RESEARCH

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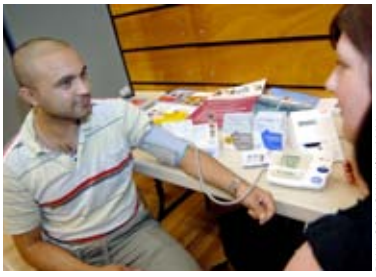

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- Barriers to providing end of life care for people with dementia: a whole-system qualitative study http://spcare.bmj.com/content/2/2/103
- Time to end the distinction between mental and neurological illnesses http://www.bmj.com/content/344/bmj.e3454
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Cardiovascular safety of central nervous system stimulants in children and adolescents

In this cohort study US researchers analysed automated healthcare claims data from 1 219 847 children and young people eligible for 28 state Medicaid programmes. They found that treatment with central nervous stimulants was not significantly associated with an increase in the short term risk of severe cardiac events. However, as the authors point out, analyses cannot be generalised to children with long term use of stimulants, and long term effects of slight increases in heart rate or blood pressure are unknown.
(*BMJ* 2012:345:e4627)

Validation of treatment strategies for enterohaemorrhagic *Escherichia coli* O104: H4 induced haemolytic uraemic syndrome: case-control study

Haemolytic uraemic syndrome induced by enterohaemorrhagic *E coli* is a severe self limiting acute condition. The findings of this case-control study question the benefit of eculizumab and of plasmapheresis with or without glucocorticoids. Patients with established haemolytic uraemic syndrome seemed to benefit from antibiotic treatment and this should be investigated in a controlled trial, say the authors.
(*BMJ* 2012:345:e4565)

RESEARCH RESPONSE ON BMJ.COM

"This interesting study fails to show any benefit from psychosocial intervention. In the future there should be modification of the type of intervention. Psychosocial intervention should always be part of the management of dementia because of the chronicity and the disabling and long term consequences of treatment of dementia."

Rizaldy Pinzon, neurologist, Bethesda Hospital, Yogyakarta, Indonesia, in response to "Efficacy of psychosocial intervention in patients with mild Alzheimer's disease: the multicentre, rater blinded, randomised Danish Alzheimer Intervention Study (DAISY)." (*BMJ* 2012;345:e4693)

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Lay perspectives on hypertension and drug adherence: systematic review of qualitative research

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EDITORIAL by Altiner

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Cite this as: *BMJ* 2012;344:e3953
doi: 10.1136/bmj.e3953

This is a summary of a paper that was published on bmj.com as *BMJ* 2012;344:e3953

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- Antihypertensive drugs and risk of incident gout among patients with hypertension: population based case-control study (*BMJ* 2012;344:d8190)
- Effect of pay for performance on the management and outcomes of hypertension in the United Kingdom: interrupted time series study (*BMJ* 2011;342:d108)
- Nurse led interventions to improve control of blood pressure in people with hypertension: systematic review and meta-analysis (*BMJ* 2010;341:c3995)

doc2doc
- doc2doc forum discussion: How do you explain the causes of hypertension to patients? http://bit.ly/OTbV9r

STUDY QUESTION How does patients' understanding about hypertension affect their drug taking behaviour?

SUMMARY ANSWER Patients from many countries and different ethnic groups perceived that hypertension was caused principally by stress, and resulted in symptoms. Many reduced or stopped treatment in response to a reduction in symptoms or stress.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS Many qualitative studies have been done to explain poor control of hypertension, particularly in ethnic minority groups. Contrary to the conclusions of individual studies, this review found no evidence of differences in understanding between ethnic, cultural, or geographical groups.

Selection criteria for studies

We carried out a systematic review and narrative synthesis of qualitative research. Data sources were Medline, Embase, the British Nursing Index, Social Policy and Practice, and PsycInfo from inception until October 2011, and reference lists of relevant papers. We included reports of face to face qualitative interviews and focus groups looking at patients' perspectives on hypertension and drug taking; we excluded telephone interviews and quantitative questionnaire analyses. We included studies of people with uncomplicated hypertension and excluded those principally (over 50%) of people with existing cardiovascular disease or diabetes or who were pregnant. Studies were included regardless of quality. A narrative synthesis was carried out using the 2006 UK Economic and Social Research Council research methods programme guidance, and sensitivity analyses were done to examine similarities and differences due to nationality, ethnicity, and study quality.

