

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Use of driving-impairing medicines by the population: a population-based registry study.
AUTHORS	Gutierrez-Abejón, Eduardo; Herrera-Gómez, Francisco; Criado-Espejel, Paloma; Alvarez, F. Javier

VERSION 1 – REVIEW

REVIEWER	Yvonne Kaussner Wuerzburg Institute for Traffic Sciences, Germany There are no competing interests.
REVIEW RETURNED	22-May-2017

GENERAL COMMENTS	<p>This is an interesting, well structured paper. Data on the use of driving impairing medicines in the general population and as well as in drivers is very important to assess its impact on traffic safety. A comparison of this exposition data (prevalence of the drugs in the accident-free population) as compared to the prevalence in accident samples allows to identify heightened risks.</p> <p>I only have minor remarks.</p> <ol style="list-style-type: none">1. Abstract: Authors conclude that "the fact that ATC group N medicines were the most consumed highlights the need to improve dispensation tools". Please specify why resp. in what way? The same holds true for the Conclusions (page 15).2. Page 5, line 12: "Medicines can adversely affect these driving-related skills ..." The appropriate DRUID deliverable about the meta-analysis of empirical studies on the influence of medicines on safe driving (Berghaus et al., Work Package 1) should be cited.3. Page 6, first paragraph: With respect to the categorization of drugs the appropriate DRUID deliverable (Work Package 4) should be cited. Alternatively reference 38 should be already used in the introduction.4. References: Reference 38 is incomplete and should be revised (Authors are missing, Link is not correct); Reference 39 is also incomplete (title is missing).
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REVIEWER	Ramaekers JG Maastricht University, The Netherlands
REVIEW RETURNED	28-May-2017

GENERAL COMMENTS	<p>The is a clear and straightforward report on the prevalence of DIM medications among the general population and drivers in the Spanish region Castile & León, The work is timely and relevant and aim, results and discussion are properly presented.</p> <p>I have a few suggestions that the authors may wish to take into account. Is there any reference to show that DIM use in this particular region is comparable to DIM use in Spain or any other EU country?</p> <p>Also, it might of interest the compare the prevalence rates for benzodiazepines, z-drugs and opioids among drivers to the prevalence rate of these drugs among crash drivers as reported in DRUID.</p>
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REVIEWER	Nicola Starkey School of Psychology, University of Waikato, Hamilton, New Zealand
REVIEW RETURNED	11-Jul-2017

GENERAL COMMENTS	<p>The paper is clear, well written and addresses a topic that is of increasing importance in the context of an ageing population (and by consequence a larger number of older drivers). There are a few areas of the manuscript that that would benefit from some additional clarification:</p> <p>Abstract</p> <ol style="list-style-type: none"> 1. The abbreviations (ATC and N) need to be written in full. 2. The conclusions are not supported by the results you present in the abstract, as you haven't reported the the percentage of licensed drivers taking DIMs. <p>Strengths and Limitations</p> <ol style="list-style-type: none"> 3. The effect of drugs on driver behaviour (and crash risk) depends on when the drug was taken in relation to driving. So even though a high percentage of drivers are taking DIMs, they may be taken them at a time when their driving is unlikely to be impaired (ie before bed) - this could be acknowledged in the paper. <p>Method/Results</p> <ol style="list-style-type: none"> 4. As a key focus is on drivers taking DSIMs it would be helpful to explain when people can obtain a driving licence (and drive unaccompanied) to provide some context for the study. 5. Target population (p8, line 27; p10 line 37 and Table 1). Could you explain how you worked out the percentage of drivers taking DSIMs? Did you calculate the proportion of licensed drivers for each age group, and adjust the numbers of those taking medication accordingly? 6. As you focus is DSIMs and driving, I wondered why you included children in the analyses? I don't think they are needed (unless you want to consider them as pedestrians or cyclists?) <p>Discussion</p> <ol style="list-style-type: none"> 7. Taking drugs with alcohol may be more problematic than combinations of prescription drugs. This issue could be incorporated into the discussion (p13 line 20).
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Yvonne Kaussner

Institution and Country: Wuerzburg Institute for Traffic Sciences, Germany Competing Interests: There are no competing interests.

This is an interesting, well structured paper. Data on the use of driving impairing medicines in the general population and as well as in drivers is very important to assess its impact on traffic safety. A comparison of this exposition data (prevalence of the drugs in the accident-free population) as compared to the prevalence in accident samples allows to identify heightened risks.

I only have minor remarks.

1. Abstract: Authors conclude that "the fact that ATC group N medicines were the most consumed highlights the need to improve dispensation tools". Please specify why resp. in what way? The same holds true for the Conclusions (page 15).

Response: Abstract, conclusion section (page 3), and conclusion section (page 17, 2nd paragraph) has been re-written.

2. Page 5, line 12: "Medicines can adversely affect these driving-related skills ..." The appropriate DRUID deliverable about the meta-analysis of empirical studies on the influence of medicines on safe driving (Berghaus et al., Work Package 1) should be cited.

Response: done, see new reference 5.

3. Page 6, first paragraph: With respect to the categorization of drugs the appropriate DRUID deliverable (Work Package 4) should be cited. Alternatively reference 38 should be already used in the introduction.

Response: done, see new references 15 and 16.

4. References: Reference 38 is incomplete and should be revised (Authors are missing, Link is not correct); Reference 39 is also incomplete (title is missing).

Response: Thanks, done. Please see references 45 and 46.

