Issue 77 – October 2015

This month in Eyes on Evidence

Intra-arterial treatment for acute ischaemic stroke
A Dutch randomised controlled trial found that people with acute ischaemic stroke who received mechanical thrombectomy, intra-arterial thrombolysis, or both, plus usual care were more likely to be independent and free from disability at 3 months than people who received usual care alone.

Drugs with anticholinergic effects and risk of cognitive impairment, falls and all-cause mortality
A systematic review and meta-analysis reported that drugs with anticholinergic effects were associated with an increased risk of cognitive impairment and all-cause mortality in older people, and some drugs were linked to an increased risk of falls.

Suicide prevention programmes in schools
A randomised controlled trial in 10 European countries found that an interactive programme for all pupils that raised awareness of factors associated with suicide and taught mental health coping skills (Youth Aware of Mental Health Programme) reduced the incidence of suicide.

Pregnancy outcomes in women who have had bariatric surgery
A Swedish population-based cohort study found that pregnant women who had previously undergone bariatric surgery for obesity had a lower risk of gestational diabetes, smaller infants, shorter gestation, and were at slightly higher risk of stillbirth or neonatal death than pregnant women with obesity who had not undergone surgery.

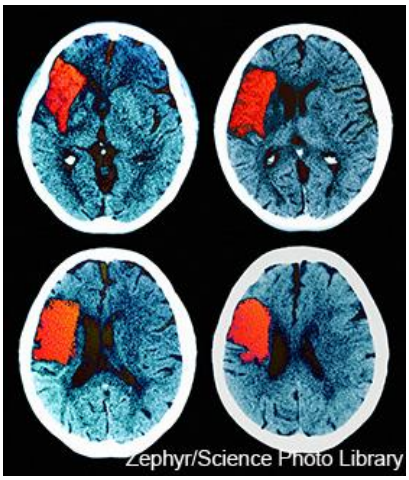
Physical and mental health of carers
A cross-sectional study in England reported that around 20% of carers experienced common mental disorders, and this poor mental health was directly related to caring rather than other stressors. A cohort study in Australia reported that more than a third of carers experienced deterioration of their physical or mental health after starting caring.

Evidence summaries from NICE's Medicines and Prescribing Programme
NICE has recently published medicines evidence summaries on:

- Prucalopride for chronic constipation
- Chronic pain: unintentional overdose in people receiving opioid analgesics for non-cancer pain
- Chronic obstructive pulmonary disease: the effect of roflumilast on exacerbations in people with severe disease – the REACT study.

Changes to the BNF
Changes have been introduced to the British National Formulary (BNF) to improve access to the latest information about medicines.

Intra-arterial treatment for acute ischaemic stroke



Overview: A stroke occurs when the blood supply to part of the brain is cut off, either by a blood clot (ischaemic stroke) or when a weakened blood vessel supplying the brain bursts (haemorrhagic stroke; NHS Choices 2014).

People with acute ischaemic stroke can be treated with intravenous thrombolysis, such as alteplase, which dissolves the blood clot and restores the flow of blood to the brain. However, alteplase is effective only if used very soon after onset of stroke (Emberson et al. 2014) and has limited efficacy in opening blockages of the major arteries in the brain (Bhatia et al. 2010).

Treatments that are delivered directly to the area of the blood clot are an alternative approach. Intra-arterial treatments can be broadly divided into those that apply thrombolytic agents to the affected area to dissolve the clot (intra-arterial thrombolysis) and those that break up or remove the clot using mechanical devices (mechanical thrombectomy).

Data from randomised trials indicate no advantage for intra-arterial thrombolysis over intravenous thrombolysis (IMS-3 trial and Synthesis trial). The efficacy of mechanical clot removal for treating acute ischaemic stroke is also not clear, and the procedure is associated with risks of serious complications (NICE 2013).

Current advice: The NICE guideline on stroke recommends thrombolysis with alteplase in people with acute ischaemic stroke. The technology appraisal on alteplase adds that treatment should be started as early as possible within 4.5 hours of onset of stroke symptoms. NICE does not have guidance on intra-arterial thrombolysis.

