

Clinical reviews

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

Reviewers

Addiction

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substance misuse

Cardiovascular disease

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Diabetes

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practitioner in diabetic
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Mental health

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Obstetrics and gynaecology

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Paediatrics

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Sexual health

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GP with an interest
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Smoking cessation

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Urology

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Obstetrics and gynaecology

Lifestyle factors associated with risk of gestational diabetes

Maintaining a healthy lifestyle before pregnancy is associated with a substantially lower risk of developing gestational diabetes mellitus (GDM), a large prospective cohort study has found.

The Nurses Health Study II recruited 116,671 female nurses aged 24-44 in 1989. Data were collected at baseline and regularly thereafter on a variety of lifestyle factors.

For the purposes of the analysis a low-risk group was identified who had normal weight before pregnancy, took regular exercise, ate a healthy diet and who did not smoke.

Each lifestyle variable was carefully defined and scored. For example, a healthy diet was based on the US Department of Agriculture Healthy Eating Index and measured using food frequency questionnaires. Individual nurse's scores were then ranked in quintiles. Data on time spent on physical activity, BMI and smoking were handled similarly.

After ten years' follow-up, 20,136

singleton pregnancies had occurred in 14,437 women. There were 823 pregnancies affected by GDM.

Each lifestyle factor was found to be significantly and independently associated with the risk of developing GDM. The associations remained significant after adjustment for other known risk factors (increasing maternal age, high parity, family history of diabetes).

The incidence of GDM in the women with the healthiest lifestyles (non-smoking, most physically active i.e. ≥ 150 min/week of moderate to vigorous physical activity, healthiest eaters, BMI < 25 kg/m²) was 52% lower compared with all other pregnancies RR 0.48 (95% CI: 0.38-0.61).

When compared with the women with the lowest lifestyle scores, who met none of the healthy lifestyle criteria (in other words the women who might be a target group for GPs to identify) the healthiest had an 83% lower risk of GDM, RR 0.17 (95% CI: 0.12-0.25).

In 2001, a paper from the Nurses Health Study looking at incident diabetes in a cohort of nearly 85,000 female nurses over 16 years concluded that 91% of cases of diabetes could be attributed to habits and forms of behaviour that did not conform to the low-risk pattern.¹

Now the Nurses Health Study II has shown that similar lifestyle factors raise the risk of GDM.

GDM increases a woman's risk of hypertension, pre-eclampsia, and developing type 2 diabetes after pregnancy. It causes fetal macrosomia, is associated with congenital abnormalities, and the children of GDM pregnancies are also at higher risk of developing diabetes.

This large well conducted study revealed significant associations between modifiable lifestyle factors and the occurrence of GDM. It seems highly likely that the link is significantly causal too.

The message for GPs is, as in many

other conditions we see, to promote healthy lifestyle change effectively rather than just treat the consequences of its absence.

DR CHRIS BARCLAY

● **Zhang C, Tobias DK, Chavarro JE et al. Adherence to healthy lifestyle and risk of gestational diabetes mellitus: prospective cohort study. *BMJ* 2014;349:g5450 doi: 10.1136/bmj.g5450**

REFERENCE

1 Hu FB, Manson JE, Stampfer MJ et al. Diet, lifestyle and the risk of type 2 diabetes in women. *N Engl J Med* 2001;345(11):790-7

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Cardiovascular disease

Do beta-blockers benefit patients with early CHD?

The use of beta-blockers in patients with new-onset coronary heart disease (CHD) is associated with a lower risk of cardiac events only in those who have had a recent myocardial infarction (MI), a study has shown.

The researchers examined the effectiveness of beta-blockers in preventing further cardiac events in patients with new onset coronary artery disease.

The trial enrolled 26,793 patients discharged after the index coronary event (acute coronary syndrome or coronary revascularisation) between 2000 and 2008 who did not use beta-blockers in the year before entry. Of these, 19,843 patients had a beta-blocker commenced within seven days of discharge from their initial coronary event.

Over an average of 3.7 years' follow-up, 6,968 patients had an MI or died. Beta-blocker therapy was associated with an adjusted hazard ratio (HR) for mortality of 0.90 (95% CI:0.84-0.96), and an adjusted HR for death or MI of 0.92 (95% CI:0.87-0.97).

The association between beta-blockers and outcomes differed significantly between patients with and without a recent MI; HR for death 0.85 vs 1.02 and HR for death or MI 0.87 vs 1.03.

Beta-blockers are often used as a first-line drug both in the management of suspected or established coronary disease and post-MI. Despite the usefulness of this class of drugs in the management of angina they are often used in asymptomatic patients with coronary disease in the belief that they will reduce the incidence of further

coronary events. However, the effectiveness of beta-blockers in preventing cardiac events has been questioned for patients who have CHD without a prior MI.

The authors conclude that the use of beta-blockers in patients with new-onset CHD was associated with a lower risk of cardiac events but only among those patients with a recent MI.