Primary outcome

Patients' understanding and experiences of hypertension and drug taking.

Main results and role of chance

59 papers reporting 53 qualitative studies were included in the synthesis from 16 countries (United States, United Kingdom, Brazil, Sweden, Canada, New Zealand, Denmark, Finland, Ghana, Iran, Israel, Netherlands, South Korea, Spain, Tanzania, and Thailand). A large proportion of participants thought that hypertension was principally caused by stress and produced symptoms, particularly headache, dizziness, and sweating. Participants widely intentionally reduced or stopped taking drugs without consulting their doctor. Participants commonly perceived that their blood pressure improved when symptoms abated or when they were not stressed, and that treatment was not needed at these times. Participants disliked drugs and their side effects, and feared addiction. These findings were consistent across countries and ethnic groups. Participants also reported various external factors that prevented adherence, including being unable to find time to take the drugs or see their doctor; having insufficient money to pay for drugs, the cost of appointments, and the costs of healthy food; a lack of health insurance; and forgetfulness.

Bias, confounding, and other reasons for caution

We included studies from peer reviewed journals only, to retrieve the highest quality research. It seems likely that a body of qualitative research also exists in book chapters, university theses, and conference presentations. Although we applied no language restriction for inclusion and included some non-English language papers, we would have missed those not listed on English language databases. Certain groups were represented in the research disproportionately: nearly half of the studies looked at an ethnic minority population and nearly half were carried out in the United States. Although a potential source of bias, the themes in these papers did not differ substantially from those from other countries, or from studies without restriction to an ethnic group.

Study funding/potential competing interests

IJM was employed as a clinical editor for *Clinical Evidence* at BMJ Group from 2008 to March 2010. This article presents independent research commissioned by the National Institute for Health Research (NIHR) under its programme grants for applied research funding scheme (RP-PG-0407-10184). The views expressed in this article are those of the authors and not necessarily those of the National Health Service, the NIHR, or the Department of Health.

Symptoms most widely associated with hypertension

Symptom	Countries (no of studies)
Headache	Brazil (4), Canada (1), Denmark (1), Ghana (1), Netherlands (2), South Korea (1), Sweden (2), UK (2), USA (8)
Dizziness	Brazil (3), Canada (1), Denmark (1), Ghana (1), Netherlands (1), New Zealand (1), South Korea (1), Sweden (1), Tanzania (1), Thailand (1), UK (3), USA (9)
Palpitations/racing heart	Brazil (3), Canada (1), Netherlands (1), Sweden (1), Tanzania (1), USA (3)
Sweating	Brazil (1), Canada (1), Netherlands (1), Tanzania (1), UK (1), USA (1)
Tiredness	Brazil (3), Canada (1), Denmark (1), Ghana (1), Sweden (2), UK (1), USA (2)

Derivation and validation of age and temperature specific reference values and centile charts to predict lower respiratory tract infection in children with fever: prospective observational study

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EDITORIAL by Kilonback

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Cite this as: *BMJ* 2012;344:e4224
doi: 10.1136/bmj.e4224

This is a summary of a paper that was published on bmj.com as *BMJ* 2012;344:e4224

STUDY QUESTION Can reference values and centile charts for respiratory rate, based on age and body temperature, accurately predict the presence of lower respiratory tract infection in children with fever?

SUMMARY ANSWER Cut-off values at the 97th centile of charts based on age and body temperature performed better than existing respiratory rate thresholds for detecting the presence of lower respiratory tract infection.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS Respiratory rate is an important predictor of lower respiratory tract infections, and is affected both by underlying respiratory disease and the presence of fever. Age specific and temperature dependent reference values for respiratory rate reduce misclassification of tachypnoea in children with fever, and are more useful for detecting lower respiratory tract infections than existing threshold values, which do not adjust for the presence of fever.

Participants and setting

We developed age specific and temperature dependent reference values for respiratory rate using data from febrile children attending the paediatric emergency department of one hospital in the Netherlands, in 2006 and 2008. We validated the reference values' predictive ability in febrile children at risk of lower respiratory tract infection who were recruited from the emergency department of a hospital in the Netherlands (n=311, 2003-05) and the paediatric assessment unit of a hospital in the United Kingdom (n=360, 2005-06).

