Hepatitis C treatment review

A systematic review of 33 randomised controlled trials and eight cohort studies on new drugs for hepatitis C virus (HCV) infection – together involving more than 19,000 patients – finds sustained virological response (SVR) rates of up to 95% from just 12 weeks' treatment. Previous treatments involving peg-interferon and ribavirin have achieved SVRs of up to 50%–80%, with lengthy treatment regimes and adverse side effects. The review concludes that patients with HCV genotype 1 should receive either: sofosbuvir with pegylated interferon and ribavirin, because of the shorter duration of therapy and high SVR rates (89%–90%); or simeprevir with pegylated interferon and ribavirin (SVR = 79%–86%). Those with HCV genotypes 2 and 3 should receive sofosbuvir and ribavirin alone (genotype 2, 12 weeks' treatment – SVR = 82%–93%; genotype 3, 24 weeks' treatment – SVR = 80%–95%). Studies published up to May 2014 are included; it should be noted that new evidence is rapidly emerging, with recent trials involving interferon-free regimes reporting impressive SVRs (see below). In the UK, genotypes 1 and 3 are the most common. UK healthcare workers carrying HCV are restricted from carrying out exposure-prone procedures until they have responded successfully to treatment.

- *JAMA 2014; 312(6): 631–640. doi: 10.1001/jama.2014.7085*
- *http://jama.jamanetwork.com/article.aspx?articleid=1895252*

HCV treatment without interferon

A randomised controlled clinical trial of an interferon-free treatment regimen for patients with hepatitis C virus (HCV) infection achieved high rates of sustained virological response (SVR) using a once-daily combination of the protease inhibitor simeprevir and the nucleotide analogue sofosbuvir. The trial involved 167 patients with HCV genotype 1 who were either untreated or who had not previously responded to interferon therapy. They were randomised to the following groups: simeprevir and sofosbuvir with or without ribavirin for 24 weeks; simeprevir and sofosbuvir with or without ribavirin for 12 weeks. Ninety-two per cent of all patients achieved a SVR 12 weeks after the end of the treatment, with no improvement either by extending the regime to 24 weeks or adding ribavirin. The treatments were generally well tolerated, with headache, fatigue and nausea the most frequently reported side effects (none deemed clinically important).

- *Lancet 2014; 384: 1756–65. doi: doi.org/10.1016/S0140-6736(14)61036-9*
- *http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(14)61036-9/abstract*

Arthritis and return to work

A Cochrane evidence review concludes that workplace interventions aimed at promoting job retention among workers with inflammatory arthritis (including rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis) have 'potential' to succeed, with no evidence of any adverse effects. The review included randomised controlled trials of non-pharmaceutical workplace interventions, including workplace adaptations, vocational counselling, advice and education, but just three trials met the inclusion criteria, and when taken together provided only very low quality evidence. Two trials looked at job loss as the main outcome, and one considered absence and work functioning. Although job loss was significantly reduced in one of the trials (relative risk = 0.35; 95% confidence interval (CI) = 0.18–0.68) the evidence quality was poor.

- *Cochrane Database of Systematic Reviews 2014; 11: CD010208. doi: 10.1002/14651858.CD010208.pub2*
- *http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD010208.pub2/abstract*

Depression and return to work

Workers off sick with depression can return to work sooner if given appropriate workplace interventions, such as work modifications and coaching in addition to their regular care, according to this Cochrane systematic review. It included randomised controlled trials (RCTs) and cluster RCTs of both work-directed and clinical interventions where the outcome measure was sickness absence. Twenty-three studies were included, involving nearly 6,000 participants; 14 papers were assessed as having a high risk of bias and nine were assessed as having low risk of bias. There is moderate quality evidence from three studies that a work-directed intervention on top of a clinical intervention reduces sickness absence compared to a clinical intervention alone (standardised mean difference (SMD) = -0.40; CI -0.66–-0.14). There is moderate quality evidence from three studies that online or telephone-based cognitive behavioural therapy is more effective than usual care (SMD = -0.23; CI -0.45–-0.01), and high quality evidence from one paper that a structured telephone outreach and care management programme, which systematically assessed, facilitated and monitored treatment needs, was more effective in reducing sickness absence than usual care (SMD = -0.21; CI -0.37– -0.05).

