 12 months. Intervention components were delivered electronically, supported by a local practice champion nominated for the trial. The primary outcome was the rate of antibiotic prescriptions for RTI from electronic health records. Serious bacterial complications were evaluated as safety outcomes. Analysis was by Poisson regression with general practice as a random effect, adjusting for covariates. Prespecified subgroup analyses by age group were reported.

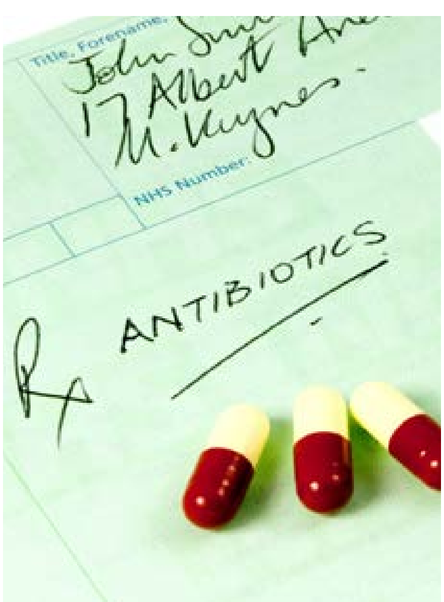
Study answer and limitations The trial included 41 AMS practices (323 155 patient years) and 38 usual care practices (259 520 patient years). During 12 months' follow-up, antibiotic prescribing reduced by 12% (95% confidence interval 1% to 22%). The prescribing rate was 98.7 per 1000 patient years for the AMS arm (31 907 prescriptions in 323 155 patient years) and 107.6 per 1000 patient years for usual care (27 923 prescriptions in 259 520 patient



Covariate	Antibiotic prescribing rate per 1000 patient years for RTI: AMS	Usual care	Rate ratio (95% CI)
Total	98.7	107.6	0.88 (0.78 to 0.99)
Age group (years)			
<15	139.3	139.8	0.96 (0.82 to 1.12)
15-24	83.6	94.3	0.92 (0.81 to 1.04)
25-34	78.2	86.4	0.90 (0.79 to 1.02)
35-44	78.6	83.4	0.90 (0.79 to 1.03)
45-54	79.9	86.0	0.84 (0.73 to 0.96)
55-64	99.6	112.8	0.79 (0.69 to 0.91)
65-74	113.8	132.8	0.80 (0.70 to 0.91)
75-84	121.7	146.1	0.79 (0.69 to 0.91)
≥85	114.7	115.5	0.97 (0.79 to 1.18)
Sex			
Male	80.0	87.7	0.90 (0.80 to 1.01)
Female	117.3	127.3	0.87 (0.77 to 0.98)
Comorbidity			
Absent	60.9	72.5	0.86 (0.74 to 1.00)
Present	287.0	314.7	0.88 (0.79 to 0.99)

Effect of antimicrobial stewardship (AMS) or usual care on primary outcome of antibiotic prescribing rate for self limiting respiratory tract infection (RTI). Estimates adjusted for random effect of general practice and covariates including sex, age group, comorbidity, region, quarter in study, practice specific rate at baseline, and interaction with period of randomisation

COMMENTARY The design and delivery of feedback is critical



Outpatient prescriptions account for an estimated 85-95% of the volume of antibiotics used in people, and antibiotics are frequently overused and misused in outpatient settings.[1-3] Optimising antibiotic use in outpatient settings is increasingly recognised as an opportunity to improve patient safety.[4]

In this issue, Gulliford and colleagues share findings from the REDUCE trial, a large cluster randomised trial in 79 general practices in the UK examining the effect of a low cost, electronic health record based, antibiotic stewardship intervention leveraging antibiotic use data.[6] The intervention included a short webinar,

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Optimising antibiotic use in outpatient settings is an opportunity to improve patient safety

practice level monthly feedback reports on antibiotic prescribing for respiratory tract infections (RTIs), RTI decision support tools embedded in the electronic health record, and stewardship champions at each practice. After 12 months, this multifaceted intervention resulted in a 12% reduction in the antibiotic prescription rate for RTIs in intervention compared with control practices. However, the intervention did not result in any differences in the consultation rate for RTIs, the proportion of RTI visits with antibiotics prescribed, or the total antibiotic prescribing rate for all conditions.

