

THIS WEEK'S RESEARCH QUESTIONS

- 1403** Is ticagrelor or clopidogrel more effective for non-invasive management of acute coronary syndromes?
- 1404** Do intensive care units and hospitals in Asia comply with resuscitation and management bundles from the Surviving Sepsis Campaign?
- 1405** Does the rate of injuries caused by violence fall when emergency departments report violent injuries to police and local authorities?
- 1406** How common is high risk prescribing in primary care, and which patient and practice characteristics are associated with it?

High risk prescribing in primary care

Bruce Guthrie and colleagues used multilevel modelling to review data from 315 Scottish general practices with 1.76 million patients, of whom nearly 140 000 (around 8%) received one or more high risk prescriptions (p 1406).

They looked at obvious risks associated with NSAIDs and warfarin, but also flagged up the perils of prescribing risperidone or olanzapine for over 65s with dementia and giving methotrexate without explicit instruction to take it weekly. After adjustment for patient level variables (age, sex, deprivation, polypharmacy), there was still considerable—and potentially modifiable—variation between practices. This variation wasn't explained by practice list size, single handedness, contract type, training status, rurality, dispensing status, and Quality and Outcomes Framework indicator scores for the management of medicines.

The authors acknowledge that not all high risk prescribing is inappropriate or avoidable. They point out, however, that “as all the prescribing examined is stated in national guidance to be contraindicated or to be avoided in routine practice, the high rates and large variation between practices suggest significant opportunities for improvement.” And they reckon that their methodology is generalisable, at least across UK primary care.

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PETER BARRITT/ALAMY

Choosing antiplatelet treatment for acute coronary syndrome

Invasive management is recommended for most patients with acute coronary syndromes, but a conservative approach is often taken in lower risk patients (something like a third of patients with non-ST elevation acute coronary syndrome are managed non-invasively). However, such patients rarely receive attention from trialists, so it's nice to see Stefan K James and colleagues' report of a planned subgroup analysis of patients enrolled in the PLATelet inhibition and patient Outcomes (PLATO) trial who were initially allocated to non-invasive treatment (p 1403).

They compared clinical outcomes with two antiplatelet agents, the second generation thienopyridine clopidogrel and the novel non-thienopyridine ticagrelor, both given in conjunction with aspirin. Ticagrelor achieved a clinically important reduction in ischaemic events and mortality compared with clopidogrel, without increasing major bleeding. The authors report that the benefits of ticagrelor over clopidogrel were consistent with those from the overall PLATO results, and they conclude that the benefits of the newer drug apply across different management strategies.

In his linked editorial (p 1371) Adam Timmis is particularly impressed that ticagrelor seems to have “achieved the elusive goal of enhancing platelet inhibition and improving cardiovascular outcomes without increasing the risk of bleeding” but warns that these are still early days.

Continuing the antiplatelet theme in their Therapeutics article on page 1415, Gabriella Passacuale and Albert Ferro discuss the use of clopidogrel and prasugrel (a third generation thienopyridine) for the prevention of cardiovascular events, covering how and how well such agents work.

Sharing information on violent injury

Curtis Florence and colleagues (p 1405) report on an information sharing partnership between health services, police, and local government in Cardiff, in which anonymised information about injuries from violence treated in emergency departments was passed to the partnership. For all patients attending an emergency department who reported injury in a violent incident, the hospital captured information about the precise location of the incident, time and day, and type of weapon, stripped it of personal identifiers, and shared it with the partnership crime analyst. The hospital data were then combined with police data and used to target violence prevention resources.

The study found that sharing of information was associated with a significant reduction in violence related hospital admissions and in woundings recorded by the police in Cardiff, relative to comparison cities. The study also showed that less serious assaults recorded by the police increased significantly.

In his linked editorial Alexander Butchart applauds this new approach to violence prevention, pointing out that such community level programmes should be more cost effective than programmes that operate at the levels of individuals, close relationships, or families (p 1372).



CORDELIA MOLLOY/SPL

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

Priorities for women with lymphoedema after treatment for breast cancer Afaf Girgis and colleagues explored the perceived unmet needs of women treated for breast cancer with symptoms and signs of lymphoedema (doi:10.1136/bmj.d3442).

