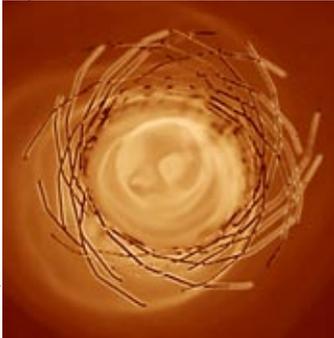


THIS WEEK'S RESEARCH QUESTIONS

- 459** Is stenting more effective than endarterectomy for carotid artery stenosis in the short and long term?
- 460** Which management approach for borderline abnormal cervical smear has the best psychosocial outcomes: HPV DNA testing, repeat smear testing, or informed choice of the two?
- 461** Does the UK Clinical Aptitude Test improve the selection process for school leaver applicants to medical and dental school?
- 462** Can a multifaceted quality improvement project lead to long term reductions in rates of catheter related bloodstream infection?
- 463** Does the risk of cancer associated with immunosuppression for kidney transplantation fall after immunosuppression is stopped?



ZEPHYR/SPL

PROMs: How to get patients' perspectives

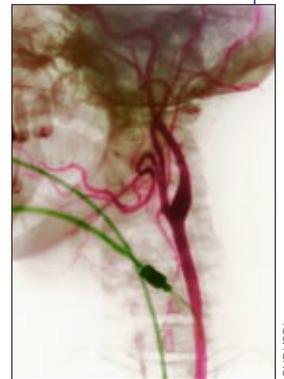
In our Research Methods and Reporting section, Jill Dawson and colleagues look at the role of patient reported outcome measure (PROMs) in investigating, monitoring, and delivering health care. These standardised, validated questionnaires can capture important clinical information that traditional evaluations cannot, such as a patient's perception of improvement in pain and mobility. Their article (p 464) follows the release in December 2009 of guidelines from the Food and Drug Administration (FDA), explaining to the drug industry how it evaluates PROM instruments used to measure endpoints in clinical trials. The guidance describes procedures for trial sponsors to generate their own PROM tools, and it cautions against measuring "general concepts" (such as overall physical health), saying that measurement of more specific concepts (such as improvement in pain) is more likely to generate useful data to support labelling claims (www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM193282.pdf).

UK Clinical Aptitude Test in selection of medical students

The UK Clinical Aptitude Test (UKCAT) was introduced to increase diversity and fairness in the selection of medical and dental students by UK universities. David James and colleagues did a cohort study of applicants in the first year of UKCAT's operation and found that the test had an inherent bias in favour of men and students from a higher socioeconomic class or from independent or grammar schools (p 461). However, the test scores did provide a reasonable proxy for A level results. The accompanying editorial from David Powis says that selectors should also take into account non-academic personal qualities that are not assessed by UKCAT. In a Rapid Response to the paper, Rachel Greatrix, the chief operating officer of UKCAT, welcomes the findings and suggests that a combination of UKCAT results and A level achievement may offer a fairer tool for selection than A levels alone.

Endarterectomy v stenting for carotid artery stenosis

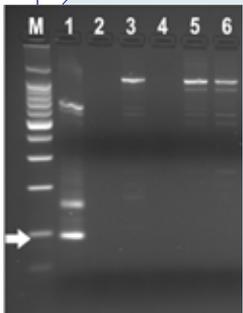
This systematic review and meta-analysis shed some light on the comparative effectiveness of the two interventions in the long term. Pascal Meier and colleagues found that carotid endarterectomy was better than carotid artery stenting in the short term—but the difference was not significant for intermediate term outcomes, since it was mainly driven by non-disabling stroke (p 459). However, stenting resulted in fewer cranial nerve injuries and myocardial infarctions. In an editorial, A Halliday and J W Norris say that although carotid artery stenting is not yet ready to replace endarterectomy, randomisation between the two interventions is still ethical when experienced surgeons are involved and both procedures are feasible.