Design, size, and duration

In this prospective observational study, we used the derivation population (n=1555) to produce respiratory rate centile charts, and calculated 50th, 75th, 90th, and 97th centiles of respiratory rate at a specific body temperature. Multivariable regression analysis explored associations between respiratory rate, age, and temperature. Results were validated in the validation population (n=671) by calculating diagnostic performance measures, z scores, and corresponding centiles of children with diagnoses of pneumonic lower respiratory tract infection (confirmed by chest radiograph), non-pneumonic lower respiratory tract infection, and non-lower respiratory tract infection.

Main results and the role of chance

Respiratory rate increased overall by 2.2 breaths/min per 1°C rise (standard error 0.2), after accounting for age and temperature in the model. Age and temperature dependent cut-off values at the 97th centile were more useful to rule in lower respiratory tract infections (specificity 0.94 (95% confidence interval 0.92 to 0.96), positive likelihood ratio 3.66 (2.34 to 5.73)) than existing respiratory rate thresholds such as Advanced Pediatrics Life Support (APLS) values (0.53 (0.48 to 0.57), 1.59 (1.41 to 1.80)). However, centile cut-off values could not discriminate between pneumonic and non-pneumonic lower respiratory tract infections.

Respiratory rate values expected at different temperatures in children (aged 1 month to <16 years). *Values above age specific upper thresholds as defined by APLS

Temperature (°C), by age group	Respiratory rate centiles (breaths/min)			
	50th	75th	90th	97th
Age 1 to <12 months				
36.0 to 36.9	37	45*	55*	65*
37.0 to 37.9	38	48*	57*	69*
38.0 to 38.9	40*	50*	60*	72*
39.0 to 39.9	42*	52*	63*	75*
Age 12 to <24 months				
36.0 to 36.9	28	35	41*	49*
37.0 to 37.9	32	39*	47*	55*
38.0 to 38.9	35	42*	50*	60*
39.0 to 39.9	36*	44*	53*	62*
Age 24 months to <5 years				
36.0 to 36.9	23	27	31*	36*
37.0 to 37.9	25	30	35*	40*
38.0 to 38.9	27	32*	38*	44*
39.0 to 39.9	29	35*	41*	48*
Age 5 to <16 years				
36.0 to 36.9	19	23	27*	32*
37.0 to 37.9	21	26*	30*	36*
38.0 to 38.9	23	28*	34*	41*
39.0 to 39.9	24	30*	36*	44*

Bias, confounding, and other reasons for caution

We measured respiratory rate by clinical counting, which can vary depending on the observer's expertise and is less accurate than other more objective methods. Also, a detailed description of the child's wellbeing, other than just crying or distress, would have added to the validity of the centiles. Both procedures, however, reflect common clinical practice, and increase the face validity of the centile charts and external generalisability to routine practice.

Generalisability to other populations

Our findings can be applied to the general population of febrile children visiting most emergency care settings. We did not assess the centile charts' validity or diagnostic performance in primary care or in low or middle income countries.

Overdiagnosis and mistreatment of malaria among febrile patients at primary healthcare level in Afghanistan: observational study

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Cite this as: *BMJ* 2012;345:e4389
doi: 10.1136/bmj.e4389

This is a summary of a paper that was published on bmj.com as *BMJ* 2012;345:e4389

STUDY QUESTION Using conventional microscopy or clinical diagnosis based on symptoms alone, how accurate is the diagnosis and treatment of vivax and falciparum malaria in basic clinics in Afghanistan?

SUMMARY ANSWER Even when parasite based diagnosis of malaria is available, most patients treated with a malaria drug do not have malaria and true cases do not receive appropriate treatment, a result of inaccurate microscopy and poor clinician adherence to negative slide results. With clinical diagnosis, over 99% of those treated for malaria had no parasites. In a context where vivax malaria predominates most cases of falciparum malaria were missed.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS Assessments in African settings show that malaria drugs are often poorly targeted; this study shows that in this vivax predominant part of Asia the results were similar. Malaria is often overdiagnosed, adherence to test results is poor, and cases of falciparum malaria are not identified and consequently patients are not treated with artemisinin combination therapy.