Predicting risk of osteoporotic and hip fracture in the United Kingdom QFractureScores are useful tools for predicting the 10 year risk of osteoporotic and hip fractures in UK patients, say Gary Collins and colleagues (doi:10.1136/bmj.d3651).

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ALISTAIR HEAP/ALAMY

Ticagrelor versus clopidogrel in patients with acute coronary syndromes intended for non-invasive management: substudy from prospective randomised PLATElet inhibition and patient Outcomes (PLATO) trial

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EDITORIAL by Timmis

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STUDY QUESTION What was the randomised outcome of the 5216 patients who were specified as planned for non-invasive management in the PLATO trial?

SUMMARY ANSWER In patients with acute coronary syndrome who were initially intended for non-invasive management, the benefits of ticagrelor over clopidogrel were consistent with those from the overall PLATO results.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS Half of all patients admitted with non-ST elevation acute coronary syndrome in the Western world do not initially have revascularisation treatment. In patients initially intended for non-invasive management, ticagrelor caused a clinically important reduction in ischaemic events and mortality without increasing major bleeding compared with clopidogrel, so the benefits of intensified P2Y12 inhibition apply across different management strategies.

Design

This was a pre-specified analysis of a subgroup of a prospective randomised clinical trial defined before randomisation.

Participants and setting

Of the 18 624 patients admitted to hospital with acute coronary syndrome, 5216 (28%) were specified as planned for non-invasive management.

Primary outcome(s)

The primary outcomes were a composite end point of cardiovascular death, myocardial infarction, and stroke; their individual components; and PLATO defined major bleeding during one year.

Main results and the role of chance

In all, 2183 (41.9%) patients had coronary angiography during the initial hospital admission, 1065 (20.4%) had percutaneous coronary intervention, and 208 (4.0%) had coronary artery bypass surgery. Cumulatively, 3143 (60.3%) patients

were managed non-invasively by the end of follow-up. The incidence of the primary end point was lower with ticagrelor than with clopidogrel (12.0% v 14.3%; hazard ratio 0.85, 95% confidence interval 0.73 to 1.00; P=0.04). Overall mortality was also lower (6.1% v 8.2%; 0.75, 0.61 to 0.93; P=0.01).

Harms

The incidences of total major bleeding (11.9% v 10.3%; 1.17, 0.98 to 1.39; P=0.08) and major bleeding not related to coronary artery bypass grafting (4.0% v 3.1%; 1.30, 0.95 to 1.77; P=0.10) were numerically higher with ticagrelor than with clopidogrel.

Bias, confounding, and other reasons for caution

This was a subgroup analysis not powered for the primary end point.

Generalisability to other populations

The intended non-invasive cohort of the trial was representative of a trial population with primarily non-ST elevation myocardial infarction acute coronary syndrome but with a lower mean age compared with a general population with acute coronary syndrome.

Study funding/potential competing interests

This work was supported by AstraZeneca, who funded the PLATO trial. Representatives of the sponsor were involved in study design; data gathering, analysis, and interpretation; and revision of the report. Support for the analysis and interpretation of results and preparation of the manuscript was provided through funds to the Uppsala Clinical Research Center and Duke Clinical Research Institute as part of the Clinical Study. JH is an employee of AstraZeneca. SKJ, MTR, CPC, JHC, SH, HK, JM, PGS, RFS, LW, RAH declare various grants and fees from a variety of organisations.

Trial registration number Clinical trials NCT00391872.

EFFICACY AND SAFETY OF TREATMENT IN PATIENTS WITH ACUTE CORONARY SYNDROME INTENDED FOR NON-INVASIVE MANAGEMENT

End point	Ticagrelor (n=2601)	Clopidogrel (n=2615)	Hazard ratio (95% CI)	P value*
Cardiovascular death + myocardial infarction (excluding silent) + stroke (primary objective)	12.0 (295)	14.3 (346)	0.85 (0.73 to 1.00)	0.045
All cause death	6.1 (147)	8.2 (195)	0.75 (0.61 to 0.93)	0.010
Total major bleeding (primary safety objective)	11.9 (272)	10.3 (238)	1.17 (0.98 to 1.39)	0.079
Non-CABG related bleeding	4.0 (90)	3.1 (71)	1.30 (0.95 to 1.77)	0.103
CABG related bleeding	8.3 (189)	7.5 (174)	1.11 (0.90 to 1.36)	0.335

CABG=coronary artery bypass grafting.