The NICE interventional procedure guidance on mechanical clot retrieval for treating acute ischaemic stroke states that clot removal can be used in patients with acute ischaemic stroke for whom thrombolysis is unsuitable or has failed. The procedure should be used with special arrangements for clinical governance, consent and audit or research. Selection of patients for mechanical clot removal should be

done by clinicians experienced in the use of thrombolysis for stroke. The procedure should be carried out in specialist centres by experienced interventional neuroradiologists with appropriate facilities and support.

The NICE pathway on stroke brings together all related NICE guidance and associated products on the condition in a set of interactive topic-based diagrams.

New evidence: An open-label randomised controlled trial at 16 centres in the Netherlands compared intra-arterial treatment plus usual care with usual care alone in acute ischaemic stroke. The Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands (MR CLEAN) by Berkhemer et al. 2015 recruited people with acute ischaemic stroke caused by a proximal occlusion in the anterior circulation of the brain.

People randomised to the intra-arterial treatment group received mechanical thrombectomy, intra-arterial thrombolysis or both. Usual care could include intravenous administration of alteplase. The primary outcome was degree of disability or dependence at 90 days, measured by the modified Rankin scale (7-point scale, with a score of 2 or less indicating functional independence).

A total of 233 (46.6%) people were randomly assigned to intra-arterial treatment plus usual care (intervention group) and 267 (53.4%) to usual care alone (control group). Intra-arterial treatment was performed in 196 (84.1%) people in the intervention group: 195 had mechanical thrombectomy and 1 had intra-arterial thrombolysis. Nearly all participants received intravenous alteplase (87.1% of the intervention group and 90.6% of the control group).

At 90 days, people in the intervention group were more likely to have a lower score on the modified Rankin scale than people in the control group (adjusted odds ratio [OR]=1.67, 95% confidence interval [CI] 1.21 to 2.30). A third (32.6%) of patients in the intra-arterial treatment group were functionally independent (modified Rankin score 0 to 2) compared with 19.1% of the control group (adjusted OR=2.16, 95% CI 1.39 to 3.38).

The proportion of people who had serious adverse events during the 90-day follow-up was similar in the intervention group (47.2%) and the control group (42.3%, p=0.31). No significant difference was seen in mortality at 7, 30 or 90 days of follow-up.

Strengths of this study include that intracranial arterial occlusion was confirmed with imaging. Limitations include that the control group was larger than the intervention group, and participants were not blinded to treatment allocation.

Commentary by Phil White, Professor of Neurointerventional and Diagnostic Neuroradiology, Newcastle University and Honorary Consultant Neurointerventionist, Newcastle upon Tyne NHS Foundation Trust:

“The MR CLEAN trial has had a major impact worldwide on stroke research and clinical practice. Since this study was first reported, 5 ongoing trials of intra-arterial treatment reviewed their data and stopped early because a pre-specified end point had been reached (ESCAPE, EXTEND-IA, REVASCAT, SWIFT-PRIME and THRACE trials). These recent thrombectomy data are compelling, generalisable and robust. Although trials that stop early do tend to overestimate effect size, this caveat does not apply to MR CLEAN.

“What is most exciting and striking regarding thrombectomy is the consistency among trials in reporting a large clinical benefit despite different protocols, populations and imaging criteria for selection of participants. To improve outcome by 1 point on the modified Rankin scale, just 3 to 4 patients need to be treated within 6 hours, compared with more than 10 patients treated within 4.5 hours for intravenous thrombolysis (Brunström and Carlberg 2015).

“Typically in large-vessel occlusive stroke, less than 40% of patients treated with intravenous thrombolysis alone will be alive and independent at 90 days. However, with appropriate tissue-based imaging selection, intravenous thrombolysis combined with early thrombectomy increases the proportion of people alive and independent at 90 days to 61–71% (EXTEND-IA and SWIFT-PRIME). Furthermore, the major advantage

for thrombectomy is in reducing the proportion of people with severe disability after stroke, so the health economic advantage is likely to be greater still.