The authors concluded that this intervention was moderately effective in years). Prescribing was reduced in patients aged 15-84 years (adjusted rate ratio 0.84, 95% confidence interval 0.75 to 0.95), with one antibiotic prescription per year avoided for every 62 patients (95% confidence interval 40 to 200). No evidence of reduced prescribing was seen for children younger than 15 years (adjusted rate ratio 0.96, 95% confidence interval 0.82 to 1.12) or adults aged 85 years and older (0.97, 0.79 to 1.18). There was no evidence of an increase in any of 12 different serious bacterial complications (0.92, 0.74 to 1.13). The imprecise effect estimate suggests that a smaller effect might be possible, but even a smaller effect could be of public health importance. Although this study was larger than previous studies, it did not have sufficient statistical power to provide conclusive evidence of safety with respect to rare outcomes.

What this study adds Multifaceted interventions, drawing on electronic health records data, could be scaled up at low cost to promote effective AMS in primary care. The needs of very young or old patients require special consideration.

Funding, competing interests, and data sharing Funded by the National Institute for Health Research Health Technology Assessment Programme (13/88/10). The authors have no competing interests. Full details on data sharing are on bmj.com.

Trial registration ISRCTN95232781.

Antimicrobial stewardship

Effectiveness of electronically delivered prescribing feedback and decision support on antibiotic use in primary care

Summary
The intervention resulted in moderate reductions of antibiotic prescribing overall and in patients aged 15 to 18, with no evidence that serious bacterial complications increased

Population
All patients registered at one of 79 participating general practices

Population numbers shown are "person years of follow-up"

582 675 | 50.2% female | Age <15: 16.5% | Comorbidity: 16.0%

Comparison

323 155
Training webinar
Monthly prescribing reports
Decision support tools

Antimicrobial stewardship intervention

259 520 Control

Usual care

Outcomes

	Intervention	Adjusted prescribing rate ratio	95% CI	Control
Prescribing rate (0-14 year olds)	139.3	0.96	0.82 to 1.12	139.8
Prescribing rate (15-84 year olds)	89.9	0.84	0.75 to 0.95	100.2
Prescribing rate (≥85 year olds)	114.7	0.97	0.79 to 1.18	115.5

Primary outcome
Rate of antibiotic prescriptions for respiratory tract infections

Scale
Antibiotic prescribing rate per 1000 person years

Clinical significance
One antibiotic prescription avoided for every 62 patients aged 15-85

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reducing antibiotic prescribing for RTIs in adults, but did not affect overall antibiotic prescribing. Although RTIs are the most common diagnoses leading to outpatient antibiotic prescriptions, most outpatient antibiotic prescriptions are for other diagnoses. In order to drive antibiotic prescribing improvements and prevent diagnostic shifting (that is, clinicians changing a code to justify prescribing), antibiotic stewardship interventions should ideally incorporate prescribing audit and feedback for both high priority conditions and overall.[4]

Lessons learnt from behavioural science might shed some light on the modest effect of the REDUCE trial. Firstly, owing to data limitations, Gulliford and colleagues were only able to track and provide feedback on antibiotic prescribing data at the practice level. While audit and feedback at the practice level have been effective, especially when included in a package of interventions,[7] variation in antibiotic prescribing is driven primarily by differences in prescribing patterns between individual clinicians.[8] Therefore, when possible, providing clinician level feedback is preferable.

Secondly, the design and delivery of feedback is critical, and the incorporation of behaviour change strategies into audit and feedback interventions appears to improve efficacy.[9,10] Comparing clinicians' antibiotic prescribing practices with those of their peers has been shown to be quite effective and is based on the idea that providing information about social norms (how others normally behave) drives individuals to bring their behaviour in line with the norm.[9] Additionally, comparing clinicians to top performing peers drives performance towards the goal rather than towards the mean.[10] Intervention practices in the REDUCE trial were given comparisons of their current prescribing against their own baseline data. Providing social norm feedback with comparisons to top performing practices could have provided benefit.

Antibiotic stewardship leaders, clinicians, and researchers can apply lessons learnt from the REDUCE trial to leverage data for action and improve antibiotic use. Prescribing is as much a behaviour as a rational clinical decision.[11,12] Thus, the way in which antibiotic prescribing is measured and fed back to clinicians must be carefully considered.