CNR/SPL

Catheter related bloodstream infections in intensive care

Peter J Pronovost and colleagues have already reported in the *New England Journal of Medicine* that the Keystone ICU project, a Michigan-wide quality improvement initiative to minimise use of central venous catheters and ensure they were inserted hygienically, successfully reduced infection rates. After that 18 month project ended intensive care units were encouraged to integrate these evidence based practices into their normal routines. Most did so, and this cohort study shows that very low infection rates were largely sustained (p 462). As one reviewer told us, "Few safety or quality improvement initiatives have demonstrated sustained change. This paper is therefore of major importance, both in the battle to reduce infection and in providing an example of how large scale improvement programmes should be evaluated over time."



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

XMRV in chronic fatigue syndrome The findings of a fast track paper published online this week cast doubt on the suggestion that xenotropic murine leukaemia virus-related virus (XMRV) could be a cause of chronic fatigue syndrome. Researchers in the United States recently detected the retrovirus in blood from patients with the condition, but Frank van Kuppeveld and colleagues found no evidence of it in samples from a well defined Dutch cohort (doi:10.1136/bmj.c1018). British researchers very recently reported similar findings in *PLoS ONE* (See News, doi:10.1136/bmj.c1033), although they used a different set of primers from those used by the American group.

Short term and intermediate term comparison of endarterectomy versus stenting for carotid artery stenosis: systematic review and meta-analysis of randomised controlled clinical trials

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EDITORIAL

by Halliday and Norris

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STUDY QUESTION What are the short term and long term efficacies of carotid artery stenting versus carotid endarterectomy?

SUMMARY ANSWER Carotid endarterectomy was superior to carotid artery stenting for short term outcomes but had similar benefits in the long term.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS Findings from previous studies that compared carotid artery stenting with endarterectomy have been controversial because little is known about longer term outcomes. This study presents a comprehensive analysis of all existing data, including intermediate term outcome, and so has increased statistical power compared with single trials.

Selection criteria for studies

We searched BIOSIS, Embase, Medline, the Cochrane central register of controlled trials, International Pharmaceutical Abstracts database, ISI Web of Science, and Google scholar from 1 January 1990 to 25 July 2009. Eligible trials were randomised controlled studies that compared carotid endarterectomy with carotid artery stenting in patients with carotid artery stenosis with or without symptoms.

Primary outcome(s)

The primary end point was a composite of mortality or stroke. Secondary end points were death, stroke, myocardial infarction, and facial neuropathy (individual end points) and mortality or disabling stroke (composite end point).

Main results and role of chance

The periprocedural risk of mortality or stroke was lower for carotid endarterectomy (odds ratio 0.67, 95% confidence interval 0.47 to 0.95; $P=0.025$) than for carotid stenting, mainly because of a decreased risk of stroke (0.65, 0.43 to 1.00; $P=0.049$). The risk of death (1.14, 0.56 to 2.31; $P=0.727$) did not differ noticeably between the two interventions. The odds of periprocedural myocardial infarction (2.69, 1.06 to 6.79; $P=0.036$) or cranial nerve injury (10.2, 4.0 to 26.1; $P<0.001$) was higher in the carotid endarterectomy group than in the carotid stenting group. In the intermediate term, the two treatments did not differ significantly for stroke or death (hazard ratio 0.90, 95% confidence interval 0.74 to 1.1; $P=0.314$).