*Values are Kaplan-Meier estimates of percentage rate of end point (numbers) at 12 months unless stated otherwise.

Management of severe sepsis in patients admitted to Asian intensive care units: prospective cohort study

The MOSAICS Study Group

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STUDY QUESTION Do intensive care units and hospitals throughout Asia comply with the resuscitation and management bundles from the Surviving Sepsis Campaign?

SUMMARY ANSWER The overall rate of compliance with the resuscitation and management bundles in Asian intensive care units and hospitals was less than 8% and 4% respectively.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS Severe sepsis is a prevalent, costly, and often fatal condition. There is poor compliance with management guidelines for sepsis and limited resources in Asia.

Participants and setting

All adult patients with severe sepsis who were admitted to 150 intensive care units in 16 Asian countries in July 2009 were enrolled.

Design, size, and duration

This prospective cohort study followed 1285 patients until discharge from or death in the hospital, recording organisational characteristics of participating centres and the patients' baseline characteristics. The primary outcome measure was compliance with the resuscitation (six hours) and management (24 hours) bundles. The secondary outcome measure was all cause hospital mortality.

Main results and the role of chance

Hospital mortality was 44.5% (572/1285). Compliance rates for the resuscitation and management bundles were 7.6% (98/1285, 95% confidence interval 6.2% to 9.1%) and 3.5% (45/1285, 2.5% to 4.5%) respectively. The figure summarises achievement of individual targets within these bundles. On logistic regression analysis, compliance with blood cultures, broad spectrum antibiotics, and central venous pressure independently predicted decreased mortality. High income countries, university hospitals, intensive care units with an

accredited fellowship programme, and surgical intensive care units were more likely to comply with the resuscitation bundle. Many centres lacked the facilities to measure lactate and central or mixed venous oxygen saturation and did not have access to drotrecogin alfa.

Bias, confounding, and other reasons for caution

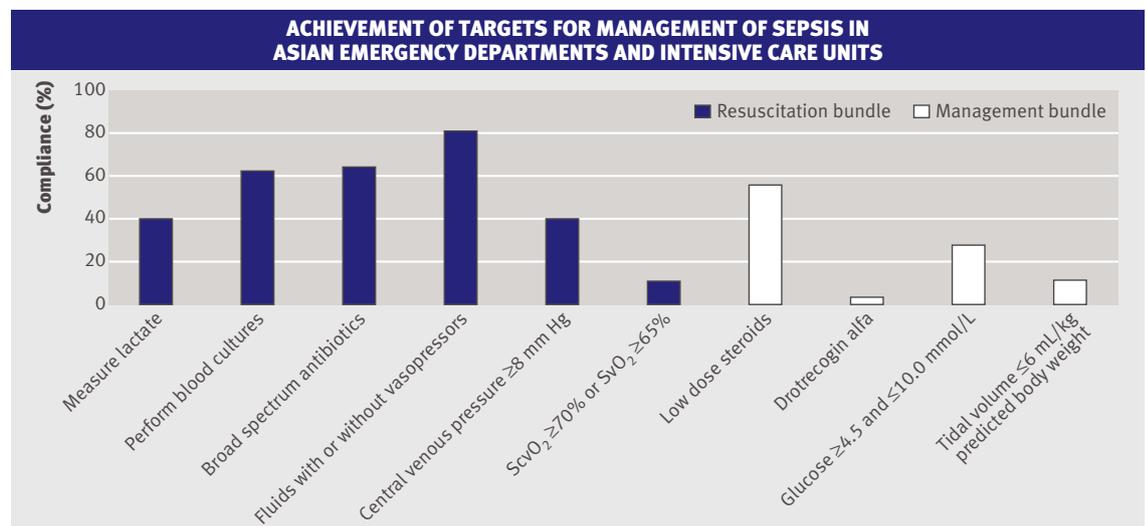
This study is subject to selection bias. The snowball method used to identify suitable units might select for centres with a greater interest in sepsis management. While there was a good representation of countries across the World Bank income categories, intensive care units with fewer than six beds were excluded, many of the United Nations' least developed countries did not participate, university hospitals accounted for half of the centres, and about three quarters of the patients were enrolled in six of the 16 countries.