“Selecting participants on the basis of imaging findings was key to the positive results of MR CLEAN. Replicating these results in the NHS would mean at the very least obtaining vascular imaging (CT angiography) and systematically recording any changes on CT head imaging (via Alberta Stroke Program Early CT [ASPECTS] score) in all acute stroke patients potentially eligible for intra-arterial treatment. In addition, NHS stroke care services would need to be reconfigured for patients with large-vessel occlusive stroke to facilitate rapid access to thrombectomy that can be delivered within published standards of care.

“Although the findings of this study are positive, some uncertainties remain around how best to implement intra-arterial treatment – for example, whether to treat large-vessel occlusive stroke with thrombectomy on basis of CT or CT angiography findings alone, or whether to refine selection further with brain perfusion imaging.”

Study sponsorship: Dutch Heart Foundation, AngioCare Covidien/ev3, Medac/Lamepro and Penumbra.

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Drugs with anticholinergic effects and risk of cognitive impairment, falls and all-cause mortality


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Overview: Drugs with anticholinergic effects block the neurotransmitter acetylcholine to inhibit smooth muscle function, such as in the lungs, gastrointestinal tract and urinary tract. These drugs are prescribed for a wide range of conditions, including Parkinson’s disease, overactive bladder, chronic obstructive pulmonary disease, nausea and vomiting, depression and psychosis.

Drugs with anticholinergic effects can cause a broad range of adverse events, including constipation, dry mouth, dry eyes, urinary retention, confusion, falls and agitation. A recent prospective cohort study suggested an increased risk of dementia with long-term exposure to drugs with anticholinergic effects, most commonly tricyclic antidepressants, sedating antihistamines and anticholinergic drugs used to treat bladder conditions (Gray et al. 2015).

Current advice: NICE guidance on falls in older people recommends that people who have had a fall or are at increased risk of falling should have their medication reviewed as part of a multifactorial risk assessment. The guidance recommends that older people on psychotropic medications (including neuroleptics, sedatives, hypnotics and antidepressants) should have their medication reviewed and if possible discontinued to reduce their risk of falling.

The NICE guidance on dementia (currently being updated) recommends that a diagnosis of dementia should be made only after a comprehensive assessment, including a medication review to identify and minimise use of drugs that may adversely affect cognitive functioning.

New evidence: A systematic review and meta-analysis assessed the effect of drugs with anticholinergic effects on cognitive impairment, falls and all-cause mortality in older people (Ruxton et al. 2015). The investigators examined drugs with anticholinergic effects as a class, compared individual drugs, and assessed different scoring systems that measure exposure to drugs with anticholinergic effects.

The authors included 18 studies (total n=124,286) in the systematic review, with the results of 11 studies included in the meta-analysis. The majority of the studies were of people aged 65 years and over and were conducted in Europe (n=12), the USA (n=4), Canada (n=1) and Australia (n=1). Follow-up ranged from 1 month to 6 years.

The systematic review found that the individual studies had conflicting results on the effects of drugs with anticholinergic effects as a class.

Meta-analysis of 3 studies showed that exposure to drugs with anticholinergic effects as a class was associated with a significant increase in cognitive impairment (odds ratio [OR]=1.45, 95% confidence interval [CI] 1.16 to 1.73). Details of risks associated with specific drugs were not reported.

Four studies that assessed risk of falls were included in the meta-analysis, which examined the effects of 5 drugs – amitriptyline, olanzapine, paroxetine, risperidone and trazodone. The risk of falling was significantly increased with olanzapine (OR=2.16, 95% CI 1.05 to 4.44) and trazodone (relative risk [RR]=1.79, 95% CI 1.60 to 1.97), with some heterogeneity present in the trazodone analysis (I^2=28.2%). Exposure to amitriptyline, paroxetine and risperidone was not associated with an increased risk of falls.

The authors did not report the effect on all-cause mortality of drugs with anticholinergic effects as a class or of individual drugs. They did report on all-cause mortality relative to score on the Anticholinergic Cognitive Burden (ACB) scale, a system that scores drugs with anticholinergic effects from 1 (possible anticholinergic effects based on in vitro data) to 3 (known anticholinergic effects that may cause delirium). This analysis showed a significant association between ACB scale and all-cause mortality, with an increase of 1 point on the scale approximately doubling risk (OR=2.06, 95% CI 1.82 to 2.33).