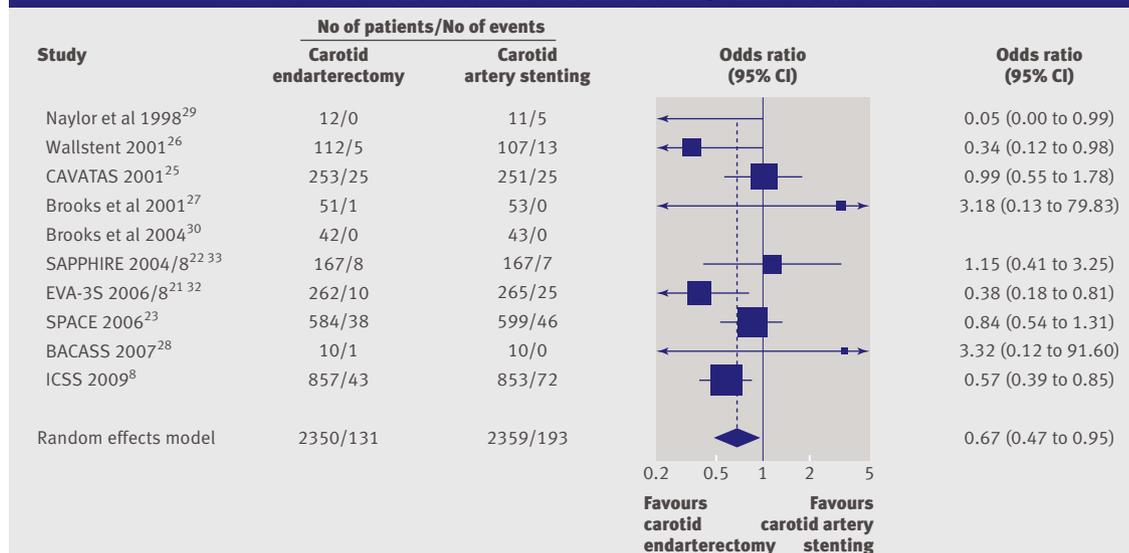
Bias, confounding, and other reasons for caution

Two of the included studies have only been presented at scientific meetings or published as abstracts, so the quality assessment of these studies is limited. Most trials needed surgeons with extensive experience of doing carotid endarterectomy, but the corresponding requirements for interventionalists carrying out carotid stenting were less stringent.

Study funding/Potential competing interests

SC is a consultant for Abbott Vascular. PM was supported by a postdoctoral fellowship grant from the Swiss National Research Foundation and the Schweizerische Stiftung für Medizinisch-Biologische Stipendien. The funding organisations had no role in the design and conduct of the study; the collection, management, analysis, and interpretation of the data; or the preparation, review, or approval of the manuscript.

ODDS OF COMPOSITE OF STROKE OR DEATH WITHIN 30 DAYS OF PROCEDURE



This is a summary of a paper that was published on bmj.com as *BMJ* 2010;340:c467

Psychosocial outcomes of three triage methods for the management of borderline abnormal cervical smears: an open randomised trial

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STUDY QUESTION Which of three triage strategies for women with a borderline abnormal cervical smear results in the best psychosocial outcomes: human papillomavirus (HPV) DNA testing, repeat smear testing, or women's informed choice of either test?

SUMMARY ANSWER Over the full year of follow-up, HPV testing was better than repeat smear testing for women's psychosocial health.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS As an alternative to repeat smear testing for the management of borderline cervical smears, HPV testing might have important psychosocial consequences for women and provides an opportunity to give women an informed choice of management. The effect of HPV testing or informed choice had not been assessed in randomised trials. We found that management by HPV testing was better for women's psychosocial wellbeing over a year than repeat smear testing. Little benefit was offered by informed choice except for some cognitive outcomes.

Design

Randomised trial with women allocated to HPV DNA testing; repeat smear testing at six months (conventional management), or an informed choice of either test supported by a decision aid.

Participants and setting

314 women aged 16 to 70 years who attended routine cervical screening at 18 publicly funded women's health clinics across Australia and who had an index borderline abnormal cervical smear.

Primary outcome(s)

Health related quality of life (SF36 mental health subscales).

Main results and the role of chance

Two weeks after triage, health related quality of life was worse for women in the HPV testing group than in the repeat smear testing group ($t=-1.63$, $df=131$, $P=0.10$; effect size=0.33) and the informed choice group ($t=-2.00$, $df=141$, $P=0.05$, effect size 0.27). However, women's satisfaction with health care in general and care for their cervical abnormality was higher in the HPV testing group over the entire follow-up period than in the smear testing group (table). Emotional outcomes improved in all groups but the HPV testing group had lower scores (least distressed) than the repeat smear testing group on the cervical screening questionnaire specific distress measure over one year. Among cognitive measures, the HPV testing group reported poorer outcomes than the other groups on intrusive thoughts at two weeks.

