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Benzodiazepine and Z-drug prescribing in Ireland. Global guidelines recommend that benzodiazepines (BZD) should be limited to short-term use (≤4 weeks) to minimise the risk of adverse outcomes (e.g. dependence, withdrawal symptoms). Long-term BZD use has also been associated with cognitive and psychomotor impairment and an increased risk of falls in people ≥65 years. However, despite these guidelines, many countries still report a small reduction in the prescribing of BZD; moreover, changes in BZD prescribing were associated with increases in Z-drug prescribing (e.g. zopiclone, zolpidem) in some countries. Although previous Irish studies on BZD prescribing focused on older people, long-term BZD use can also lead to adverse outcomes for other age groups (e.g. mortality in polysubstance misusers and cases of deliberate self-harm); therefore it would be important to examine the prescribing patterns of BZD and Z-drugs across the entire adult population. A recent repeated cross-sectional study ***(Br J Clin Pharmacol 2018;DOI:10.1111/bjcp.13570)*** assessed the prescribing trends for BZD and Z-drugs from 2005 to 2015, using the PCRS pharmacy claims database in Ireland. The study found that the **prescribing rates of BZD decreased significantly by 27% between 2005 and 2015 (p<0.0001), however there was a significant increase in the prescribing rates of Z-drugs of 14% during the same time period (p=0.048)**. Approximately 1/3 of patients were receiving long-term prescriptions for BZD or Z-drugs. The **five most commonly dispensed drugs** during the study period were diazepam, alprazolam, temazepam, zopiclone and zolpidem; there was an increase in the prescribing rates of alprazolam, zopiclone and zolpidem, while the prescribing rate of diazepam decreased slightly. **Patients receiving combinations of BZD and Z-drugs significantly increased from 12% in 2005 to 15% in 2015**. The highest rates for prescribing of BZD and Z-drugs throughout the study period were for older women (≥65 years). The authors noted that although there was an overall decrease in BZD prescribing during the study period, there was a significant increase in the prescribing of Z-drugs, co-prescribing of both drug classes was common, and that a sizeable proportion of patients received long-term prescriptions. They concluded that targeted interventions are required to further reduce the prescribing of these medicines.
[**Editors' note**: the **HSE** Medicines Management Programme **(MMP)** website has a useful "**Tips and Tools**" section for the prescribing of BZD and Z-drugs, including patient support leaflets: **www.hse.ie/yourmedicines**]

Impact of HPV vaccine on prevalence of type-specific HPV.
Cervical cancer is caused by persistent human papilloma virus (HPV) infection. In the UK a national HPV vaccination programme was introduced in 2008 (routinely to 12 to 13 year old girls and as catch-up vaccination to girls up to 18 years). The programme initially used the bivalent vaccine (against high-risk (HR) types HPV 16 / 18, responsible for around 80% of cervical cancer in the UK); in 2012 this was changed to the quadrivalent vaccine (additional efficacy against HPV 6 / 11). A recent paper reported on the trends in prevalence of various HPV types in England during 2010 – 2016 (***JID 2018;DOI:10.1093/infdis/jiy249***). The study tested >15,000 residual vulva-vaginal swab specimens (taken from women, 16 to 24 years old, attending for chlamydia screening in England) for HPV DNA. Vaccine effectiveness was estimated for those with known vaccination status. **Results showed a reduction in prevalence of HR HPV 16 / 18** between 2010/2011 and 2016, from 8.2% to 1.6% in 16 to 18 year olds and from 14% to 1.6% in 19 to 21 year olds. **Vaccine effectiveness for HPV 16 / 18 was 82%**. There was also evidence of a decrease in the prevalence of other HPV types (31 / 33 / 45, vaccine effectiveness of 48.7%), most likely attributable to cross-protection. Although there were limitations with the data used, which might impact on the study validity, the findings are in keeping with other studies carried out in Scotland and Europe. The authors conclude that after 8 years of the national HPV programme, substantial declines have occurred in the prevalence of high risk HPV 16 / 18, which cause the majority of cervical cancer cases in the UK.