- *Cochrane Database of Systematic Reviews 2014; 12: CD006237. doi: 10.1002/14651858.CD006237.pub3*
- *http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD006237.pub3/abstract*

Stress and the risk of coronary heart disease

Work stress increases the risk of recurrent coronary heart disease (CHD) events by two-thirds (65%), according to this systematic review and meta-analysis. It focused on papers with follow-up greater than three years, where end points were either cardiac death or myocardial infarction, and where work stress was measured using validated instruments; five papers met these criteria. Work stress – as defined according to the demand–control or effort–reward imbalance models – was associated with a significant raised risk of CHD events (hazard ratio (HR) = 1.65; CI = 1.23–2.22). The pooled HRs for high demand and low control were 1.42 (CI 1.02–1.99) and 1.44 (CI 1.04–1.99) respectively; and for high effort and low reward were 1.17 (not significant) and 1.77 (CI 1.16–2.71), respectively. Workplace interventions aimed at improving the psychosocial work environment are warranted, say the authors.

- *International Journal of Occupational Medicine and Environmental Health 2014; online first: doi: 10.2478/s13382-014-0303-7*
- *http://link.springer.com/article/10.2478%2Fs13382-014-0303-7*

Stress reduction in healthcare workers

An updated Cochrane systematic review of occupational stress in healthcare workers (HCWs) finds that cognitive-behavioural training, mental relaxation (eg mindfulness) and physical relaxation (such as massage) all have moderately beneficially effects in lowering stress levels. It also recommends that organisational interventions should focus on addressing specific stress-causing factors. Fifty-eight randomised controlled trials were included. There is: low quality evidence that cognitive behavioural interventions compared to no intervention reduced stress in seven studies with follow up of one to six months (standardised mean difference (SMD) = -0.38; CI -0.59–-0.16); low quality evidence that relaxation-based interventions reduced stress in studies with follow-up of less than one month (SMD = -0.48; CI -0.89–-0. 08) or greater than six months (SMD = -1.89; CI -2.65–-1. 13); and moderate quality evidence that relaxation-based interventions reduced stress in 12 studies with more than six months' follow-up (SMD = -0.49; CI -0.78–-0. 21). There is low-quality evidence that changing work patterns can reduce stress levels; for example, evidence from two trials found that, for intensive care staff, work schedules with weekend breaks reduced stress

compared with continuous work schedules (SMD = -0.55; CI -0.84–-0.25). Improving working conditions, enhancing communication skills or organising peer-support did not reduce stress (though the number of studies was small). Publication bias and lack of methodological precision contributed to the generally low quality evidence.

- *Cochrane Database of Systematic Reviews 2014; 12: CD002892. doi: 10.1002/14651858.CD002892.pub4*
- *http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002892.pub4/abstract*

Bricklayers' lung cancer risk

There is clear evidence that length of time working as a bricklayer is associated with an increased risk of lung cancer, this pooled analysis of case–control studies reveals. The SYNERGY study is based on case–control occupational lung cancer studies carried out in 13 European countries, plus Canada, Hong Kong and New Zealand. It included 15,608 cases and 18,531 controls, of which 695 cases and 469 controls had ever worked as bricklayers. Sometime employment as a bricklayer, after adjustment for age and tobacco smoking, is associated with a 50% raised risk of lung cancer (OR = 1.47; CI 1.28–1.68). The raised risk remained significant after adjusting for educational level (ie primary or secondary school, college). Length of employment is also associated with greater risk ($p < 0.001$), with a gradual rise until 25 years in the job, plateauing thereafter.