This study has a number of limitations. The majority of studies included were observational, with only 2 randomised controlled trials included, 1 of which was available only as an abstract. Significant heterogeneity was observed in the meta-analysis of some drugs or scoring systems. Limited data were available on the relative risks associated with specific drugs, with results available for only 5 named drugs.

Commentary by Dr Martin Duerden, GP and Clinical Senior Lecturer, Centre for Health Economics and Medicines Evaluation, Bangor University, North Wales:

“The growing problem of multimorbidity and its associated polypharmacy is creating a major challenge for modern healthcare. Most of the evidence for medicines comes from trials of individual drugs in the context of highly selected individuals who may not be representative of the ‘real world’ patients we treat. Furthermore, the guidelines we use tend to be focused on individual conditions, when the reality is that people may have several conditions.

“Of late there has been a lot of interest in the potential harm caused by drugs that have anticholinergic effects. Concerns exist that several treatments with some anticholinergic activity might have cumulative harmful effects when given to a person with more than one clinical condition. This potential for harm increases with frailty and age. Various anticholinergic burden or risk scales have been devised to aid medication reviews so that certain drugs can either be stopped, or the medication regimen altered to reduce this burden.

“This systematic review and meta-analysis by Ruxton and colleagues examines the evidence of cognitive impairment, falls and mortality from drugs with anticholinergic effects. The evidence is not very strong, but there does appear to be an association between some individual drugs and these harms. There also seems to be a correlation between overall anticholinergic burden and mortality.

“Taken alongside the other known adverse effects of these drugs, it seems sensible to be cautious when prescribing any medication with anticholinergic effects. The catch is that there is surprisingly little evidence to show that using measures of anticholinergic burden to reduce exposure reduces the harm from these drugs. Researching this area is very difficult, and it may be that we have to continue hoping that this process, which sounds worthy, may be beneficial.

“Anticholinergic risk scales are currently contained in various toolkits for polypharmacy, such as those by NHS Scotland and the All Wales Medicines Strategy Group. The findings of the Ruxton et al. study provide reasonable support to continue using these tools when deciding on and reviewing treatments for older or frail people, or people with complex multimorbidities.”

Study sponsorship: None.

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Suicide prevention programmes in schools

Overview: In high-income countries, suicide accounts for 17.6% of all deaths among young people aged 15−29 years and represents the leading cause of death for both sexes (World Health Organization 2014). Mental health problems in young people are often predictors of poor mental health in adulthood, making adolescence a key period for early preventive interventions (Patton et al. 2014, see also Eyes on Evidence September 2014).

Providing interventions in schools may be one approach to reducing the risk of suicide in young people, but little evidence is available on the effectiveness of school-based programmes (Katz et al. 2013).

Current advice: The NICE guideline on depression in children and young people recommends that healthcare professionals in schools should be trained to detect symptoms of depression, and to assess children and young people who may be at risk of depression. In the assessment of a child or young person with depression, healthcare professionals should always ask the patient and their parent(s) or carer(s) directly about self-harm and ideas about suicide.

Active suicidal ideas or plans, and high recurrent risk of acts of self-harm or suicide, are criteria for referral of children and young people with depression to specialised child and adolescent mental health services.

The NICE pathway on depression brings together all related NICE guidance and associated products on the condition in a set of interactive topic-based diagrams.

New evidence: Wasserman et al. (2015) conducted a randomised controlled trial of 3 school-based approaches to suicide prevention in young people called the Saving and Empowering Young Lives in Europe (SEYLE) study. This study recruited young people aged 15 years on average from schools in 10 European countries. Schools were randomly assigned to a 4-week intervention programme or to a control group. The intervention programmes were:

- Question, Persuade, and Refer (QPR): a ‘gatekeeper’ training programme for teachers and other school staff on recognising and reducing suicidal behaviour in pupils;
- The Youth Aware of Mental Health Programme (YAM): an interactive programme for all pupils that raised awareness of factors associated with suicide and taught mental health coping skills;
- Screening by Professionals (ProfScreen): a programme of assessment and referral of young people identified as at risk of suicide.