DR PETER SAVILL

● **Andersson C, Shilane D, Go AS et al. Beta-blocker therapy and cardiac events among patients with newly diagnosed coronary heart disease. *J Am Coll Cardiol* 2014;64(3):247-52. doi: 10.1016/j.jacc.2014.04.042**

Smoking cessation

E-cigarettes help smokers to quit

Early evidence suggests that e-cigarettes help smokers interested in quitting to stop or cut down, a systematic review has found.

The researchers searched Medline, PsycINFO, Cochrane Methodology Register, Health Technology Assessment and NHS economic evaluation database, Google Scholar, EMBASE and CINAHL up to February 2014. They found 81 papers they deemed relevant as they presented original data and provided evidence that could guide regulatory decisions.

The use of e-cigarettes had increased rapidly over the past five years. In the UK, use in smokers increased from 2.7% in 2010 to 6.7% in 2012 and 11% in 2013. In the US general population, use increased from 0.6% in 2009 to 2.7% in 2010 and 6.2% in 2011. E-cigarette users tended to be younger, more educated and have higher incomes than non-users.

There has been speculation that

e-cigarette use will spread to non-smokers who want to experiment with nicotine use without the dangers of smoking. The reviewers found that e-cigarette ever use in non-smokers ranged from 0.1 to 3.8% (median 0.5%), and use within the past 30 days from 0 to 2.2% (median 0.3%).

Smokers consistently reported that e-cigarettes helped them to quit (42-99%) or to cut down (60-80%).

E-cigarettes, are designed to deliver a nicotine dose by inhalation from a cigarette-like device, but without the other harmful ingredients of tobacco smoke. They are made using nicotine containing e-liquids. For the major e-liquid brands the labelling of nicotine content was accurate and consistent, though the authors comment that the practical features of the actual device, including the size of the battery, the nature of the heating element, the ventilation holes and individual inhalation characteristics all have a substantial influence on the nicotine levels actually delivered.

Other contents of the aerosols included some toxicants, though in much lower concentrations than tobacco smoke, and some ingredients such as propylene glycol that have been implicated in other environments in reducing lung function and exacerbating rhinitis and asthma.

No long-term study has investigated passive inhalation associated with e-cigarettes, but the authors conclude that the risk is likely to be much lower than that associated with tobacco smoking.

Several small studies and case studies have suggested that e-cigarettes reduce the urge to smoke and that their use facilitates both reducing and quitting smoking in smokers interested in stopping.

In England, the growth of e-cigarette use has been accompanied by an increase in smoking cessation rates and no increase in smoking uptake. The devices are most frequently used by dependent smokers who want to reduce their risks.

The authors conclude by saying that regulatory verdicts on e-cigarettes and advice given by health professionals regarding their use need to follow the evidence base.

DR JEZ THOMPSON

● **Hajek P, Etter J-F, Benowitz N et al. Electronic cigarettes: review of use, content, safety, effects on smokers and potential for harm and benefit. *Addiction* 2014;109:1801-1810**

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Diabetes

Interval walking improves glycaemic control in type 2 diabetes

A small Danish study of patients with type 2 diabetes has shown that interval walking training has a beneficial effect on glycaemic control by increasing insulin sensitivity while maintaining insulin secretion.

Twenty men and 12 women, with type 2 diabetes of at least two years' duration, took part in this open, randomised, partial crossover trial. Exclusion criteria included the use of insulin, weight instability, high levels of physical activity (> 150 min/wk), evidence of liver, renal or cardiopulmonary disease or of diseases precluding physical activity.

Participants were randomly allocated to a control group with no exercise intervention, a continuous walking training group and an interval walking training group. After completing the control programme, five patients were re-randomised to one or other of the active arms. This gave eight patients in the control group, 12 in the continuous walking group and 12 in the interval walking group.

The exercise sessions were 60 minutes long and for five days a week. Step recorders were used to ensure the amounts of exercise were equivalent in the two exercise groups.

$\text{VO}_{2\text{max}}$ was used to demonstrate the increased aerobic intensity of the interval exercise training. Concordance with the exercise regimens was high. The study duration was four months.

Although HbA_{1c} was measured, this was not the main outcome measure for the glycaemic control. The subjects

underwent continuous glucose monitoring over 48 hours and had fasting insulin measurements. They were also tested with a hyperglycaemic clamp. This maintained the blood at a post-prandial level of glucose, and the further addition of a GLP-1 agonist infusion completed the simulation of the post-prandial state. Sophisticated biochemical testing (including biopsies of skeletal muscle) was performed to assay whether insulin signaling was having its effect on cell markers, and whether there were changes in mitochondrial metabolism.

Improvements in glycaemic control, measured by these detailed investigations, were only seen in the interval training group. In this group insulin secretion remained the same, but the sensitivity to insulin as measured by the fall in glucose rose by $49.8 \pm 14.6\%$; $P < 0.001$, and the peripheral glucose disposal increased by $14.5 \pm 4.9\%$; $P < 0.05$.

No changes were seen to suggest mitochondrial metabolism was altered, and the authors postulate that the improvements are the result of increased sensitivity to insulin in the interval exercise group.

