# Clinical reviews

Our panel of GPs review recent research papers in their specialist areas that may influence the way you practise

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**Urology**
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GPwSI Urology, Bristol

## Mental health

# Should we abandon the PHQ-9?

It is uncertain whether the use of structured assessment tools (PHQ-9, HADS-D or BDI-III) improves outcomes for depressed patients and the QOF depression severity indicators should be abandoned, a systematic review has concluded.

Eight studies met the inclusion criteria. There was only one (quasi) randomised controlled trial; the rest were observational studies.

The rationale for the assessment of depression severity at the onset of treatment is to improve the targeting of treatment to those who will benefit in accordance with the NICE stepped care guideline. In particular, antidepressants should not be used for the initial treatment of mild depression but should be routinely used for those with moderate to severe depression.

There was low quality evidence that severity assessments facilitate appropriate interventions but none of the studies looked at depression-related outcomes. Patients felt that the assessment tools improved diagnostic accuracy and made them feel they were being taken seriously. However, GPs preferred to rely on their clinical judgement and generally ignored severity scores which did not agree with their assessment.[1]

An analysis of medical records from 38 UK practices found that exactly the same proportion of patients assessed with the PHQ-9 and HADS were prescribed antidepressants despite a large difference in the severity scores (83.5% and 55.6% respectively rated moderate to severe).[2]

GPs are right to question the validity and utility of depression severity scores. A recent study compared severity measures obtained with the four commonly used structured assessment tools with a psychiatrist's assessment using the Hamilton Rating Scale for Depression (HRSD).

The HADS underestimated severity whereas the PHQ-9 and the BDI overestimated severity; to avoid this the authors recommend revised cut-off scores of 9, 12 and 23 respectively. However, even with the revised cut-offs none of these tools was sufficiently accurate to be used in clinical settings.[3]

The rationale for follow-up severity assessments is first to identify non-responders and adjust treatment accordingly and second to encourage patients to continue treatment for an adequate length of time (at least six months after remission).

There was conflicting evidence on whether follow-up severity scores influenced management. The American COMET study found that they did not[4] whereas a UK retrospective cohort study found that patients with an inadequate response to treatment (fall in PHQ-9 score $\leq 1$) were nearly five times as likely to have their treatment adjusted than those with an adequate response (fall in PHQ-9 score $\geq 5$).[5]

Surprisingly, the COMET study did find that follow-up severity assessments increased the likelihood of response to treatment and remission. One possible explanation is that patients were encouraged to continue their treatment for longer.

Should we continue to use severity assessment questionnaires? I think a case can still be made for using the PHQ-9, for the following reasons:

- It encourages us to apply the DSM IV diagnostic criteria
- A score $\leq 10$ can be used to rule out moderate depression (negative likelihood ratio 0.04)[6] in the same way that BNP levels below the cut-off value are used to rule out heart failure
- It enhances patients' confidence in our diagnosis, thereby potentially increasing adherence to treatment
- The main value of follow-up scores is that they encourage case management which in my opinion is the key to improving outcomes in depression.

**DR PHILLIP BLAND**

- **Shaw EJ, Sutcliffe D, Lacey T, Stokes T. Assessing depression severity using the UK Quality and Outcomes Framework depression indicators: a systematic review. *Br J Gen Pract* 2013;DOI: 10.3399/bjgp13X667169**

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**3** Cameron IM, Cardy A, Crawford JR et al. Assessing the validity of the PHQ-9, HADS, BDI-III and QIDS-SR16 in measuring of depression in a UK sample of primary care patients with a diagnosis of depression. Healthcare Improvement Scotland. Edinburgh. 2011
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## Urology

# Severity of erectile dysfunction predicts CVD risk

Erectile dysfunction (ED) is a risk marker for cardiovascular disease (CVD), a large prospective population-based study from Australia has found.

The 45 and Up Study linked data derived from postal surveys, carried out between 2006 and 2009, with hospitalisation and death data, up to June and December 2010, respectively, on 95,038 men in this age group.

The aim of this part of the study was to examine the relationship between the severity of ED and CVD-related hospital admission or all cause mortality.

The authors found that ED increased in prevalence with age. The rate of severe ED was:

- 2.2% age 45-54
- 6.8% age 55-64
- 20.2% age 65-74
- 50% age 75-84
- 75.4% age ≥ 85 years

There were 7,855 admissions for CVD and 2,304 deaths during the follow-up period.