Pupils completed a questionnaire on suicidal thoughts and behaviours at baseline, 3 months and 12

months. The primary outcome was incident suicide attempt(s). Severe suicidal ideation in the 2 weeks before follow-up was a secondary outcome.

A total of 168 schools (11,110 pupils) were recruited and randomly assigned to QPR (40 schools, 2692 pupils), YAM (45 schools, 2721 pupils), ProfScreen (43 schools, 2764 pupils) or control (40 schools, 2933 pupils). At 3 months, 333 (3.4%) of the 9724 pupils who answered the questionnaire reported either a suicide attempt or ideation, and 85 (0.9%) reported both. At 12 months, 261 (2.9%) of the 8885 pupils who completed the questionnaire reported either a suicide attempt or ideation, and 55 (0.6%) reported both. No completed suicides were reported.

At 3 month follow-up, no significant difference was seen between any of the intervention groups and the control group in suicide attempts or severe suicidal ideation. At 12 month follow-up, young people in the YAM group were significantly less likely than those in the control group to report a suicide attempt (odds ratio [OR]=0.45, 95% confidence interval [CI] 0.24 to 0.85, p=0.014) or suicidal ideation (OR=0.50, 95% CI 0.27 to 0.92, p=0.025). A total of 167 pupils would need to receive the YAM intervention to prevent one suicide attempt a year. Neither QPR nor ProfScreen had an effect on suicide attempts or ideation at 12 months.

Strengths of this study include its large sample size and the good rates of follow-up (88% of pupils at 3 months and 80% at 12 months). Limitations are that it is not clear whether all participants completed their assigned intervention, and the outcome measures relied on self-report.

Commentary by Dr Georgina Cox, Research Fellow in Suicide Prevention, Orygen, National Centre of Excellence in Youth Mental Health, University of Melbourne, Australia:

“Evidence is limited for the long-term effectiveness of universal school-based suicide prevention programmes (up to and following 12 months), in terms of a reduction in suicidal ideation or attempts in young people who undertake them. The SEYLE study had a large sample size, good follow-up retention rate, and measured appropriate suicide-related outcomes, which are only in recent years becoming more commonplace to measure. It provides evidence that students who received the YAM reported fewer suicide attempts, and instances of severe suicidal ideation, compared with students who did not receive the programme.

“However, there is debate as to whether students exposed to suicide-related curricula experience distress immediately after sessions (Robinson et al. 2013), and whether those who are currently experiencing thoughts of suicide are adversely affected by such programmes. Despite the results of the SEYLE study, this question remains unanswered. Before implementation of such programmes in secondary schools, it is critical that we know the potential positive and adverse effects that such programmes may have on individual students, of varying levels of risk. It is also important that we understand exactly what parts of the YAM are most effective (for example, teaching coping skills versus knowledge about risk factors), so that future programmes can deliver the most critical elements to young people.

“The study also concluded that the gatekeeper training programme (QPR) and ProfScreen screening intervention did not have a significant effect on numbers of suicide attempts, or suicidal ideation, in students. However, that is not to say that such interventions did not have other positive effects. For example, the study did not measure whether young people’s help-seeking behaviour was affected, or whether gatekeeper training improved attitudes or increased confidence in dealing with suicidal behaviour.”

Study sponsorship: European Union.

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Pregnancy outcomes in women who have had bariatric surgery

Overview: An estimated 5% of pregnant women in the UK are obese (BMI ≥35 kg/m^2; Centre for Maternal and Child Enquiries 2010). The risk of fetal death, stillbirth and infant death is higher in pregnant women with obesity than in pregnant women of normal weight (Aune et al. 2014). Obesity in pregnancy is also linked to preterm delivery (Cnattingius et al. 2013), congenital abnormalities (Stothard et al. 2009) and infants who are large for gestational age (Surkan et al. 2004).

Bariatric surgery – such as gastric banding and gastric bypass – can be used to treat people who are dangerously obese (NHS Choices 2015). Becoming pregnant after bariatric surgery may affect the risks of adverse infant outcomes, such as small-for-gestational-age birth, but existing evidence is mixed (Kjaer and Nilas 2013).

