

THIS WEEK'S RESEARCH QUESTIONS

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Reducing bleeding during prostate surgery

Tranexamic acid has become an established treatment in cardiac surgery to reduce the rate of bleeding, and thus the need for perioperative blood transfusion. Unsurprisingly, its potential use has also been investigated in orthopaedic and liver surgery—



TEK IMAGE/SPL

and now in radical prostatectomy (p 885). Antonella Crescenti and colleagues conducted a randomised placebo controlled trial to assess the efficacy of low dose tranexamic acid in reducing the rate of blood transfusion in 200 patients undergoing open radical retropubic prostatectomy (still the standard surgical treatment for localised prostate cancer) and the long term safety of this treatment.

The results are promising if not startling: 34% of patients needing transfusion with active treatment compared with 55% of controls, and no significant difference in (rare) adverse events at six months' follow-up. Being relatively inexpensive and simple to administer are other definite pluses for tranexamic acid.

Research in the *BMJ*

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HIV: outlook in UK shows the drugs work

There are common questions from patients with HIV, or those considering an HIV test, that doctors are expected to answer: How long have I got? What difference do antiviral drugs make? What's the point of being tested for a terminal disease?

The reality and image of life with HIV and AIDS has changed with the development of antiretrovirals, and continues to evolve. We now have more drugs, better drugs, and drugs with fewer side effects than in the past—we also have a better understanding of HIV, and specialist services to care for patients living with the infection. But what has been the overall effect of these improvements?

In search of some modern, crunchy numbers to estimate the life expectancy for people undergoing HIV treatment, compared with that of the general population in the UK, Margaret May and colleagues examined outcomes for



FRANCIS SHEEHAN/SPL

patients in the UK Collaborative HIV Cohort (p 886). The take home message is that the drugs work, say Elena Losina and colleagues in their accompanying editorial (p 856). And starting treatment early is associated with better outcomes. All good reasons to encourage testing; particularly in males, who, unlike women of child bearing age, are not routinely offered screening.

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

Risk of venous thromboembolism from use of oral contraceptives containing different progestogens and oestrogen doses
In this cohort study by Øyvind Lidegaard and colleagues, oral contraceptives with desogestrel, gestodene, or drospirenone were associated with twice the risk of venous thromboembolism compared with those containing levonorgestrel, after adjustment for length of use (doi:10.1136/bmj.d6423).

Factors associated with variability in the assessment of UK doctors' professionalism

J A Simpson and colleagues investigated potential biases arising in the assessment of doctors' professionalism using multisource feedback, a method that is likely to be used in revalidation processes in the UK (doi:10.1136/bmj.d6212).

Honorary and ghost authorship in high impact biomedical journals

A study by Joseph Wislar and colleagues showed that 21% of articles published in six high impact, general medical journals in 2008 had honorary authorship, ghost authorship, or both, a decline from 29% in 1996 (doi:10.1136/bmj.d6128).



Intraoperative administration of tranexamic acid to reduce transfusion rate in patients undergoing radical retropubic prostatectomy: double blind, randomised, placebo controlled trial

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STUDY QUESTION Can tranexamic acid reduce the rate of perioperative blood transfusions in patients undergoing radical retropubic prostatectomy?

SUMMARY ANSWER Intraoperative treatment with low dose tranexamic acid is effective in reducing the rate of perioperative blood transfusions in patients undergoing radical retropubic prostatectomy.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS Tranexamic acid reduces mortality in trauma patients with severe haemorrhage and reduces the rate of perioperative blood transfusions in cardiac surgery and other surgical settings, but its efficacy in urological surgery is unknown. Our results indicate that tranexamic acid can reduce transfusion rate in urological surgery.

Design

In this double blind, parallel group, randomised, placebo controlled trial with block randomisation and a 1:1 allocation generated by computer, patients received an intravenous infusion of tranexamic acid or placebo (saline) according to the following protocol: a loading dose of 500 mg of tranexamic acid 20 minutes before surgery, followed by a continuous infusion of tranexamic acid at 250 mg/h during surgery (or equivalent volumes of saline). Analysis was by intention to treat.

Participants and setting

We included 200 patients older than 18 years, undergoing radical retropubic prostatectomy, and who provided written informed consent at Vita-Salute San Raffaele University, Milan, Italy. Exclusion criteria were atrial fibrillation, coronary artery disease treated with drug eluting stent, severe chronic renal failure, congenital or acquired thrombophilia, and known or suspected allergy to tranexamic acid.

Primary outcome(s)

Number of patients receiving blood transfusions perioperatively (from surgery to hospital discharge).

Main results and the role of chance

All patients completed treatment. 34/100 patients in the tranexamic acid group and 55/100 in the control group received transfusions (absolute reduction of transfusion rate 21% (95% confidence intervals 7% to 34%), relative reduction 38% (14% to 55%); relative risk of receiving transfusions for patients treated with tranexamic acid 0.62 (0.45 to 0.85); number needed to treat 5 (3 to 14); $P=0.004$) (table).