Harms

None.

Bias, confounding, and other reasons for caution

Potential confounding was assessed in all analyses and did not affect interpretation of the results. Women in the HPV group were well informed about HPV infection, which may have mitigated some negative psychosocial sequelae observed in previous studies.

Generalisability to other populations

Women who decided to participate in the study might have been more interested in HPV testing and informed choice than the general population. In the informed choice group, 65% of women preferred HPV testing, compared with 85% in a nationally representative sample of Australian women. We suggest that the offer of informed choice may be best suited to women who desire it in their health care, which would make our sample appropriate.

Study funding/potential competing interests

This work was supported by an Australian National Health and Medical Research Council (NHMRC) grant 402764 to the Screening and Test Evaluation Program. KMcC is supported by a NHMRC Career Development Award 402836. The NHMRC had no role in the writing of this paper.

Trial registration number:

12605000111673

PSYCHOSOCIAL OUTCOMES OVER ONE YEAR

	Trial arm mean scores			Overall P value	P value for pairwise comparisons*		
	HPV	IC	RS		HPV v RS	HPV v IC	RS v IC
Quality of life							
SF36: mental health combined score	46.2	48.5	45.5	0.16	–	–	–
Cognitive							
Intrusive thoughts†	25%	13%	17%	0.19	–	–	–
Satisfaction generally	14.5	14.4	13.5	0.03	0.01	–	0.03
Satisfaction with care	8.4	8.0	7.6	0.02	0.01	–	–
Emotional							
CSQ (distress)†	16.6	17.5	18.4	0.01	<0.01	–	–

RS=repeat smear, IC=informed choice, CSQ=cervical screening questionnaire.

*Pairwise comparisons were made only if $P<0.1$.

†Higher scores represent poorer psychological wellbeing.

Comparison of A level and UKCAT performance in students applying to UK medical and dental schools in 2006: cohort study

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EDITORIAL by Powis

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STUDY QUESTION Does the UK Clinical Aptitude Test (UKCAT) add value to the selection process for school leavers applying to medical and dental school, and in particular does it reduce the socioeconomic bias known to affect A levels?

SUMMARY ANSWER UKCAT scores can provide a reasonable proxy for A levels in the selection process before A level results are available, but these scores show an inherent favourable bias to male candidates and to those from a higher socioeconomic class and from independent or grammar schools.

WHAT IS known and what this paper adds Discriminating between large numbers of highly able applicants on their academic achievement alone is increasingly difficult, and participation needs to be widened. For UK domiciled students with three or more A levels, UKCAT scores are modestly correlated to A level tariff scores and continue to show inherent gender and socioeconomic bias.

Participants and setting

We studied applicants to 23 UK medical and dental schools in 2006.

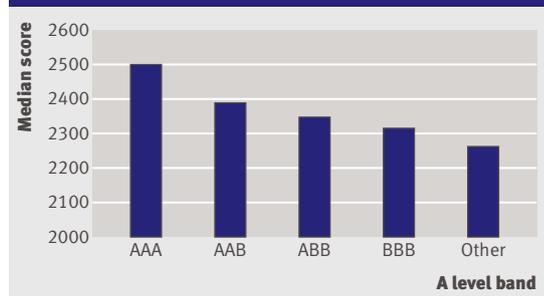
Design, size, and duration

This was a cohort study of applicants who took the UKCAT in the United Kingdom and who had recently achieved at least three passes at A level in their school leaving examinations (n=9884, 53% of all applicants). The analysis was designed to explore the relation between UKCAT and A levels and to identify the independent predictors of higher scores in both.