The risk of CVD and death increased steadily with increasing severity of ED. Men were divided into two groups, with and without a previous record of CVD. In those without previous CVD, those with severe versus no ED had increased risks of: ischaemic heart disease risk ratio (RR) 1.60, heart failure RR 8.0, peripheral vascular disease RR 1.92, and all cause mortality RR 1.93. RRs for men with previous CVD were 1.70, 4.40, 2.46, and 2.37, respectively (see table 1, below).

This is a large study and adds further weight to the argument that all men presenting with ED should be considered as high risk for CVD unless proved otherwise.

ED can be considered as a form of 'penile angina' with atherosclerosis affecting the small penile arteries typically a few years before larger coronary arteries are affected.

The authors state clearly that ED is not a cause of CVD but is a risk marker serving as an indicator of underlying common pathophysiological processes such as atherosclerosis and endothelial dysfunction.

While the risk of CVD increases with ED severity it is clear that even those men with mild or moderate ED are at significantly increased risk and should undergo full cardiovascular risk assessment using risk scores.

**DR JONATHAN REES**

● **Banks E, Joshy G, Abhayaratna WP et al. Erectile dysfunction severity as a risk marker for cardiovascular disease hospitalisation and all-cause mortality: a prospective cohort study. *PLOS Medicine* 2013:10 (1):e1001372**

**Table 1**

**Increased risks of outcomes in those with severe versus no erectile dysfunction**

| | Men without previous CVD | | Men with previous CVD | |
|---|---|---|---|---|
| | Risk ratio | 95% CI | Risk ratio | 95% CI |
| Ischaemic heart disease | 1.60 | 1.31-1.95 | 1.70 | 1.46-1.98 |
| Heart failure | 8.0 | 2.64-24.2 | 4.40 | 2.64-7.33 |
| Peripheral vascular disease | 1.92 | 1.12-3.29 | 2.46 | 1.63-3.70 |
| All cause mortality | 1.93 | 1.52-2.44 | 2.37 | 1.87-3.01 |

## Cardiovascular disease

# Why do patients take aspirin for primary prevention?

A primary care study has shown that many patients continue to use aspirin for primary prevention, with almost two thirds doing so on the advice of their family doctor, despite studies showing an unfavourable risk/benefit profile.

The study was a cross-sectional, self-reported, waiting room questionnaire in two North American primary care clinics. Patients were 50 years of age or older.

Data were collected on the overall prevalence of aspirin use, the proportion used for primary or secondary cardiovascular prevention, and use by patient age and sex. The proportion who initiated aspirin on the advice of a physician and patient beliefs about the role of aspirin were also recorded.

Overall 807 patients completed the questionnaire with a response rate of 89.1%.

A total of 318 patients (39.8%) were taking aspirin regularly, 274 (87.0%) of whom took it for the prevention of cardiovascular disease. More than half (53.1%) of these took it for primary prevention and 46.9% for secondary prevention. In the primary prevention cohort 62.0% took aspirin on the advice of their family doctor.

However, of the 200 patients who had underlying cardiovascular disease only 62.5% took aspirin.

Nearly three quarters of patients (70.9%) who took aspirin for cardiovascular prevention believed that the benefits outweighed the risks. This view did not differ between those patients taking it for primary and »

those taking it for secondary prevention.

Low dose aspirin has an established role in the secondary prevention of cardiovascular disease but the picture is far from clear in primary prevention. Many professional societies and guidelines now discourage the use of aspirin in people with no underlying cardiovascular disease. This is the result of a number of large studies showing an unfavourable risk/benefit profile in such patients.

Patients can of course continue to self-medicate with aspirin and physicians are often slow to change historical patterns of prescribing or may remain unconvinced by the growing evidence base.

The authors conclude that aspirin use is common and more than half take it for the primary prevention of cardiovascular disease with primary care physicians continuing to support this strategy.

They postulate that more education as to the risk/benefit profile of aspirin is required for both patients and doctors. This would help to target aspirin use to those patients who are most likely to derive the greatest overall benefit.

**DR PETER SAVILL**

● **Kolber M, Sharif N, Marceau R, Szafran O et al. Family practice patients' use of acetylsalicylic acid for cardiovascular disease prevention. *Can Fam Physician* 2013;59(1):55-61**

## Smoking cessation

# Women who quit before 40 significantly improve mortality risk

Women who give up smoking before the age of 40 reduce their excess mortality risk by 90% and those who stop before 30 by > 97%, results from the Million Women Study have shown.