Current advice: The NICE guideline on obesity recommends considering bariatric surgery in people who have a BMI of 40 kg/m^2 or more, and in people who have a BMI of between 35 kg/m^2 and 40 kg/m^2 and other significant disease (for example, type 2 diabetes or high blood pressure) that could be improved if they lost weight. Surgery should be considered once all appropriate non-surgical measures have been tried but the person has not achieved or maintained adequate, clinically beneficial weight loss.

The NICE guideline on weight management before, during and after pregnancy recommends that women with a BMI of 30 kg/m^2 or more should be encouraged and helped to reduce their weight before becoming pregnant. Dieting during pregnancy is not recommended.

The NICE pathway on obesity brings together all related NICE guidance and associated products on the condition in a set of interactive topic-based diagrams.

New evidence: A population-based cohort study by Johansson et al. (2015) investigated fetal outcomes among pregnant women in Sweden who had previously undergone bariatric surgery. A total of 628,778 singleton pregnancies were identified from the Swedish Medical Birth Register. The Scandinavian Obesity Surgery Registry was used to find 596 pregnancies in women who had previously undergone bariatric surgery (mean pre-surgery BMI=43.7 kg/m^2; 98% had gastric bypass surgery). These women were then matched to a control group of 2356 pregnancies in women with no history of bariatric surgery and who had a BMI similar to the pre-surgery BMI of those who had undergone surgery (mean BMI=41.8 kg/m^2). Fetal outcomes were established from the Medical Birth Register and the National Patient Register.

Women who had previously undergone bariatric surgery were less likely to develop gestational diabetes than control women (1.9% versus 6.8%; odds ratio [OR]=0.25, 95% confidence interval [CI] 0.13 to 0.47, p<0.001). Pregnancies in women who had previously undergone bariatric surgery had a lower risk of resulting in large-for-gestational-age infants (8.6% versus 22.4% in control women; OR=0.33, 95% CI 0.24 to 0.44, p<0.001) or big babies (macrosomia; 1.2% versus 9.5%; OR=0.11, 95% CI 0.05 to 0.24, p<0.001). However, women who had undergone surgery were at higher risk of having small-for-gestational-age infants (15.6% versus 7.6%; OR=2.20, 95% CI 1.64 to 2.95, p<0.001).

Gestation was shorter for pregnancies in women who had undergone surgery than in those who had not (273.0 days versus 277.5 days; mean difference=−4.5 days, 95% CI −2.9 to −6.0, p<0.001), although the risk of preterm birth was not significantly different (10.0% versus 7.5%; OR=1.28, 95% CI 0.92 to 1.78, p=0.15). Women who had a history of bariatric surgery had a slightly higher risk of stillbirth or neonatal death (1.7% versus 0.7%; OR=2.39, 95% CI 0.98 to 5.85, p=0.06).

Limitations of this study include its observational nature and that it could not control for all possible confounding factors. The Swedish population is mostly white, and nearly all women in this study who had a history of surgery had gastric bypass rather than banding surgery, so the results may not be generalisable to other populations.

Commentary by Dr Anna Lawin-O'Brien, Subspecialty Trainee in Fetal and Maternal Medicine, and Dr Christoph Lees, Clinical Reader in Obstetrics and Honorary Consultant in Obstetrics, Head of Fetal Medicine, Queen Charlotte's and Chelsea Hospital, Imperial College Healthcare NHS Trust, London:

"Obesity in pregnancy is associated with significant health risks to mother and fetus. However, data on the effectiveness of interventions to reduce pre-pregnancy weight remain limited and controversial. Bariatric surgery has been shown to reduce weight substantially but is associated with serious complications such as malabsorption and possibly increased perinatal mortality.

"This study by Johansson et al. (2015) is the largest data set comparing pregnancy outcomes in obese women after bariatric surgery with no-surgery matched controls. Pregnancies after bariatric surgery had a significantly lower incidence of gestational diabetes and large-for-gestational-age fetuses. Pregnancies after bariatric surgery also had higher rates of small-for-gestational-age neonates and a slightly higher rate of perinatal mortality. Prematurity and congenital anomalies were similar in the two cohorts.