Main results

The UKCAT scores showed a consistent drop in performance with each decrease in A level band, and this was highly significant in all cases ($P < 0.001$, Kruskal-Wallis test). Most of the distributions were non-normal, so median scores are shown in the figure. The only exception to the downward trend was for the abstract reasoning sub-test, in which the BBB band performed better than expected. Independent predictors of obtaining grades of at least AAB at A level were white ethnicity (odds ratio 1.58, 95% confidence interval 1.41 to 1.77), professional or managerial background (1.39, 1.22 to 1.59), and independent or grammar schooling (2.26, 2.02 to 2.52) (all $P < 0.001$). Independent predictors of achieving UKCAT scores at or above the 30th centile for the whole test were male sex (odds ratio 1.48, 1.32 to 1.66), white ethnicity (2.17, 1.94 to 2.43), professional

MEDIAN UKCAT TOTAL SCORE BY A LEVEL BAND



or managerial background (1.34, 1.17 to 1.54), and independent or grammar schooling (1.91, 1.70 to 2.14) (all $P < 0.001$).

Bias, confounding, and other reasons for caution

One major limitation of the study was that the socioeconomic status was not volunteered by about 30% of the applicants. People who withheld data on socioeconomic status were notably different from those who provided that information. This might have caused bias in analysis.

Generalisability to other populations

Only 53% of the total population that sat the UKCAT in 2006 were included in the study. Although the applicants that remain still represent a large cohort, the exclusions reduce the diversity of the study group and the generalisability of the results. Similarly, to preserve the simplicity and ease of understanding of the analysis, we collapsed the many variables for the binary regression. Although this provided a broad overview of UKCAT performance, such simplifications might hide subtle but important differences, for example, between the performance of different ethnic groups.

Study funding/potential competing interests

The UKCAT Board is responsible for an overall research and evaluation programme, but the named authors are responsible for the study design, data analysis and interpretation, and writing of the paper as submitted. UKCAT is responsible for the database and agreed with the decision to submit the article for publication. This research was commissioned and approved by the UKCAT Board as part of their ongoing research programme evaluating UKCAT. JY was funded by the UKCAT Board to complete the analysis. SN was elected as chair of the UKCAT Board in December 2008. No author has any ongoing financial interests in the publication of these results.

Sustaining reductions in catheter related bloodstream infections in Michigan intensive care units: observational study

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STUDY QUESTION Can a multifaceted quality improvement project sustain reductions in rates of catheter related bloodstream infection for up to three years after implementation?

SUMMARY ANSWER After reducing rates of catheter related bloodstream infections in intensive care units during the 18 month post-implementation study period, the use of a multifaceted quality improvement project was associated with sustained reductions in infection rates for an additional 18 months.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS Few reports show that the benefits associated with quality improvement projects can be sustained. This study shows that they can, suggesting that broad and sustained improvements in quality of health care are possible.

Participants and setting

Ninety intensive care units predominantly located in the state of Michigan, USA, participated in this study.

Design, size, and duration

In this collaborative cohort study, participating intensive care units implemented interventions to improve culture and teamwork and to translate research into practice by increasing the extent to which five evidence based recommendations to reduce rates of catheter related bloodstream infection were applied. We analysed data on rates of catheter related bloodstream infection from the initial 18 month post-implementation period and a new, subsequent 18 month sustainability period.

Main results and the role of chance

Ninety (87%) of the original 103 intensive care units participated, reporting 1532 intensive care unit months of data and 300 310 catheter days during the 18 month sustainability period. The mean and median rates of catheter related bloodstream infection decreased from 7.7 and 2.7 (interquartile range 0.6-4.8) at baseline to 1.3 and 0 (0-2.4) at 16-18 months and to 1.1 and 0 (0.0-1.2) at 34-36 months post-implementation. Multilevel regression analysis showed that the incidence rate ratio decreased from 0.68 (95% confidence interval 0.53 to 0.88) at 0-3 months to 0.38 (0.26 to 0.56) at 16-18 months and 0.34 (0.24 to 0.48) at 34-36 months post-implementation. During the sustainability period, the mean bloodstream infection rate was reduced by 1% (95% confidence interval -9% to 7%) from the initial 18 month post-implementation period.