- *International Journal of Cancer 2014; online first: doi: 10.1002/ijc.28986*
- *http://onlinelibrary.wiley.com/doi/10.1002/ijc.28986/abstract*

Law enforcement increases police officers' risk of sudden cardiac death

Stressful law enforcement duties are associated with a raised risk of sudden cardiac death in police officers, this US case-distribution analysis reveals. Physical restraint, for example, is associated with a 69-fold raised risk. Information on sudden cardiac death in serving police officers was obtained from the US National Law Enforcement Officers Memorial Fund, a database tracking all police officer deaths in the line of duty. A total of 441 sudden cardiac deaths were recorded over the 25 years to 2010. One quarter (25%) were associated with restraints or altercations; 23% with routine duties; 20% with physical training; 12% with pursuit of suspects; and 19% on other activities. Taking account of the amount of time spent on different police duties, relative risks (RR) were calculated for the various activities, with routine, non-emergency work as the reference. Significant raised risks for frontline officers were associated with: restraint/physical altercation – RR = 69.0 (CI 52.6–90.5); pursuit – RR = 50.8 (CI 36.4–70.8); physical training RR = 23.3 (CI 17.5–30.9); medical/rescue operations – RR = 8.98 (CI 6.09–13.3); transporting/supervising prisoners – RR = 6.27 (CI 3.80–10.4); and serving warrants – RR = 2.87 (CI 1.26– 6.55). The contribution of other risk factors (eg obesity, hypertension) was not assessed. The study notes that for many police officers most of the day is spent on sedentary work 'punctuated by unpredictable short periods of stressful activities'. The findings may be applicable to other relatively sedentary occupations with similar bursts of activity.

- *BMJ 2014; 349:g6534. doi: 10.1136/bmj.g6534*
- *http://www.bmj.com/content/349/bmj.g6534*

Chronic fatigue syndrome review

A systematic review by the US Agency for Healthcare Research and Quality finds a lack of clear aetiology for chronic fatigue syndrome (CFS, sometimes known as myalgic encephalomyelitis), with considerable overlap with other conditions hampering diagnosis. There is no single reliable

diagnostic tool or reference standard and a risk of incorrectly labelling patients with CFS. The review includes 36 observational studies of diagnostic methods and 35 treatment trials. It finds low quality evidence that the immune modulator drug rintatolimod improves exercise performance in some patients; low to moderate strength evidence that counselling and behavioural therapies and graded exercise therapy can be beneficial, but these 'have not been adequately tested in more disabled populations'; and insufficient evidence on the efficacy of a range of other drugs and alternative treatments. There is some evidence that receiving a CFS diagnosis can be associated with perceived stigma in terms of financial instability, reduced work opportunities, social isolation, and interaction with the healthcare system. Limitations of existing research include poor diagnostic criteria and low patient numbers in the trials, and inconsistent outcome measures.

- *Agency for Healthcare Research and Quality. Evidence. Report/Technology Assessment no. 219. Rockville, MD: AHRQ 2014*
- *http://www.effectivehealthcare.ahrq.gov/search-for-guides-reviews-and-reports/?pageaction=displayproduct&productid=2005*

Asleep at the wheel

A study of 497 professional truck and bus drivers in Italy supports the use of the Chalder Fatigue Questionnaire – a 14-item self-administered scale of physical and mental fatigue – in identifying those at risk of falling asleep at the wheel. Questionnaires were administered during drivers' mandatory periodic professional development training courses. Forty-one per cent of the drivers – whose confidentiality was assured – reported at least one episode per month of 'sudden onset sleep at the wheel'. Predictive factors were: age over 55 years (odds ratio (OR) = 4.91; CI 1.79–13.50, $p < 0.01$), travelling more than 40,000 miles per year (OR = 1.86; CI 1.08–3.22, $p < 0.05$); body mass index of at least 30 (OR = 2.16; CI 1.01–4.64, $p < 0.05$); self reported fatigue – ie chronic fatigue questionnaire score greater than 22 (OR = 3.93; CI 1.90–8.14, $p < 0.001$). Coffee and tobacco consumption were not significant factors. Working hours, sleep disorder and sleep loss were not assessed. The report notes that regulations limiting the amount of driving hours are often flouted.

- *International Journal of Occupational Medicine and Environmental Health 2014; online first: doi: 10.2478/s13382-014-0327-z*
- *http://link.springer.com/article/10.2478%2Fs13382-014-0327-z#page-1*