Generalisability to other populations

As the centres included in this study might not be fully representative of Asian intensive care, true compliance with the sepsis bundles is likely to be even lower than the data suggest. In view of the heterogeneity of the study population, it would be prudent to interpret compliance rates stratified according to the World Bank income classification of the participating countries.

Study funding/potential competing interests

This study was conducted under the auspices of the Asia Ventilation Forum, an independent non-profit working group. Covidien (supplier of medical devices, supplies and pharmaceuticals) provided support for meeting room expenses and access to the data collection website. Several of the contributing authors are directors of the Asia Ventilation Forum and have received travel support and honoraria for lectures from Covidien. One author is employed by Covidien. See the full version on bmj.com for further details.



Effectiveness of anonymised information sharing and use in health service, police, and local government partnership for preventing violence related injury: experimental study and time series analysis

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EDITORIAL by Butchart

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STUDY QUESTION When shared by emergency departments and used by city government and police partners, can anonymised information about violence location, times, and weapons derived from emergency patients reduce rates of violence related injury?

SUMMARY ANSWER This information sharing and use was associated with sustained and substantially lower rates of violence related hospital admissions and serious violence recorded by the police in Cardiff compared with cities where this information was not shared.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS A substantial proportion of violence that results in treatment by doctors is not known to the police, but it is not known whether the use of information derived from patients injured in violence can improve violence prevention. This study provides evidence that this information can, when combined with police intelligence, be used to prevent violence to a greater extent than is achievable using police intelligence alone.

Participants and setting

Cardiff, Wales, and 14 comparison cities in England and Wales selected on the basis of a range of socioeconomic variables.

Design, size, and duration

This experimental study incorporated a time series analysis of violence recorded by the police (“woundings”) in 15 cities over 84 months (33 months before and 51 months after intervention) and of violence related hospital admissions in four cities over 72 months (36 months before and 36 months after intervention).

Main results and the role of chance

Information sharing and use were associated with a substantial and significant reduction in violence related

hospital admissions (adjusted incidence rate ratio 0.58, 95% confidence interval 0.49 to 0.69) from seven to five a month per 100 000 population in Cardiff compared with an increase from five to eight a month in comparison cities; and substantially fewer woundings recorded by the police (0.68, 0.61 to 0.75) from 54 to 82 a month per 100 000 population in Cardiff compared with an increase from 54 to 114 a month in comparison cities. There was a significant increase in violence resulting in no injury or very minor injury recorded by the police in Cardiff relative to comparison cities (1.38, 1.13 to 1.70). These results suggest that a mechanism underlying the reduction in violence related injury is earlier and more frequent police intervention brought about by use of information collected in the emergency department.

Bias, confounding, and other reasons for caution

While we controlled for major confounders, other factors could have influenced the change in rates of violence in the study cities. It is not possible from these findings to determine whether the effectiveness of this intervention varied by violence category.

Generalisability to other populations

Cultural and political differences might affect the utility of this approach in other cities. The partnership activity described here depends on sustained and continuous data capture, sharing, and use; absence or disruption of any of these steps is likely to reduce effectiveness.

Study funding/potential competing interests

The development of the prototype partnership was funded in part by a grant from the Home Office targeted policing fund. The study was funded in part by the Wales Office for Research and Development in Health and Social Care (WORD), grant No R/98/037.

NUMBERS AND RATES OF VIOLENCE RELATED HOSPITAL ADMISSIONS AND WOUNDINGS AND MINOR VIOLENCE (COMMON ASSAULTS) RECORDED BY POLICE IN CARDIFF AND COMPARISON CITIES BEFORE AND AFTER IMPLEMENTATION OF INFORMATION SHARING AND USE

	Violence related hospital admissions		Woundings recorded by police		Common assaults recorded by police	
	Cardiff	Comparison cities	Cardiff	Comparison cities	Cardiff	Comparison cities
Unadjusted count (monthly average)						
Before intervention	21.0	21.2	168.5	181.0	47.8	142.7
After intervention	16.9	33.4	256.8	382.5	61.1	110.9
Population adjusted rate of violence (per 100 000 population)						
Before intervention	6.7	5.3	53.8	53.9	15.3	42.4
After implementation	5.4	8.4	82.0	113.8	19.5	33.0

High risk prescribing in primary care patients particularly vulnerable to adverse drug events: cross sectional population database analysis in Scottish general practice

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STUDY QUESTION How common is high risk prescribing (potentially inappropriate prescribing of drugs to patients particularly vulnerable to adverse drug events) in primary medical care, and which patient and practice characteristics are associated with it?

