NHS
Frimley
Clinical Commissioning Group

Hypnotics patient decision aid

What this decision aid is for

This decision aid is intended to assist health professionals in consultations with people aged 60 years or over with insomnia and otherwise free of psychiatric or psychological disorders when drug treatment with hypnotics (benzodiazepines, zaleplon, zolpidem or zopiclone) is being considered. Leaflets for patients explaining the causes, symptoms and prevention of insomnia can be found on the CKS website Insomnia | Health topics A to Z | CKS | NICE[i]

When should hypnotic treatment be considered?

Although currently available hypnotic drugs are marginally effective in promoting better sleep in the short term, there is little evidence to support their efficacy during longer term use. Indeed, because of concerns about adverse effects including the risk of dependence, in 1988 the Committee on Safety of Medicines advised that these drugs should be prescribed only for insomnia which is severe and disabling or is subjecting the patient to extreme distress. As a general principle, prescribers should always use the lowest effective dose and for a maximum of two to four weeks only.[ii] Whenever possible, any underlying cause of insomnia should be identified before considering hypnotics. NICE recommends that non-pharmacological measures (e.g., avoiding stimulants and maintaining regular sleeping hours with a suitable environment for sleep) should be considered first, but that hypnotics may be considered for a short period for patients with severe insomnia which is interfering with daily life.[iii] If hypnotics are used they should be used intermittently if possible and gradually tapered off towards the end of the course of treatment in order to avoid rebound insomnia.

Which hypnotic should be used?

NICE guidance on the use of Z-drugs (zaleplon, zolpidem and zopiclone) for the short-term management of insomnia was published in 2004. NICE reviewed data from 24 randomised controlled trials (RCTs) and concluded that there was no compelling evidence of a clinically useful difference between Z-drugs and shorter acting benzodiazepines in respect of their effectiveness, adverse effect, or potential for dependence or abuse. They therefore recommended that the drug with the lowest purchase cost should be prescribed and that switching from one to another should only occur if a patient experiences adverse effects thought directly related to specific agent. This might include, for example, metallic taste with zopiclone. They added that patients who have not responded to one of these drugs should not be prescribed any of the others as there was no evidence that switching to another drug would improve the chances of the patient experiencing better sleep as a result.

What are the benefits of hypnotics?

A meta-analysis (24 RCTS, n=2,417) (see technical note below) looked at the potential benefits and risks of hypnotics in people aged 60 years or more with primary insomnia, who took hypnotics for at least five consecutive nights.4 It found that on average, around 13 people would have to be treated with a hypnotic instead of placebo in order for one to obtain any notable improvement in sleep quality. With pooled data for any sedative compared with placebo, total sleep time was increased by an average of only 25 minutes (range 12.8 to 37.8 minutes) and the average number of night time awakenings decreased by less than one per night (mean 0.63, range 0.48 to 0.77). When benzodiazepines were compared with placebo, there was a modest improvement in sleep quality and total sleep time increased by around 34 minutes.

The usefulness of this analysis is limited by the fact that it combined data from studies of short- and long-acting agents without consideration of the dose used or relative potency of the different agents. Furthermore, there was some evidence of publication bias having favoured the publication of studies with positive outcome at the expense of those with negative findings.[iv]

What are the harms of hypnotics?

The meta-analysis found that on average, for every six people treated with a hypnotic drug, one person would experience an adverse effect such as drowsiness or fatigue, headache, nightmares, and nausea or gastrointestinal disturbances. In particular, cognitive effects (effects on a person's ability to think and concentrate) and morning/daytime fatigue were more common in hypnotic recipients than in the placebo groups. When comparing Z-drugs and benzodiazepines the authors found no difference in any of these outcomes between these two groups.

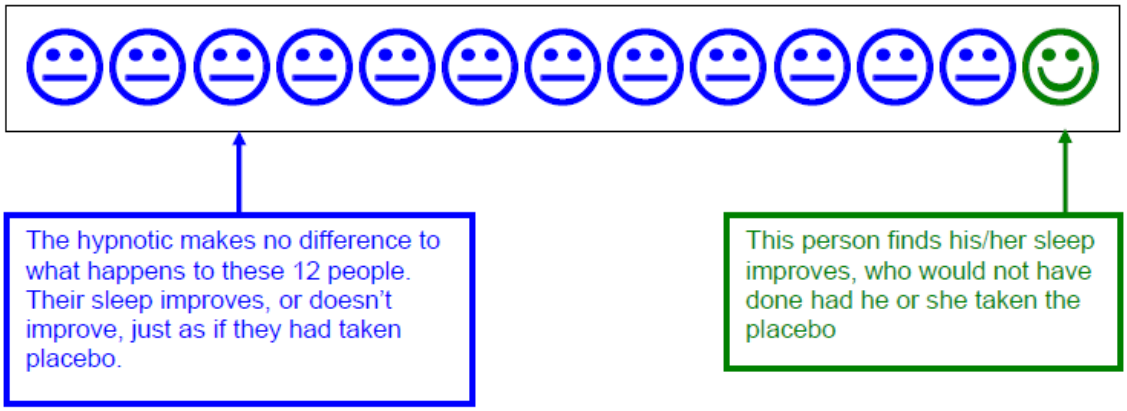
Benefits of hypnotics: sleep time and night time awakenings

Imagine a group of 13 people aged 60 years or over, with primary insomnia. If they all take a hypnotic for at least five consecutive nights:

- About one person will sleep better. This means that, on average, they will get an extra 25 minutes sleep each night and will wake up once less often every two nights (the green face).
- The hypnotic makes no difference to what happens to 12 people (the blue faces). Their sleep improves, or doesn't improve, just as if they had taken placebo. Details of the control event rate were not available in the published meta-analysis. This means that we do not know how many people slept better when taking placebo.

