Replies to Hypnotics’ association with mortality or cancer: a matched cohort study

21/06/12 14.01

With the approach applied in the present study, the amount of information on confounders accumulates over time. This could lead to impaired adjustment for confounding among those who leave the study cohorts early. We note that there was very little difference between crude and adjusted estimates. This could imply lack of confounding, but also that the adjustment was deficient. An additional reason for inefficient confounder control despite the thorough matching could be that confounders was defined in rather broad categories. One way of evaluating confounders would be to examine associations between confounders and outcome, but the use of a comparability -stratified Cox model unfortunately obscures this possibility.

In summary, we believe that the associations between hypnotic use and cancer or death in the study by Kripke et al may to a large degree be explained by selection bias affecting the controls, and to a lesser degree by suboptimal control of confounding. Kripke et al may inadvertently have introduced bias by some of the choices they have made in their study design and analysis. Furthermore, analyses taking into account time-dependent exposure and - in the analysis of cancer risk - both exposure duration and cumulative exposure would have added much to the interpretation of results.

Finally, we would like to add that we share the authors’ view on hypnotics in general. Prescription of hypnotics should generally be avoided, and these drugs should almost exclusively be reserved for short-term use in selected patients.

References

Conflict of Interest:
MA and JH has participated in research projects funded by Nycomed, the manufacturer of Nitrazepam, and Pfizer, the manufacturer of Halcion (triazolam) and Tafil (alprazolam), with grants paid to institutions where they have been employed. JH has personally received fees for teaching from Nycomed. AP and SF declare no conflicts of interest.

Is it hypnotics that kill, or is it psychiatric illness?

Kenneth G. Terkel, M.D., General Psychiatrist, Assistant Director, Behavioral Health Services
James P McGuire, M.D. and Michael B Friedman
Community Health Center of Cape Cod

Is it hypnotics that kill, or is it psychiatric illness?* Kenneth G. Terkel, M.D. General Psychiatrist, Assistant Director. * James P. McGuire, M.D. Child and Adolescent Psychiatrist Behavioral Health Services Community Health Center of Cape Cod

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Scripps Clinic Viterbi Family Sleep Center

Please note that my co-authors have approved our manuscript, but Dr. Langer and Dr. Kline have no previous publications about hypnotic drugs and no affiliation with the www.DarkSideOfSleepingPills.com website. Some people would think it scientifically proper that I participated in a

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Published 19 April 2012

Conflict of interest

Angela M Cadeia, PharmD Candidate

Dear Editor: I appreciated and read Dr. Kripke's manuscript with interest. He and his co-authors present many considerations healthcare providers should acknowledge when prescribing hypnotics. Hypnotics, like all medications, have inherent risks.

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Published 16 April 2012

Propensity score matching to minimize confounding by indication

Sujit D Rathod, PhD Candidate in Epidemiology

University of California, Berkeley

The authors made a concerted effort to control for confounding in the design and analysis phase of this paper, and correctly stated that unmeasured confounding is a limiting feature of the results. Given the understandable concerns about confounding by indication, another approach the authors may wish to consider is propensity score minus...

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Published 29 March 2012

Response: "Hypnotics' association with mortality or cancer: a matched cohort study"

Devonne M Ryan, Student

Dr. Daniel Kripke,

Thank you for your article entitled "Hypnotics' association with mortality or cancer: a matched cohort study." I enjoyed reading it and found it to be especially interesting.

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Published 16 March 2012

Re: Hypnotics and mortality: A time for action

http://bmjopen.bmj.com/content/2/1/e000850.abstract/reply#bmjopen_el_3489

Page 3 of 5

Re: Hypnotics and mortality: A time for action

Daniel F Kripke, M.D.

Scripps Clinic Viterbi Family Sleep Center

We apologize if we created confusion by saying we "adjusted" for prior cancer. Indeed, our method of adjustment was to exclude all patients with any diagnosis of major cancer prior to the interval of observation. Similarly, when examining non-melanoma skin cancers, we excluded

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Published 8 March 2012

Need for accessible non-drug treatments

Daniel F Kripke, M.D.

Scripps Clinic Viterbi Family Sleep Center

As these distinguished authors write, efforts should be made to improve the accessibility of non-drug treatments for insomnia such as cognitive-behavioral approaches. By reducing the use of hypnotics, such treatments might be life-saving.

Conflict of Interest:

Please see our BMJ Open article

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Published 8 March 2012

Insomnia in the UK: who cares?

Colin A Espie, Director, University of Glasgow Sleep Centre
Kevin Morgan, David Nutt, Nilanjan Silvadben, Derek Jen Oja, Sioban McIntyre, June Brown, John Cape, Sue Wilson, Maureen Tomeny, Andrew McGuffin, Neil Douglas

Insomnia is twice as common in the UK as anxiety or depressive symptoms(1). Indeed, chronic insomnia is a risk factor for the development of such mental health problems(2). Yet in a week when new research shows that the prevalence of insomnia is increasing in England(3), and that even

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Published 6 March 2012

Hypnotics and mortality: more evidence is needed

Victor Yarlejo-Garcia, Medical Student
Pilar Toledano-Varela, Javier Field-Sancho, Jose Madrido-Santes

University of Navarra

Dear Editor:

We have read with great interest the recent article by Kripke DF, Langer RD and Kline LE that assessed the risk of all cause mortality and cancer incidence in patients using

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http://bmjopen.bmj.com/content/2/1/e000850.abstract/reply#bmjopen_el_3489

Page 4 of 5
Why weren't people with insomnia who didn't take hypnotics included in the control group—could insomnia and not hypnotics be the factor causing excess death?? Is the dose relationship just an indication of the severity of insomnia?