Participants and setting
Participants were patients at 22 rural Afghan clinics: 12 in eastern Afghanistan, where malaria transmission is higher (incidence around 10/1000 per year) and 10 in northern Afghanistan where malaria transmission is lower (incidence <1-10/1000 per year). All clinics in the east and half of those in the north had microscopy. The remaining five clinics in the north had no parasite based means of diagnosing malaria and relied only on clinical diagnosis.

Design, size, and duration
From June to September 2009 we recruited 2357 patients who attended the study clinics with self reported fever. Clinicians enrolled the patients and recorded symptoms, took a blood slide (if available), and noted the final diagnosis and treatment given. To identify true cases of malaria we took a double read reference blood slide from all patients.

Main results and the role of chance
In health centres using clinical diagnosis, although 413 of 414 of patients were negative for malaria by reference slide, 412 (99%) received a malaria drug and 47 (11%) received an antibiotic. Using microscopy, 49.6% (729/1471) of patients with a negative reference slide result received a malaria drug and 30.3% (445/1471) an antibiotic. Among patients positive for malaria, 94% (443/472) correctly received a malaria drug but only one of six cases of falciparum malaria was detected and appropriately treated. The specificity of microscopy was between 72.9% and 79.8%. In response to negative clinic slide results, malaria drugs were prescribed to 28.5% (302/1059) of patients and antibiotics to 41.1% (446/1084). Differences were apparent between settings where microscopy was established (east) and newly introduced (north). Nurses were less likely to misprescribe than doctors.

Bias, confounding, and other reasons for caution
We examined confounding using logistic regression adjusting for preset variables: type of diagnosis (microscopy or symptoms), reference slide diagnosis (malaria or not), sex, age group, clinician type (nurse, midwife, or doctor), and clinic type (Comprehensive Health Centres or Basic Health Centres). These did not alter the conclusions of the uncorrected analysis for the primary outcome. As an observational study, this may be subject to a Hawthorne effect, where behaviour may be changed by observation.

Generalisability to other populations
Afghanistan's health service has received significant investment since 2001, and healthcare at primary level should not be assumed to be inferior to other south and central Asian health systems. The results may well be typical of rural south and central Asia, where vivax malaria predominates, the population at risk exceeds two billion, and malaria epidemiology is comparable.

Study funding/potential competing interests
We have no competing interests. This study was sponsored by the ACT Consortium at the London School of Health and Tropical Medicine with a grant from the Bill and Melinda Gates Foundation.

bmj.com
- Risk factors for mortality from imported falciparum malaria in the United Kingdom over 20 years: an observational study (*BMJ* 2012;344:e2116)
- Protective efficacy of co-trimoxazole prophylaxis against malaria in HIV exposed children in rural Uganda: a randomised clinical trial (*BMJ* 2011;342:d1617)
- Rapid testing for malaria in settings where microscopy is available and peripheral clinics where only presumptive treatment is available: a randomised controlled trial in Ghana (*BMJ* 2010;340:c930)
- Imported malaria and high risk groups: observational study using UK surveillance data 1987-2006 (*BMJ* 2008;337:a120)

Accuracy of diagnosis and treatment for malaria in 22 Afghan clinics. Values are number with outcome/number in group (percentage)

		North	
Results and treatment	East: established microscopy	New microscopy	Clinical diagnosis
Diagnostic accuracy:			
False positive result	329/1212 (27.1)	39/193 (20.2)	412/413 (99.8)
False negative result	47/451 (10.4)	—	0/1
Adherence to clinic slide result:			
Negative result, received malaria drug	270/905 (29.8)	32/154 (20.8)	—
Positive result, no malaria drug	1/733 (0.1)	2/39 (5.1)	—
Overall treatment accuracy	1056/1740 (60.7)	127/202 (62.9)	3/415 (0.7)

Predicting the 10 year risk of cardiovascular disease in the United Kingdom: independent and external validation of an updated version of QRISK2

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Cite this as: *BMJ* 2012;344:e4181
doi: 10.1136/bmj.e4181

This is a summary of a paper that was published on bmj.com as *BMJ* 2012;344:e4181