Bias, confounding, and other reasons for caution

Results may have been influenced by the fact that feedback on rates of catheter related bloodstream infection was given to participating intensive care units and that participating intensive care units met periodically during

CATHETER RELATED BLOODSTREAM INFECTION RATES FROM BASELINE UNTIL 36 MONTHS AFTER QUALITY IMPROVEMENT INTERVENTION

Study period	Mean (SD) infection rate	Incidence rate ratio* (95% CI)
Baseline (pre-implementation)	7.7 (28.9)	Reference
During implementation	2.8 (4.0)	0.81 (0.61 to 1.08)
After implementation—initial evaluation period:		
0-3 months	2.3 (4.0)	0.68 (0.53 to 0.88)
16-18 months	1.3 (2.4)	0.38 (0.26 to 0.56)
After implementation—sustainability period: 34-36 months	1.1 (2.7)	0.34 (0.24 to 0.48)

*Calculated with use of generalised linear latent and mixed model, with robust variance estimation and random effects to account for clustering of catheter related bloodstream infections within intensive care units over time and clustering of hospitals within geographical regions; rates of catheter related bloodstream infections during implementation, initial evaluation, and sustainability periods compared with baseline (pre-implementation) values, adjusted for hospital's teaching status and number of beds.

the sustainability period to discuss new safety interventions unrelated to catheter related bloodstream infection or by the Blue Cross Blue Shield of Michigan's quality incentive payment to hospitals for meeting performance thresholds for bloodstream infection rates.

Generalisability to other populations

These findings are probably generalisable to other intensive care units that can implement the culture interventions and the five evidence based recommendations to prevent catheter related bloodstream infection. Broad use of this intervention with achievement of similar results could substantially reduce the morbidity and costs associated with catheter related bloodstream infections.

Study funding/potential competing interests

This study was funded by the Agency for Healthcare Research and Quality (AHRQ) (1UC1HS14246), the Michigan Health and Hospital Association (MHA), and Blue Cross Blue Shield of Michigan. PJP, CG, and SB have support from AHRQ, and SW has support from Blue Cross Blue Shield of Michigan for the submitted work. PJP, CG, SB, SC, JB, RH, and PP have relationships with the Speakers' Bureau, National Patient Safety Agency, World Health Organization, MHA, National Institutes of Health, Robert Wood Johnson Foundation, Docusys, Merck, AdvanDx, Cubist Pharmaceuticals, Cadence Pharmaceuticals, Astellas/Theravance, Forest Laboratories, Institute for Healthcare Improvement, American Medical Association, Pascal Metrics, Edward Life Sciences, and Lilly Pharmaceuticals.

Effect of reduced immunosuppression after kidney transplant failure on risk of cancer: population based retrospective cohort study

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STUDY QUESTION Does reduction or cessation of immunosuppression after kidney transplant failure reduce cancer risk in kidney transplant recipients?

SUMMARY ANSWER Cancer risk is significantly reduced for some, but not all, cancers.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Immunosuppression in organ transplant recipients is associated with increased risk of a broad range of cancers. This increased risk is rapidly reversible on reduction of immunosuppression for some but not all cancers.

Participants and setting

A nationwide, population based, retrospective cohort study of cancer incidence in 8173 Australian kidney transplant recipients registered on the Australia and New Zealand Dialysis and Transplant Registry (ANZDATA), 1982-2003.

Design, size, and duration

Incident cancers were ascertained using linkage with national cancer registry records. Person years of follow-up (n=59 037

were accumulated from transplantation until cancer diagnosis, death, or the end of follow-up. Cancer-specific incidence ratios (standardised for five-year age group, sex, calendar year, and state or territory) were calculated for periods of transplant function and dialysis after transplant failure. Analyses were restricted to cancers or groups of cancers for which there were at least 10 cases in total. Incidence was compared between periods using multivariate incidence rate ratios adjusted for current age, sex, and duration of transplantation.