Cite this as: *BMJ* 2019;364:l289

Find the full version with references at http://dx.doi.org/10.1136/bmj.l289

Enterovirus as trigger of coeliac disease

Kahrs CR, Chuda K, Tapia G, et al

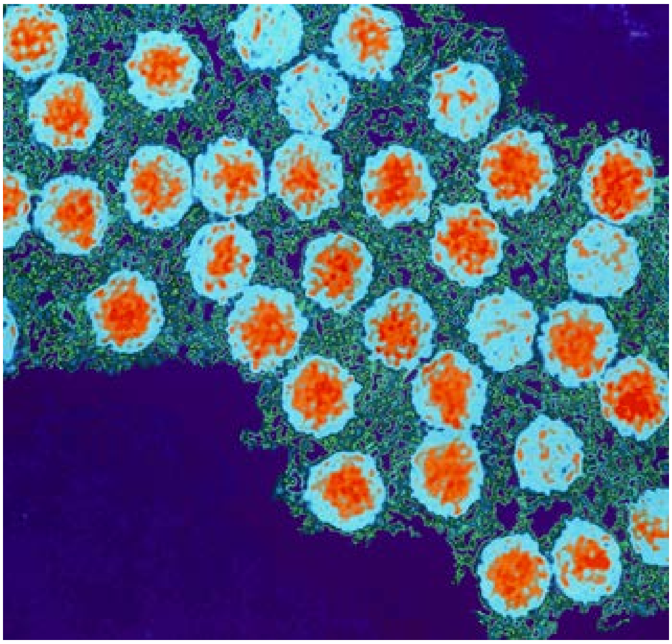
Cite this as: *BMJ* 2019;364:l231

Find this at: http://dx.doi.org/10.1136/bmj.l231

Study question Does infection with human enterovirus or adenovirus, both common intestinal viruses, predict development of coeliac disease?

Methods This was a population based case-control study nested within a Norwegian birth cohort of children carrying the HLA genotype DR4-DQ8/DR3-DQ2 conferring an increased risk of coeliac disease. Children were recruited between 2001 and 2007 and followed to September 2016. Enterovirus and adenovirus were detected using real time polymerase chain reaction in monthly stool samples from age 3 to 36 months. Coeliac disease was diagnosed according to standard criteria. Coeliac disease antibodies were tested in blood samples taken at age 3, 6, 9, and 12 months and then annually. Among 220 children, and after a mean of 9.9 (SD 1.6) years, 25 children were diagnosed as having coeliac disease after screening and were matched to two controls each.

Study answer and limitations The frequency of enteroviruses in stool samples was significantly higher before the development of coeliac disease antibodies in children later diagnosed as having coeliac disease compared with healthy controls (adjusted odds ratio 1.49, 95% confidence interval 1.07 to 2.06). Adenovirus was not associated with coeliac disease. Given the limited number of cases, a need exists for corroboration in similar studies, and preferably interventional studies, to reach conclusions about causality.

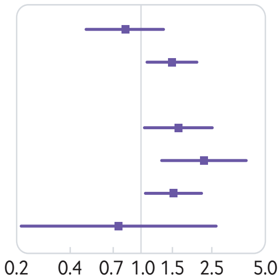


What this study adds This study suggests that enterovirus, but not adenovirus, during early childhood is associated with later coeliac disease. The finding adds new information on the role of viral infections in the cause of coeliac disease.

Funding, competing interests, and data sharing The funders listed in the full online paper had no influence on the contents of the paper.

Data supporting the presented results are available from the authors on reasonable request. No competing interests declared.

Stool sample positive for:	Positive/total samples: Cases	Positive/total samples: Control	Adjusted odds ratio (95% CI)	P value
Main analysis				
Adenovirus	47/390	111/775	0.82 (0.49 to 1.38)	0.46
Enterovirus	84/429	129/855	1.49 (1.07 to 2.06)	0.02
Enterovirus subgroup analysis				
Enterovirus A	42/387	60/787	1.62 (1.04 to 2.53)	0.03
Enterovirus B	34/379	43/770	2.27 (1.33 to 3.88)	0.003
Enterovirus after gluten introduction	66/298	99/587	1.52 (1.05 to 2.20)	0.03
Enterovirus before gluten introduction	7/64	9/113	0.75 (0.21 to 2.63)	0.65



Infections and later coeliac disease: adjusted odds ratios for positive longitudinal stool sample before development of coeliac disease antibodies in children later diagnosed as having coeliac disease (n=25) compared with healthy controls (n=49)

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