SUMMARY ANSWER High risk prescribing is common. The patient characteristic most associated with high risk prescribing was the number of repeat prescriptions a patient received, and this largely explained univariate associations with increasing age. Unexplained variation between practices was considerable and not explained by structural characteristics of the practices.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS Preventable adverse drug events related to prescribing in primary care are a common cause of hospital admission and death. This study shows that high risk prescribing is common, can be reliably measured using routine clinical data, and varies greatly between practices.

Participants and setting

315 Scottish general practices with 1.76 million registered patients.

Design

Cross sectional study using multilevel modelling.

Primary outcome(s)

Proportion of patients receiving a high risk prescription, measured using a composite of 15 individual indicators, such as the proportion of patients taking warfarin and prescribed an oral non-steroidal anti-inflammatory drug.

Main results and the role of chance

139 404 of 1 760 223 (7.92%, 95% confidence interval 7.88% to 8.00%) registered patients were defined as being particularly vulnerable to adverse drug events because of age, pre-existing disease, or co-prescription. 19 308 of the 139 404 (13.9%, 95% confidence interval 13.7% to 14.0%) patients had received at least one high risk prescription in

the past year. In univariate analysis, patients were more likely to receive a high risk prescription if they were older (15.9% of patients aged 70-79 v 6.7% aged <40), lived in more deprived postcodes (15.3% of the most deprived fifth v 12.8% of the most affluent), and were prescribed long term drugs. In multivariate analysis, the number of long term drugs remained strongly associated with high risk prescribing, whereas associations with other patient level variables were largely accounted for. After adjustment for patient level variables, considerable variation remained between practices that was not accounted for by practice related structural variables, such as list size, training status, rurality, and Quality and Outcomes Framework indicator scores for the management of medicines. As all the prescribing examined is stated in national guidance to be contraindicated or to be avoided in routine practice, the high rates and large variation between practices suggest significant opportunities for improvement.

Bias, confounding, and other reasons for caution

Although we examined 15 indicators, constraints on feasibility meant that we could not examine other important indicators. The study is therefore likely to under-estimate the true rates of high risk prescribing. Although the prescribing measured was high risk it is sometimes appropriate, as prescribers and patients often have to make decisions in situations with no ideal course of action.

Generalisability to other populations

The practices are representative of the Scottish population, and we believe the results are generalisable to the rest of the United Kingdom. Patterns of high risk prescribing may vary more between other countries.

Study funding/potential competing interests

This study was funded by NHS Quality Improvement Scotland and Scottish government Chief Scientist Office, neither of whom had any role in the conduct or reporting of the study. We have no competing interests.

PERCENTAGE OF PATIENTS RECEIVING HIGH RISK PRESCRIPTION AND MULTILEVEL MODELING OF PATIENTS RECEIVING AT LEAST ONE HIGH RISK PRESCRIPTION

No of drugs prescribed long term (No of patients)	% of patients receiving high risk prescription (95% CI)	Multilevel model	
		Univariate odds ratio (95% CI)	Adjusted odds ratio (95% CI)*
0 (19 082)	4.3 (4.1 to 4.7)	1	1
1 or 2 (21 709)	11.0 (10.5 to 11.4)	2.68 (2.47 to 2.91)	2.69 (2.47 to 2.92)
3 or 4 (30 460)	12.7 (12.3 to 13.1)	3.18 (2.94 to 3.43)	3.24 (2.99 to 3.52)
5 or 6 (30 345)	14.5 (14.1 to 14.9)	3.69 (3.42 to 3.99)	3.79 (3.49 to 4.11)
7 or 8 (20 445)	18.3 (17.8 to 18.8)	4.87 (4.50 to 5.27)	5.01 (4.61 to 5.45)
9 or 10 (10 372)	21.5 (20.7 to 22.3)	5.92 (5.44 to 6.45)	6.06 (5.54 to 6.63)
≥11 (6991)	26.6 (25.5 to 27.6)	7.81 (7.15 to 8.54)	7.91 (7.20 to 8.69)

*Adjusted for age and sex.