Reviewer: 2

Reviewer Name: Ramaekers JG

Institution and Country: Maastricht University, The Netherlands Competing Interests: none declared

This is a clear and straightforward report on the prevalence of DIM medications among the general population and drivers in the Spanish region Castile & León, the work is timely and relevant and aim, results and discussion are properly presented.

I have a few suggestions that the authors may wish to take into account. Is there any reference to show that DIM use in this particular region is comparable to DIM use in Spain or any other EU country?

Response: This issue is addressed on discussion, page 15, 12nd paragraph.

The following text has been added: “ Our study was based in a region of Spain. Current information from the CONCILYA medicines dispensation registry shows that medication use in Castile and León does not differ from other areas in Spain (as measured in Defined Daily Doses [DDD] per 1000 inhabitants-day)^{48,49} and are in line with those reported in other countries.⁷ Recently, Eurostat reported on medicine use in the European Union.⁵⁰ In the European health interview survey, conducted between 2013 and 2015, people were asked about self-reported medicine use. Our data by gender and age range agree well with these results, although figures from the Eurostat refer to medicine use in the two weeks prior to the survey, and the current data were based on any medicine dispensed in 2015. Therefore, although considered with caution due to possible country variations, the figures from the present study could be generalized to other developed countries.”

Comment: Also, it might of interest the compare the prevalence rates for benzodiazepines, z-drugs and opioids among drivers to the prevalence rate of these drugs among crash drivers as reported in DRUID.

Response: This is now addressed in discussion section, page 12, 2nd paragraph.

Reviewer: 3

Reviewer Name: Nicola Starkey

Institution and Country: School of Psychology, University of Waikato, Hamilton, New Zealand

Competing Interests: None declared

The paper is clear, well written and addresses a topic that is of increasing importance in the context of an ageing population (and by consequence a larger number of older drivers). There are a few areas of the manuscript that that would benefit from some additional clarification:

Abstract

1. The abbreviations (ATC and N) need to be written in full.

Response: done

2. The conclusions are not supported by the results you present in the abstract, as you haven't reported the the percentage of licensed drivers taking DIMs.

Response: In line with conclusion section of the study, abstract conclusion reference to drivers in the original submission has been deleted. “Conclusion: The use of DIM was frequent in the general population and among drivers in our region....”

Strengths and Limitations

3. The effect of drugs on driver behaviour (and crash risk) depends on when the drug was taken in relation to driving. So even though a high percentage of drivers are taking DIMs, they may be taken them at a time when their driving is unlikely to be impaired (ie before bed) - this could be acknowledged in the paper.

Response: this section “Strengths and Limitations” (page 4) has been fully rewritten. The issue you raised has been dealt with either in “Strengths and Limitations” and particularly in the discussion sections, limitations of the study, page 16.

Method/Results

4. As a key focus is on drivers taking DSIMs it would be helpful to explain when people can obtain a driving licence (and drive unaccompanied) to provide some context for the study.

Response: The fitness to drive evaluation and granting issue, and the relevance for DIM, is addressed in introduction (see page 7, 2nd paragraph).

The following text was added: "Fitness to drive evaluations have been applied in most developed countries^{30,31}, although the procedures differ markedly. Across the European Union, there is a minimum common regulation under Council Directive 439/EEC³⁰. Within the context of a fitness to drive evaluation, an issue to be considered is medication use (prescribed and over-the-counter) by the driver, although this should always be assessed under the complex relation between disease-medication, particularly among aged people who frequently suffer from several diseases and are poly-medicated.^{1,14-16}"

5. Target population (p8, line 27; p10 line 37 and Table 1). Could you explain how you worked out the percentage of drivers taking DSIMs? Did you calculate the proportion of licensed drivers for each age group, and adjust the numbers of those taking medication accordingly?

Response: this is now explained in detail in methods, target population, page 8, 2nd paragraph.

6. As you focus is DSIMs and driving, I wondered why you included children in the analyses? I don't think they are needed (unless you want to consider them as pedestrians or cyclists?)

Response: Please see discussion page 14th, last paragraph, and page 15, lines 1-2.

The following text was added: "Our study showed that DIM use by the population is frequent, even in young people/children, who are not motorized vehicle drivers: however, all of us are road users (pedestrians). Medicinal products authorized for use in children do not have the pictogram for medicines and driving in Spain; however, medicines that could be used by the population, including young people, include it. Although the topic of medicines and driving has focused on motorized vehicles, their use by cyclists and pedestrians²⁵ is a field of growing interest, especially involving road accidents."

Discussion 7. Taking drugs with alcohol may be more problematic than combinations of prescription drugs. This issue could be incorporated into the discussion (p13 line 20).

Response: this is certainly a relevant issue. This is now addressed in discussion section, page 13, 2nd paragraph.

The following text was added: "The combined use of DIM with alcohol is well-known to have marked effects on psychomotor performance.^{1,5,14-16} Furthermore, the risk of being seriously injured or killed while driving with these psychoactive substances was highly increased with multiple use and the risk increased severely with combined use with alcohol.^{1,36} Avoiding use of alcohol is a priority for safe driving,^{1,6} but particularly for those who take medicines, either acutely or regularly.

VERSION 2 – REVIEW

REVIEWER	Nicola Starkey School of Psychology University of Waikato Hamilton New Zealand
REVIEW RETURNED	21-Aug-2017
GENERAL COMMENTS	The authors have addressed all of the comments raised in my first review- I have no further suggestions.