Harms

Six month follow-up was completed in all 200 patients. No patients died and we did not see any difference in the frequency of thromboembolic events between the tranexamic acid group (two events) and the placebo group (five events) (relative risk for patients treated with tranexamic acid 0.4 (95% CI 0.09 to 1.74); $P=0.4$).

Bias, confounding and other reasons for caution

Safety data at six month follow-up did not have enough power to make a definitive conclusion about safety. However, our data accord with those from other studies and reviews. The concealment method of our allocation sequence might also be considered suboptimal compared with other expensive and remote methods of randomisation.

Generalisability to other populations

Intraoperative treatment with low doses of tranexamic acid is a particularly attractive intervention, because it is very simple and because tranexamic acid is a relatively inexpensive drug not covered by patent. Moreover, the trial inclusion criteria were very broad and consequently almost all patients undergoing radical prostatectomy could be treated with tranexamic acid. Intraoperative treatment with low dose tranexamic acid could also be considered in other settings of urological surgery where major perioperative bleeding could happen, such as cystectomy, nephrectomy, and renal cancer tumorectomy.

Study funding/potential competing interests

All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: the study was funded by the Department of Anaesthesia and Intensive Care of San Raffaele Hospital; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Trial registration number

ClinicalTrials.gov Identifier NCT00670345.

BLOOD PRODUCT TRANSFUSIONS DURING ENTIRE HOSPITAL STAY

	Placebo group (No (%))	Tranexamic acid group (No (%))	P	Relative risk of event (95% CI)
Any blood product	55 (55)	34 (34)	0.004	0.62 (0.45 to 0.85)
Packed red blood cells	37 (37)	22 (22)	0.02	0.59 (0.38 to 0.93)
Autologous whole blood	25 (25)	13 (13)	0.04	0.52 (0.28 to 0.96)
Fresh frozen plasma	3 (3)	2 (2)	0.9	0.66 (0.11 to 3.9)

Impact of late diagnosis and treatment on life expectancy in people with HIV-1: UK Collaborative HIV Cohort (UK CHIC) Study

UK Collaborative HIV Cohort (UK CHIC) Study

EDITORIAL by Losina and Freeberg

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STUDY QUESTION

What is the life expectancy of people with HIV undergoing treatment compared with people in the general population in the United Kingdom?

SUMMARY ANSWER

Life expectancy in people with HIV undergoing treatment has increased by over 15 years during 1996-2008 but is still about 13 years lower than that of the UK population. At the age of 20 men who started antiretroviral therapy during the study period could expect to live an average of 40 additional years to age 60, with women living 10 years longer to age 70.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Life expectancy is strongly related to the CD4 count at which people with HIV start treatment. Patients who were diagnosed late or deferred treatment until their CD4 count fell to below 200 cells/mm³ were estimated to have a life expectancy at least 10 years lower than those who conformed to current treatment guidelines.

Participants and setting

The study included adults treated for HIV infection in hospital outpatient clinics throughout the UK.

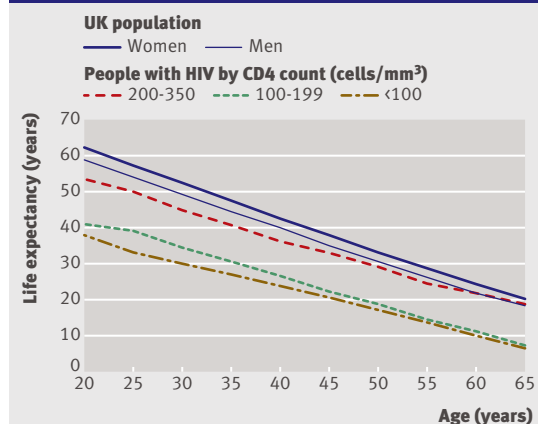
Design, size, and duration

We used data on 17 661 patients who started antiretroviral therapy with CD4 count ≤ 350 cells/mm³ during 1996 to 2008. Abridged life tables were constructed from age specific mortality rates (per 1000 person years) grouped in five year age bands. We estimated life expectancy from exact ages 20 to 65—the average additional years that will be lived by a person after that age—according to the cross sectional age specific mortality rates during the study period.