"Other authors, such as Devlieger et al. (2015), suggested that post-surgical complications could be a contributory factor to the raised perinatal mortality – a factor that Johansson et al. did not mention. The results to date of an ongoing study (www.aurorastudy.org) suggest that 14% of women who become pregnant after bariatric surgery need further surgery, which may explain the increased perinatal mortality rate. Further confounding factors include that underlying social and health differences between women opting for or against surgery were not accounted for in the Johansson et al. analysis, nor were the women's histories of gestational diabetes mellitus or preterm birth.

"A recent Cochrane review by Opray et al. (2015) evaluated the effectiveness of preconception health programmes and interventions – including surgical interventions – for improving pregnancy outcomes in obese women. This review concluded that further research was needed and that no recommendations can be given until the effectiveness of health programmes and interventions for this group is established. This paper by Johansson et al. valuably adds to what is known, but cannot answer the question as to whether bariatric surgery is advisable before pregnancy. It remains for the clinician to deliver carefully considered, balanced and individualised counselling in each case."

Study sponsorship: Swedish Research Council and Stockholm County Council.

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Physical and mental health of carers

Overview: An estimated 11.9% of women and 9.0% of men in England and Wales provide some level of unpaid care to family members, friends, neighbours or others because of long-term physical or mental ill health or disability, or problems related to old age (Office for National Statistics 2013).

Both men and women who provide unpaid care are more likely to report their general health as 'not good' than people who are not carers (Office for National Statistics 2013). Carers also experience poorer mental health than people who do not provide care (Smith et al. 2014). Some of the mental ill health reported by carers may be attributable to factors not directly associated with the act

of caring, such as difficulties with finances and employment.

Current advice: The 2014 Care Act stipulates that local authorities must assess any carer who requests an assessment or who appears to need support. A carer's assessment considers the impact of caring on the carer's physical, mental and emotional health and how caring is affecting what they want to achieve in their day-to-day life. It must also assess whether the carer is able or willing to carry on caring, whether they work or want to work, and whether they want to study or do more socially. Carers may then be eligible for support from their local authority, such as replacement care to allow the carer to take a break.

NICE is currently preparing guidance on social care of older people with complex care needs and multiple long-term conditions (anticipated publication date November 2015) and service user and carer experience (anticipated publication date January 2018).

New evidence: Stansfeld et al. (2014) used cross-sectional data to evaluate the level of common mental disorders among carers in England and whether stressors other than caring might account for poor mental health in this group.

Data from the Adult Psychiatric Morbidity Survey in England (2007) were used to compare the prevalence in carers and non-carers of common mental disorders (such as anxiety and depression), stressors (such as personal life events or alcohol misuse) and mediators (such as social support and social participation).

This analysis comprised 5170 people, 1367 (26.4%) of whom were carers. Carers were more likely to have a common mental disorder than non-carers (adjusted odds ratio [OR]=1.64, 95% confidence interval [CI] 1.37 to 1.97). Carers were also more likely than non-carers to report domestic violence (adjusted OR=1.57, 95% CI 1.14 to 2.17), debt (adjusted OR=1.60, 95% CI 1.20 to 2.13) and fatigue (adjusted OR=1.33, 95% CI 1.14 to 1.54).

In multivariate models that adjusted for a range of stressors and mediators, caring remained associated with an increased risk of common mental disorders (adjusted OR=1.58, 95% CI 1.30 to 1.91). The authors concluded that the increased risk of common mental disorders among carers could not be explained by other stressors or poor social support.

This study could not establish causation because of the cross-sectional nature of the data. In addition, people with severe mental distress or very time consuming caring duties may not have been included because they might have been less likely to fill in the Adult Psychiatric Morbidity Survey.

Kenny et al. (2014) used longitudinal cohort data from an annual survey of Australian households to assess the effect of starting caring on the physical and mental health of carers.

Care giving status and burden was measured as time spent in a typical week caring for a disabled spouse, adult relative, elderly parent or elderly parent-in-law. Health was self-assessed using the 36-item Short Form Health Survey (SF-36). The study included 424 people who were not providing care at their first annual survey (baseline) but were providing care for at least 2 subsequent surveys. These carers were matched to 424 non-carers.