The results must be interpreted with caution, because the study is small, and the lack of any improvement at all in the continuous exercise group is not consistent with other studies in the field. However, there has been considerable interest of late in the possibility that short bursts of higher intensity exercise are better than longer, lower intensity sessions, and this research adds weight to this.

In the future we will need to be more specific on the types of exercise regimens we recommend for patients to achieve the maximum benefit. In the meantime, I am still very happy to see any increase in activity levels at all in the majority of my diabetes patients.

DR MATTHEW LOCKYER

● Karstoft K, Winding K, Knudsen SH et al. Mechanisms behind the superior effects of interval vs continuous training on glycaemic control in individuals with type 2 diabetes; a randomised controlled trial. *Diabetologia* 2014;57:2081-93

Sexual health

Could urine testing be used to detect cervical HPV infection?

Urine sampling could potentially become an acceptable alternative to conventional cervical cytology for detecting cervical human papilloma virus (HPV), a systematic review and meta-analysis suggests.

The study authors searched databases including Medline, Embase, Cochrane Library, Web of Science, BIOSIS, DARE and SIGLE for articles relating to the use of urine samples in screening and detection of HPV for cervical cancer in sexually active women. Studies were excluded if they had a high prevalence of HPV, used populations comprising only patients with HIV, cervical cancer, high-grade CIN or whose age was below screening recommendations.

A total of 16 articles reporting on 14 studies, covering 1,443 women, were included in the meta-analysis.

Outcome data from the studies were pooled into a contingency table and a forest plot was used to look at heterogeneity of data across studies.

The authors looked at the sensitivities and specificities of any HPV detection, high-risk HPV, and HPV types 16 and 18, see table 1, below. »

Table 1

Urine detection of HPV in women

	Pooled sensitivity	Pooled specificity
Any HPV	87% (95% CI:78-92%)	94% (95% CI:82-98%)
High-risk HPV	77% (95% CI:68-84%)	88% (95% CI:58- 97%)
HPV 16 and 18	73% (95% CI:56-86%)	98% (95% CI:91-100%)

There was a high heterogeneity among studies; regression analysis showed the differences in diagnostic accuracy could not be explained by purpose of testing, mean age of participants, HIV status, cytology and biopsy results, detection methods, use of commercial methods, or risk bias caused by patient selection.

There was a 22-fold increase in overall accuracy in use of first-void urine compared with random or mid-stream samples; this is exclusively based on increased sensitivity of first-void urine samples. The relative sensitivity was 1.2 (95% CI:1.06-1.37; $P = 0.004$); there were no effects on specificity.

Routine screening using cervical cytology to detect and treat CIN can prevent cancers from progressing. However, despite availability of screening, cervical cancer is still the most common malignancy in women under 35. The coverage of screening in young women is also reducing.

HPV detection is being used as a method of cervical cancer screening. This can be more protective against higher-grade CINs compared with cervical smears. However, the sampling method is still invasive and time consuming and unlikely to improve the poor screening uptake.

Previous studies have shown that detection of urine HPV can be a feasible alternative to cervical sampling.

The authors of this systematic review concluded that where cervical testing for HPV is being considered for cervical cancer screening, urine-based testing can be considered instead as this may be an acceptable alternative to increase coverage for groups that are hard to reach.

The accompanying editorial¹ welcomed the suggestion of using urine HPV testing as a potentially useful self-sampling screening test. However, unlike vaginal self-samples, urine samples have not been evaluated for the detection of CIN – which is the outcome that matters most.

It may be some time before urine or vaginal self-samples can replace current cervical smears as further evaluation comparing urine testing and vaginal self-sampling in the detection of high-grade CIN as the primary endpoint needs to be done.

Until such time, women and clinicians will have to put up with the cumbersome, and for some embarrassing, procedure of cervical smears using speculum examinations.

DR RICHARD MA

● Pathak N, Dodds J, Zamora J, Khan K. Accuracy of urinary human papillomavirus testing for presence of cervical HPV: systematic review and meta-analysis. *BMJ* 2014; 349. g5264

REFERENCE

¹ Kitchener HC, Owens GL. Urine testing for HPV. *BMJ* 2014; 349: g5542

We welcome your feedback

If you would like to comment on any of the clinical reviews write to: editor@thepractitioner.co.uk



Inaugural Meeting

Tuesday 18 November 2014, 10am-3pm

**10-11 Carlton House Terrace
London SW1Y 5AH**

The Primary Care Urology Society (PCUS), led by Dr Jonathan Rees, is now established with registration open for its inaugural one day meeting on 18 November in London.

An online survey of interested healthcare professionals found that 75% of respondents wanted to increase their urology knowledge through the Society by learning with peers and 70% welcomed the opportunity to network with others in a community setting.

The Primary Care Urology Society will provide a forum for healthcare professionals working in primary and community care to discuss and debate practical and topical management issues in urology.

Further details about the PCUS and registration for its first meeting can be found at: www.primarycareurologysociety.org All interested healthcare professionals are invited to register.