Main results and the role of chance

During the 91 203 person years of follow-up, 1248 (7%) patients died. Life expectancy at exact age 20 increased from 30.0 (SE 1.2) in 1996-9 to 45.8 (SE 1.7) years in 2006-8. Among people with HIV, life expectancy was 39.5 (0.45) years for men and 50.2 (0.45) years for women compared with 57.8 and 61.6 years for men and women in the general population (1996-2006). Starting antiretroviral therapy later than guidelines suggest resulted in up to 15 years' loss of life: at age 20, life expectancy was 37.9 (1.3), 41.0 (2.2), and 53.4 (1.2) years in those starting antiretro-

LIFE EXPECTANCY IN PEOPLE WITH HIV ACCORDING TO CD4 CELL COUNT AT START OF ANTIRETROVIRAL THERAPY (2000-8) COMPARED WITH UK POPULATION (2000-6)



viral therapy with CD4 count <100, 100-199, and 200-350 cells/mm³, respectively.

Bias, confounding, and other reasons for caution

Estimates of life expectancy were based on extrapolations of the age and sex specific mortality rates observed during the study period, which were then applied to a hypothetical cohort as if they applied to individuals throughout their lives. The validity of this assumption could be greatest for patients with persistently suppressed viral loads. Underascertainment of deaths could have biased estimates of life expectancy upwards, though the UK CHIC Study was linked with the national death registry and surveillance studies from the Health Protection Agency. We excluded people with a history of use of injected drugs as they have higher mortality, particularly if they are also infected with hepatitis B or C, but some misclassification could have occurred. We could not control for smoking or socioeconomic position, which could be associated with both late treatment and poorer life expectancy.

Generalisability to other populations

Our findings might be generalisable to similar treated populations in Europe and North America. Results do not apply to untreated patients or those infected with HIV who have yet to receive a diagnosis or access care.

Study funding/potential competing interests

The study was funded by the UK Medical Research Council.

Maternal exposure to angiotensin converting enzyme inhibitors in the first trimester and risk of malformations in offspring: a retrospective cohort study

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STUDY QUESTION

Does use of angiotensin converting enzyme (ACE) inhibitors during the first trimester of pregnancy increase the risk of malformations in live born offspring?

SUMMARY ANSWER

Use of ACE inhibitors in the first trimester was associated with increased risk of congenital heart defects in offspring compared with normotensive controls, but not compared with use of other antihypertensives or with hypertensive controls.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Use of ACE inhibitors during the first trimester of pregnancy has been reported to increase the risk of birth defects, whereas use of other antihypertensives has not. However, this much larger study suggests it is the underlying hypertension, rather than antihypertensive drugs, that increases the risk of birth defects.

Participants and setting

The study included pregnant women and their live born offspring in the Kaiser Permanente Northern California region.

Design, size, and duration

A population based, retrospective cohort study included 465 754 mother-infant pairs from 1995 to 2008. By linking automated clinical and pharmacy databases including comprehensive electronic medical records, we examined maternal use of angiotensin converting enzyme (ACE) inhibitors and other antihypertensives and underlying hypertension during pregnancy in relation to the risk of birth defects in offspring.

Main results and the role of chance

The prevalence of ACE inhibitor use in the first trimester only was 0.9/1000, and the use of other antihypertensive medications was 2.4/1000. After adjustment for potential confounders, use of ACE inhibitors during the first trimester only seemed to be associated with increased risk of congenital heart defects in offspring compared with normotensive controls (15/381 (3.9%) v 6232/400 021 (1.6%) cases, odds ratio 1.54 (95% CI 0.90 to 2.62)). A similar association was observed for use of other antihypertensives (28/1090 (2.6%) cases of congenital heart defects, odds ratio 1.52 (1.04 to 2.21)). However, compared with hypertensive controls (708/29 735 (2.4%) cases of congenital heart defects), neither use of ACE inhibitors nor use of other antihypertensives in the first trimester was associated with increased risk of congenital heart defects (odds ratios 1.14 (0.65 to 1.98) and 1.12 (0.76 to 1.64) respectively).

Bias, confounding, and other reasons for caution

Our study was based on a large sample with almost half a million mother-infant pairs. However, we did not have information on many social and behavioural factors, and these could be potential confounders.

Generalisability to other populations

Members of Kaiser Permanente in northern California are an ethnically diverse population. The findings from the study should have implications for a wide range of populations.

Study funding/potential competing interests

Contract No 2900500331 from Agency for Healthcare Research and Quality, as part of the Developing Evidence to Inform Decisions about Effectiveness programme. FDA and Office of Women's Health also contributed funds.