This UK prospective cohort study aimed to quantify accurately the excess mortality associated with smoking in women, together with the effects of cessation, by reviewing a large cohort born in the 1940s.

From 1996 to 2001 participants were recruited into the Million Women Study through the NHS Breast Screening Programme. As part of the study participants completed a questionnaire which included lifestyle and smoking information. Participants were followed up by postal questionnaire at three years, when information on stopping smoking was first sought, and eight years. Date and cause of death were automatically notified to the study authors up to 2011, a mean of 12 years after entry.

Patients with a baseline history of cancer (other than some skin cancers), heart disease, stroke and current treatment for respiratory disease were excluded leaving a cohort of 1.2 million women, age 50-69 years, who were included. Mean age at recruitment was 55, and 6% died during the average 12 years of follow-up, at a mean age of 65.

At baseline 20% were current smokers, 28% former smokers and 52% never smokers. Smokers were more likely to live in deprived areas, drink more than 14 units of alcohol weekly, and not to undertake strenuous exercise. Regular exposure to second-hand smoke in never smokers was 13%. Of the current smokers at baseline, 23% had stopped at the three-year survey and 44% at eight years.

At the 12-year mortality follow-up those who were current smokers at baseline had almost three times the mortality rate of never smokers.

The risks increased steeply with the amount smoked, but even for those smoking fewer than 10 cigarettes a day at baseline mortality was doubled.

The age at which women had started smoking affected overall mortality decades later, with those starting at age 15 at greatest risk. Common causes of death included cancer, vascular and respiratory diseases. All results were adjusted for alcohol intake.

Overall, the benefits of stopping were greater for those stopping earlier. Those stopping in the 25-34 year group avoided about 97% of the excess overall mortality compared with those who continued smoking, while those who stopped by about 40 avoided 90%.

Stopping smoking, at whatever age, reduced excess mortality, though even those who had stopped at ages 25-34 years had, decades later, measurably higher lung cancer mortality than never-smokers.

Former smokers who quit at age 25-34 or 35-44 had respective relative risks of 1.05 (95% CI:1.10-1.11) and 1.20 (95% CI:1.14-1.26) for all cause mortality and 1.84 (95% CI:1.45-2.34) and 3.34 (95% CI:2.76-4.03) for lung cancer mortality.

This paper confirms the very significant excess in mortality in women who smoke, and the authors concluded that female smokers lose at least 10 years of their lifespan.

GPs now have very specific and accurate information on the harms associated with smoking in women, and the substantial benefits of stopping, particularly at a relatively young age.

**DR JEZ THOMPSON**

● **Pirie K, Peto R, Reeves GK et al. The 21st century hazards of smoking and benefits of stopping: a prospective study of one million women in the UK. *Lancet* published online Oct 27 2012. http://dx.doi.org/10.1016/S0140-6736(12)61720-6**

## Diabetes

# Is early insulin effective in type 2 diabetes?

A short course of intensive insulin therapy in certain patients with newly diagnosed type 2 diabetes may induce remission, a meta-analysis suggests.

The researchers looked for studies which assessed the use of insulin for two to three weeks, at diagnosis of type 2 diabetes, on ß-cell function and/or insulin resistance or assessed long-term drug-free remission.

Of 1,645 studies only seven, published between 2004 and 2012, covering 839 patients, met the inclusion criteria. Six of the studies were from China, the other from Taiwan. Mean baseline $HbA_{1c}$ was 9.7-11.9% and BMI 24.0-27.7kg/$m^2$.

Pooled analysis of the seven studies showed a 13% improvement in ß-cell function and a 43% decrease in insulin resistance, using modelling.

The investigators postulate that removal of glucose toxicity might improve ß-cell function and reduce insulin resistance.

Four studies assessed glycaemic remission. Two thirds of the patients (66.2%) treated with the regimen had achieved glycaemic remission at 3 months follow-up. Respective figures for remission at 6, 12 and 24 months follow-up were 58.9%, 46.3% and 42.1%.

Although interesting the meta-analysis is open to question. The number of studies eligible was small, and of the seven studies fitting the criteria five were not randomised. All the study subjects were Chinese, and type 2 diabetes in this ethnic group is characterised by a good response to acarbose and sulfonylureas, and low insulin requirements.

In an accompanying editorial, DeVries suggests that because of this the Chinese patients could be more likely to obtain remission from early insulin use than their Western counterparts.[1] He also notes that there may be a Hawthorne effect: the subjects were more likely to adhere tightly to other aspects of lifestyle change because they were in a study.