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- Predicting the 10 year risk of cardiovascular disease in the United Kingdom: independent and external validation of an updated version of QRISK2 (*BMJ* 2012;344:e4181)
- Comparing risk prediction models (*BMJ* 2012;344:e3186)
- Communicating risk (*BMJ* 2012;344:e3996)

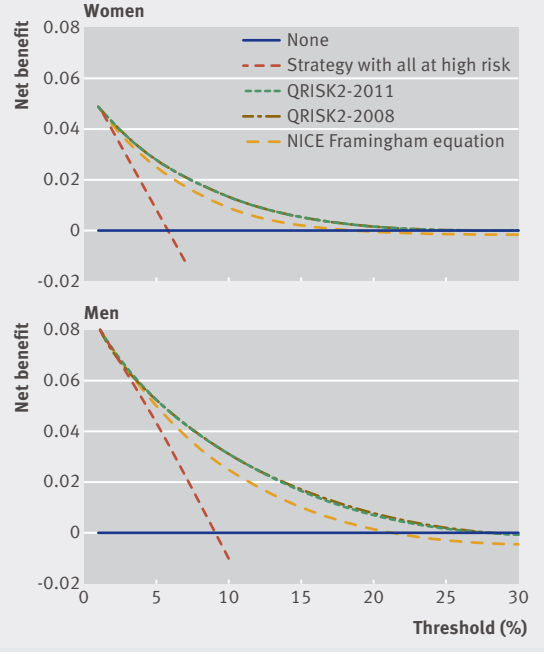
STUDY QUESTION Does the updated version of QRISK2 (QRISK2-2011) provide an improvement over the National Institute for Health and Clinical Excellence version of the Framingham risk score for predicting the 10 year risk of cardiovascular disease in the United Kingdom?

SUMMARY ANSWER QRISK2-2011 is more accurate in identifying a high risk population for cardiovascular disease in the United Kingdom than the NICE version of the Framingham equation. QRISK2-2011 is well calibrated, with reasonable agreement between observed and predicted outcomes, whereas the NICE Framingham equation seems to consistently over-predict risk in men by about 5% and shows poor calibration in women.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Cardiovascular risk assessment in the United Kingdom is currently assessed using either QRISK2 or the NICE Framingham equation. Independent evaluation and comparison of an updated version of QRISK2 against the NICE Framingham equation continue to show that QRISK2 identifies a high risk group of patients who will go on to experience more cardiovascular events over the next 10 years than a similar group identified by the NICE Framingham equation. Furthermore, the NICE Framingham equation is miscalibrated for a UK population, and current treatment thresholds seem limited when using this model.

Decision curves for participants aged 34 to 75 years in The Health Improvement Network



Participants and setting

364 general practices from the United Kingdom supplying The Health Improvement Network database, contributing two million patients (11.8 million person years and 93 564 cardiovascular events) aged 30-84 years and registered between June 1994 and June 2008.

Design, size, and duration

Prospective cohort study to validate an updated version of the QRISK2 cardiovascular risk score.

Main results and the role of chance

The results from this independent and external validation of QRISK2-2011 indicate that the updated version of QRISK2 still provides improved prediction of a patient's 10 year risk of cardiovascular disease over the NICE version of the Framingham equation in the United Kingdom. Discrimination and calibration statistics were better with QRISK2-2011 compared with the NICE Framingham equation. At the traditional treatment threshold of 20% used to designate an individual at high risk of developing cardiovascular disease, the net benefit of QRISK2-2011 is that the model identified an additional five more men and two more women per 1000 without increasing the number treated unnecessarily compared with the NICE Framingham equation. There seems to be no net benefit in using the 20% threshold for the NICE Framingham equation for identifying men or women at an increased risk of developing cardiovascular disease over the next 10 years.

Bias, confounding, and other reasons for caution

High levels of data were missing for the total serum cholesterol to HDL ratio; however, multiple imputation with 10 multiple imputed datasets appropriately dealt with the missing data. Omitting patients with missing data considerably reduces the sample size, and for studies evaluating the performance of a risk prediction model will lead to biased results.

Study funding/potential competing interests

This research received no specific grant from any funding agency in the public, commercial, or not for profit sectors.