At 2 years after baseline, a similar proportion of carers (37.3%) and non-carers (37.5%) reported a decline in physical health. At 4 years after baseline, more carers (45.7%) reported a reduction in physical health than non-carers (37.1%). For mental health: the proportions of carers (45.5%) and non-carers (41.7%) who reported worse mental health at 2 years were similar. At 4 years, around half (51.7%) of carers had a reduction in mental health, compared with 42.4% of non-carers. The effects of caring on physical and mental health differed by gender, and care-giving hours and carer work hours were important contextual factors.

Limitations of Kenny et al. (2014) include that a large number of carers were excluded because of missing or insufficient data, and carers who looked after disabled children or provided care for less than a year were excluded.

Commentary by Diane Fox, Research Officer, Personal Social Services Research Unit, University

of Kent:

“The multivariate modelling undertaken by Stansfield et al. proves useful in disentangling the diversity of circumstance that exists amongst people in caring roles. Separating out the direct effects of caring from indirect stressors (such as debt or other adverse life events) and mediators (such as perceived social support and social participation) reveals that caring is independently associated with increased risk of fatigue, common mental disorders and suicidal thoughts.

“Kenny et al. offer insights into the cumulative impact of caring on health over time and how this differs by gender, employment status and hours of care provided per week. The results indicate the circumstances in which employment could be ‘health protective’ and ‘tipping points’ at which balancing work and care becomes detrimental to health. Caring for 20 or more hours per week had a detrimental effect on women’s health at 2 years whether they were in employment or not. Men caring for 20 hours or more but not working reported improved health at 2 years, but the health of men combining working and caring for 20 hours or more declined.

“Both studies offer insights for health and social care service providers in designing assessments and targeting support for carers. For example, the risk of domestic violence could be discussed during carer assessments, because Stansfield et al. found that carers were at higher risk than non-carers.

“Providing opportunities for carers to have a break, particularly for those providing a high number care hours per week or those combining work and care, may begin to address carer fatigue. Enabling carers to combine work and care is covered by the 2014 Care Act and can make cost savings to the economy over the longer term (Department of Health 2013).

Study sponsorship: Kenny et al. (2014) was funded by the Australian National Health and Medical Research Council. Stansfeld et al. (2014) did not receive funding.

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Evidence summaries from NICE’s Medicines and Prescribing Programme

NICE has recently published the following Medicines evidence commentaries:

Prucalopride for chronic constipation
Two European randomised controlled trials have compared prucalopride with placebo in people with chronic constipation.

Chronic pain: unintentional overdose in people receiving opioid analgesics for non-cancer pain
A cohort study examined the relationship between prescribed opioids for chronic non-cancer pain and unintentional overdose among US military veterans.

Chronic obstructive pulmonary disease: the effect of roflumilast on exacerbations in people with severe disease – the REACT study
A large multicentre double-blind randomised controlled trial investigated the effectiveness of roflumilast in reducing moderate to severe exacerbations in people with severe chronic obstructive pulmonary disease who were also taking combination therapy of an inhaled corticosteroid and long acting beta-2 agonist.

Medicines evidence commentaries form part of NICE’s Medicines Awareness Service and help contextualise important new evidence, highlighting areas that could signal a change in clinical practice. They do not constitute formal NICE guidance. These commentaries were published in NICE’s Medicines Awareness Weekly service and are available online in NICE Evidence Search.

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Changes to the BNF

Over the past 18 months, the British National Formulary (BNF) has been working on a broad range of feedback to improve access to the latest information about medicines. Following feedback, a number of changes have been made to the BNF.

Improved consistency and clarity will be delivered in the print editions of BNF, BNF for Children, and the Nurse Prescribers Formulary (NPF) that will be distributed from October.

An enhanced online version of the BNF can be found through MedicinesComplete. Enhanced content and functionality will be added to the BNF content on the NICE website in the winter.

New apps are also being developed and will be available in the autumn.

To find out more about the forthcoming changes visit www.bnf.org.

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