RISK OF CONGENITAL HEART DEFECTS IN OFFSPRING BY MATERNAL USE OF ANTIHYPERTENSIVES DURING PREGNANCY

	No (%) of mother-infant pairs*	Odds ratio (95% CI)		
		Crude	Adjusted†	
Normotensive controls‡	6232/400 021 (1.6)	Reference	Reference	—
Hypertensive controls§	708/29 735 (2.4)	1.54 (1.43 to 1.67)	1.41 (1.30 to 1.53)	Reference
Antihypertensive use				
Only in 1st trimester:				
Other antihypertensives¶	28/1090 (2.6)	1.67 (1.14 to 2.43)	1.52 (1.04 to 2.21)	1.12 (0.76 to 1.64)
ACE inhibitors**	15/381 (3.9)	2.59 (1.54 to 4.34)	1.54 (0.90 to 2.62)	1.14 (0.65 to 1.98)
Any in 1st trimester††:				
Other antihypertensives¶	123/4186 (2.9)	1.91 (1.59 to 2.29)	1.67 (1.39 to 2.01)	1.24 (1.02 to 1.52)
ACE inhibitors**	24/670 (3.6)	2.35 (1.57 to 3.54)	1.39 (0.91 to 2.13)	1.10 (0.70 to 1.71)
Only in 2nd or 3rd trimesters:				
Other antihypertensives¶	566/12 349 (4.6)	3.04 (2.78 to 3.32)	2.90 (2.65 to 3.16)	2.02 (1.81 to 2.27)
ACE inhibitors**	4/48 (8.3)	5.75 (2.06 to 15.99)	4.28 (1.53 to 11.97)	3.04 (1.08 to 8.56)

*Excluding cases of other birth defects from the denominator.

†Adjusted for pre-existing diabetes, maternal age, ethnicity, parity, and maternal weight, and with different reference categories (normotensive or hypertensive controls).

‡No use of antihypertensives during pregnancy and no diagnosis of hypertension.

§No use of antihypertensives during pregnancy but with a diagnosis of hypertension.

¶Use of antihypertensives other than ACE inhibitors during pregnancy.

**Use of ACE inhibitors during pregnancy.

††Any use of antihypertensives in first trimester regardless of use in other trimesters.

Implementation and adoption of nationwide electronic health records in secondary care in England: final qualitative results from prospective national evaluation in “early adopter” hospitals

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STUDY QUESTION What were the local consequences of the government led implementation of a national electronic health records system (the NHS Care Record Service) in “early adopter” hospitals in England?

SUMMARY ANSWER Implementation proved time consuming and challenging, with as yet limited discernible benefits for clinicians and no clear advantages for patients. The national strategy had considerable unforeseen organisational and clinical consequences for “early adopter” hospitals, these being compounded by wider national political and economic developments.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

There are major challenges associated with government led “top down” implementation strategies. There is a need to move away from technology centred models of “implementation” and focus more attention on the process of “adoption,” which needs to be seen as an ongoing “working out” between staff and technology.

Rationale, design, data collection method

Countries around the world are now actively pursuing the implementation of electronic health records on a national scale. We conducted a theoretically informed longitudinal qualitative evaluation based on case studies to explore England’s national implementation of electronic health record systems.

Participants and setting

We collected qualitative data in 12 “early adopter” NHS hospitals over two and a half years. Our dataset consisted of 431 semistructured interviews with hospital staff, developers, and governmental stakeholders; 590 hours of observations; 334 sets of researcher notes; and 867 regional and national documents.

Recruitment/sampling strategy

We selected hospitals using purposive sampling to identify

diverse organisations and purposefully recruited a range of interviewees, actively seeking the broadest range of perspectives.

Data analysis method

Data were thematically analysed, initially within and then across cases; we combined deductive coding informed by sociotechnical principles and inductive coding that allowed themes to emerge from the data.

Main findings

Delays in implementation and adoption related to unrealistic expectations about the capabilities of systems; the time needed to build, configure, and customise the software; the work needed to ensure that systems were supporting provision of care; and the training and support needs of end users. Other factors included the changing milieu of NHS policy and priorities; repeatedly renegotiated national contracts; different stages of development of systems; and a complex communication process between different stakeholders, along with contractual arrangements that largely excluded NHS providers. Despite these major challenges, there was some early evidence of important learning within and between organisations and the development of relevant competencies within hospitals.

Implications

Although our results might not be directly transferable to later adopting sites because the functionalities we evaluated were new and untried in the English context, this work sheds important light on the processes involved in implementing major new IT systems. The move to increased local decision making that we advocated on the basis of our interim analysis has been welcomed by the NHS, but it is important that policymakers do not lose sight of the overall goal of an integrated interoperable solution.

Bias, limitations, generalisability

We observed problems that were being addressed for the first time by all stakeholders. These might eventually be resolved through negotiation and as subsequent implementers learn from these early experiences. The political environment resulted in restricted access to some stakeholders and also meant that information that was considered particularly sensitive and confidential was in some cases difficult to obtain.

Study funding/potential competing interests

This report is independent research commissioned by the NHS Connecting for Health Evaluation Programme.

KEY THEMES EMERGING FROM THE ANALYSIS

- Multiple translations of the original vision
- Ways in which hospitals prepared themselves
- The arrival of the software in institutional settings
- Implementation as a process
- Standardisation versus localisation
- Some early benefits for organisations and staff
- Work processes and changes in work practices
- The impact of the change in government and the economic recession