7 steps to appropriate polypharmacy. Polypharmacy (the use of several drugs) is often required to manage multi-morbid patients appropriately; however, polypharmacy may be challenging because prescribing guidance for a specific medical condition may be difficult to implement in a patient with multiple competing comorbidities. The *Scottish Government Polypharmacy Model of Care Group* recently published "**Polypharmacy Guidance, Realistic Prescribing, 3rd Ed. 2018**" to promote effective polypharmacy. It has been estimated that adverse drug events (ADE) result in 8.6 million unplanned hospital admissions in Europe each year, of which >70% occur in elderly patients on polypharmacy. Moreover, 50% of ADE-related admissions are preventable. The guide outlines **5 stages** which should be used as a trigger to ensure appropriate polypharmacy as follows: at **time of prescribing** (and risk assessment), or **medication review**, at time of **dispensing and administration**, during **communication and patient interaction** or during **medication reconciliation**. The guide stresses that no list can be comprehensive, therefore the individual prescriber's clinical judgement is essential in identifying the needs of each individual patient. However it provides a "***7-Steps"*** **medication review** to aid healthcare professionals to ensure appropriate polypharmacy

(1) **Aim** - what matters to the patient (in terms of goals of therapy)?
(2) **Need** - what are the essential drugs, and
(3) **Need** - are there unnecessary drugs?
(4) **Effectiveness** - are therapeutic goals being achieved?
(5) **Safety** - is there a risk of ADE with therapies?
(6) **Efficiency** - is the drug(s) cost-effective?
(7) **Patient-centred** - is the patient willing and/or able to take the drug regimen as intended?

The full guide is available at: **www.therapeutics.scot.nhs.uk/wp-content/uploads/2018/04/Polypharmacy-Guidance-2018.pdf**

Are PPIs associated with an increased risk of pneumonia?

Proton pump inhibitors (PPIs) are prescribed widely to reduce gastric acid secretion and for gastroprotection. Gastric acid plays a vital role in the innate response to bacterial infection; therefore the reduced acid secretion with PPIs increases the risk of bacterial micro-aspiration and pulmonary colonisation. Some studies have shown increased rates of pneumonia in the 30 days post-prescription of PPIs. However a recent primary care study showed that pneumonia rates were even higher in the 30 days preceding PPI prescription, which could bias post-PPI initiation results in terms of true pneumonia risk. A recent study sought to estimate **possible association between long-term use of PPIs and pneumonia incidence** in older adults in primary care using a UK GP database (***J Am Geriatr Soc 2018; DOI:10.1111/jgs.15385***). Individuals (n=75,000) aged 60+ years, receiving PPIs for ≥1 year, with medical records available for >1 year prior to PPI use were matched with non-PPI users from the same database; the incidence of pneumonia prior to, and after PPI initiation was calculated and compared with the results from the matched controls. **Results showed that the PPI group had greater overall comorbidity compared with controls**. In the PPI group, unadjusted pneumonia incidence rates were <6/1,000 person years from 24 to 6 months prior to PPI use but then increased to 22/1,000 in the 6 months before PPI therapy. In the 12 months post PPI initiation, pneumonia rates declined to a stable 8/1,000 by the end of that year; thereafter, the trend increased once more, reaching up to 12/1,000 by 24 months' PPI treatment. In comparison, the control group showed a steady pneumonia rate of <4/1,000 throughout the study period. The authors state that the study was designed to reduce confounding in relation to risk of pneumonia with short-term PPI usage by focusing on the longer-term outcomes. Therefore while short-term PPI / pneumonia associations may be confounded, longer-term associations were found in older adults in primary care. They note that 40% of elderly adults receive PPIs, and appropriate clinical indications may be lacking in up to 85% of cases. **They conclude that the study findings support the need for caution in long-term prescribing of PPIs (>1 year) to older adults.**

Every effort has been made to ensure that this information is correct and is prepared from the best available resources at our disposal at the time of issue. References are available on request. This ***newsletter is produced by the National Medicines Information Centre, St. James's Hospital (SJH) Dublin 8 and Dept of Therapeutics Trinity College, Trinity Centre, SJH.*** *Tel: Direct Line (01) 473 0589 or 1850 727 727 Email: nmic@stjames.ie*