The conclusion is that more studies are needed, with control groups and possibly across different ethnic groups, but at present there is no indication to deviate from existing guidelines. It may be that we will need to keep an open mind in the future about the timing of the use of insulin.

**DR MATTHEW LOCKYER**


● **Kaercher Kramer C, Zinman B, Retnakaran R. Short-term intensive insulin therapy in type 2 diabetes mellitus: a systematic review and meta-analysis. *Lancet Diabetes Endocrinol* Published online January 30 2013. http://dx.doi.org/10.1016/S2213-8587(13)70006-8**

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## Obstetrics and gynaecology

# Identifying risk factors for cerebral palsy

A population-based case control study from Sweden has identified different potential risk factors for the subtypes of cerebral palsy.

A total of 356 cases of cerebral palsy were identified in children, aged four years or older, born at term, during the period 1983-1994, in Sweden. Of these, 47 cases were excluded, because of postnatal causes of cerebral palsy and spinal malformation. This included 25 children with ataxic cerebral palsy as this condition can be difficult to differentiate from non-cerebral palsy syndromes.

The remaining 309 cases were included in the study. Two matched controls were selected for each case. Cerebral palsy was classified as dyskinetic or spastic. Spastic cerebral palsy was subdivided into hemiplegic, diplegic and tetraplegic cerebral palsy.

Case records were scrutinised and data associated with maternal history (e.g. maternal smoking and alcohol consumption, pre-eclampsia, hypertension and gestational diabetes), obstetric catastrophe (e.g. ruptured uterus, prolapsed cord, placental abruption) and postpartum neonatal encephalopathy were extracted. Encephalopathy was deemed present if the baby had neonatal seizures or any of the following lasting > 24 hours: altered consciousness; breathing or feeding difficulties; abnormal tone or reflexes.

Demographic and other data, such as results of antenatal ultrasound scanning were also collected.

Significant factors associated with cerebral palsy included obstetric catastrophe, low birthweight and meconium staining of liquor. Emergency caesarean section, an Apgar score < 7 at 5 minutes and neonatal encephalopathy were very strongly associated with cerebral palsy.

Birthweight, not living with the baby's father, admission to NICU, maternal weight and neonatal encephalopathy appeared to be risk factors for cerebral palsy in general, see table 1, below.

When sub-types of cerebral palsy were analysed in a multivariate analysis, see table 2, below, spastic diplegia and tetraplegia were most associated with gestational diabetes, mother not living with baby's father, emergency caesarean section and admission to NICU.

For spastic hemiplegia small head circumference and admission to NICU were the strongest associations.

A low Apgar score and admission to NICU were most associated with dyskinetic cerebral palsy which, unlike the spastic forms of cerebral palsy, was associated only with intrapartum and postnatal factors.

The authors were unable to identify a single risk factor that was pre-eminent. Rather they observed a mix of antenatal, intrapartum and postnatal factors which differed according to cerebral palsy subtype.

The authors conclude that the risk factors identified may be useful indicators for identifying children at risk of developing cerebral palsy and help to target individuals for early intervention programmes.

**DR CHRIS BARCLAY**

● **Ahlin K, Himmelmann K, Hagberg G et al. Non-infectious risk factors for different types of cerebral palsy in term-born babies: a population-based, case-control study. *BJOG* 2013;120:724-731**

**We welcome your feedback**

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**Table 1**

**Risk factors for cerebral palsy in term infants (multivariate analysis)**

| Risk factors | Odds ratio | 95% Confidence interval |
|---|---|---|
| Birthweight | 0.54 | 0.4-0.7 |
| Not living with the baby's father | 2.58 | 1.1-6.0 |
| Admission to NICU | 4.43 | 3.0-6.5 |
| Maternal weight at 34 weeks gestation | 1.02 | 1.0-1.03 |
| Neonatal encephalopathy | 69.22 | 9.4-511.9 |

**Table 2**

**Risk factors for spastic diplegia and tetraplegia (multivariate analysis)**

| Risk factors | Odds ratio | 95% Confidence interval |
|---|---|---|
| Gestational diabetes | 13.13 | 1.2-135.30 |
| Not living with the baby's father | 5.69 | 1.54-21.00 |
| Birth length | 0.83 | 0.7-0.9 |
| Emergency caesarean section | 19.72 | 2.27-171.7 |
| Admission to NICU | 3.18 | 1.7-6.0 |