Main results and the role of chance

A total of 892 cancers were identified, after excluding 33 cancers that occurred in the first three months of each period (as these cancers would almost certainly have developed in the preceding period). All 10 cases of Kaposi's sarcoma occurred during transplant function. Standardised incidence ratios were significantly elevated during transplant function, but not during dialysis after transplant failure, for non-Hodgkin's lymphoma, lip cancer, and melanoma. For each of these cancers, incidence was significantly lower during dialysis after transplant failure in multivariate analysis. In contrast, standardised incidence ratios during dialysis after transplant failure remained significantly elevated for leukaemia and lung cancer, and for cancers related to end stage kidney disease (kidney, urinary tract, and thyroid cancers). Indeed, thyroid cancer incidence was significantly higher during dialysis after transplant failure than during transplant function. There was no significant difference in incidence by transplant function for other cancers.

Bias, confounding, and other reasons for caution

The main limitation was the limited statistical power with which to examine incidence beyond the period of first transplantation for the less common cancers.

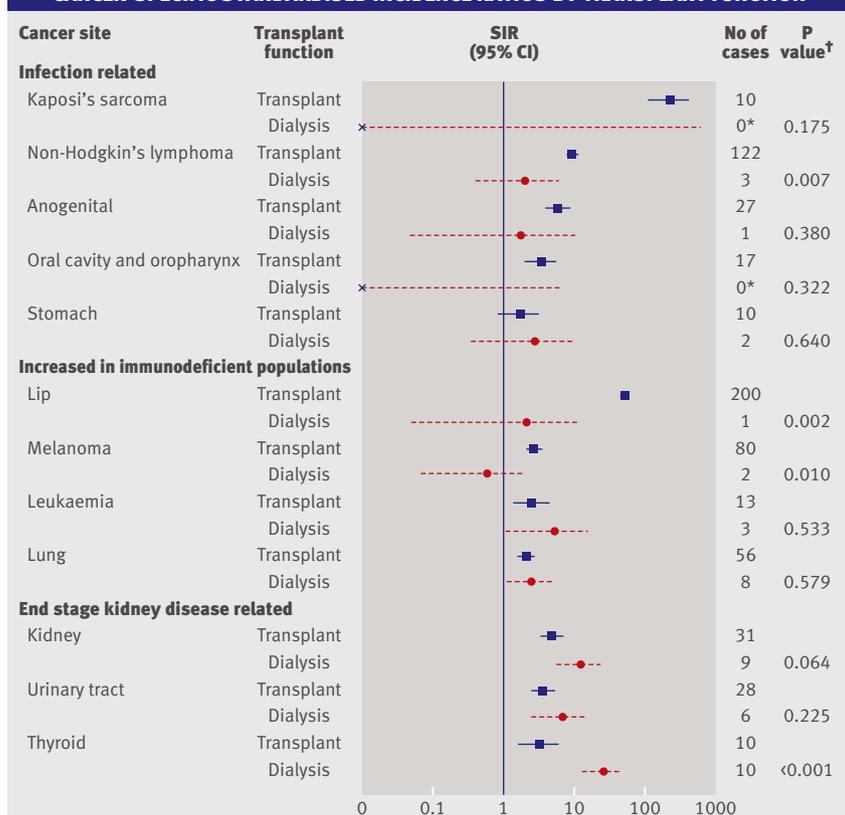
Generalisability to other populations

This is the first epidemiological study to examine cancer-specific incidence after transplant failure. The findings offer insight into the role of current functional immunity in cancer prevention and may help inform the management of cancer risk in other immunosuppressed populations.

Study funding/potential competing interests

This work was funded by Cancer Council New South Wales, National Health and Medical Research Council, and Cancer Institute New South Wales. ANZDATA is supported by the Australian and New Zealand governments, and Kidney Health Australia. The National Centre in HIV Epidemiology and Clinical Research is funded by the Australian government. JRC and AEG have financial links with pharmaceutical companies involved in this study (see full paper for details).

CANCER-SPECIFIC STANDARDISED INCIDENCE RATIOS BY TRANSPLANT FUNCTION



*Upper CI of standardised incidence ratio presented when zero cases observed

[†]P value for multivariate incidence rate ratio comparing transplant and dialysis periods