But remember:

- It is impossible to know for sure what will happen to each individual person.
- All 13 people will have to take the hypnotic.



Harms of hypnotics

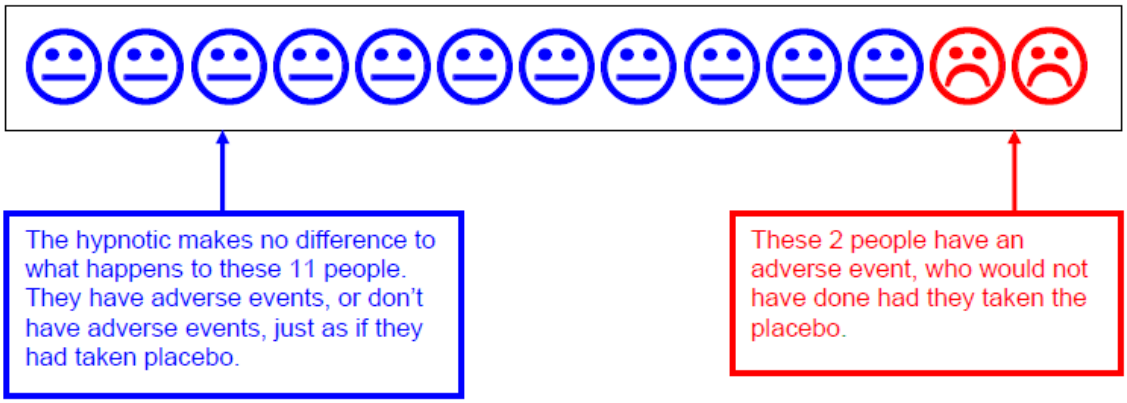
Imagine a group of 13 people aged 60 years or over, with primary insomnia. If they all take a hypnotic for at least five consecutive nights:

- About two will have adverse effects such as drowsiness or fatigue, headache, nightmares, nausea or gastrointestinal disturbances who would not have done had they taken placebo (the red faces).
- The hypnotic makes no difference to what happens to 11 people (the blue faces). They have adverse events, or don't have adverse events, just as if they had taken placebo. Details of the control event rate were not available in the published meta-analysis for total adverse effects.

This means that we do not know how many people suffered adverse effects when taking placebo.

But remember:

- It is impossible to know for sure what will happen to each individual person.



Technical note

The meta-analysis aimed to quantify and compare potential benefits (subjective reports of sleep variables) and risks (adverse events and morning-after psychomotor impairment) of short term treatment with sedative hypnotics in older people with insomnia. It included RCTs of any pharmacological treatment for insomnia for at least five consecutive nights in people aged 60 years or over with insomnia who were otherwise free of psychiatric or psychological disorders. (see references)

Twenty-four studies (n=2417) were included. In 20 studies considering benefits of hypnotics, 830 participants were treated with a benzodiazepine, 106 with zopiclone, 384 with zolpidem, 609 with zaleplon, 14 with diphenhydramine, and 468 with placebo. Sleep quality improved (effect size 0.14, P<0.05), total sleep time increased (mean 25.2 minutes, P<0.001), and the number of night time awakenings decreased (0.63, P<0.001) with sedative use compared with placebo. Adverse events were more common with sedatives than with placebo: adverse cognitive events were 4.78 times more common (95% confidence interval 1.47 to 15.47, P<0.01) and reports of daytime fatigue were 3.82 times more common (1.88 to 7.80, P<0.001) in people using any sedative compared with placebo.

Details of the control event rate were not available in the published meta-analysis. This means that we do not know how many people slept better when taking placebo.

The study authors concluded that improvements in sleep with sedative use are statistically significant, but the magnitude of effect is small. The increased risk of adverse events is statistically significant and potentially clinically relevant in older people at risk of falls and cognitive impairment. In people over 60, the benefits of these drugs may not justify the increased risk, particularly if the patient has additional risk factors for cognitive or psychomotor adverse events.

The authors acknowledge that interpretation of this meta-analysis must take into account that all sedatives or all benzodiazepines were grouped together for analyses, irrespective of differences in half life, potency, or dosage. In addition, no standard method of collecting subjective sleep variables is available. The studies used various measures: ordinal scales (three, five, or seven point), visual analogue scales, and combined scales. Though subjective reports create more variable results than objective measures, the authors focused on subjective ratings of sleep variables as the primary outcome measure because consumption of healthcare resources is driven by subjective report rather than objective measures of sleep. Another potential source of variability was the health status of the

participants in the studies. Some were community dwelling ambulatory patients attending a health clinic and others were inpatients on a geriatric ward.

Taken from National Prescribing Centre Date of preparation March 2010

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[i] CKS. Insomnia. Clinical Knowledge Summaries. Last revised February 2022 Accessed from Insomnia | Health topics A to Z | CKS | NICE

[ii] con2024428.pdf (nationalarchives.gov.uk)

[iii] NICE. Guidance on the use of zaleplon, zolpidem and zopiclone for the short-term management of insomnia. TA77. April 2004. Accessed from www.nice.org.uk/ta77

[iv] Glass J, Lanctot KL, Herrmann N, et al. Sedative hypnotics in older people with insomnia: meta-analysis of risks and benefits. BMJ 2005;331:1169. Accessed from www.bmj.com/cgi/content/abstract/331/7526/1169