Author’s response to reviews

Title: Longitudinal pharmacoepidemiological and health services research for substance users in treatment: protocol of the Belgian TDI-IMA linkage

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Brussels, October 23th 2017,
Dear Editors of Archives of Public Health,

Thank you for inviting us to submit a revised version of our manuscript entitled: “Longitudinal pharmacoepidemiological and health services research for substance users in treatment: protocol of the Belgian TDI-IMA linkage”. All the reviewer’s comments were important to improve the manuscript. We carefully considered all comments and suggestions from the three reviewers. Please find below our point-by-point reply to the each revision. Our reply is in blue, under each comment. We also modified the manuscript accordingly and all the changes are also highlighted in track changes.

In addition to the suggestions of the reviewers, we made few corrections in the text to improve the understanding by the readers. They are also highlighted in blue.

We are looking forward to your final decision.

Kind regards,

Luk Van Baelen

Reviewer reports:

Reviewer #1: This paper describes the protocol that was followed to allow linkage between the Treatment Demand Indicator Database, a database containing information about people entering drug treatment and the Intermutualistic Database, a database containing information on the use of reimbursed medication and health services. Furthermore it explains how it may facilitate the understanding of care pathways of people with a substance disorder.

The topic is undoubtedly relevant. Not only will this linkage allow in depth analysis of the trajectories of people with a substance use disorder in terms of health service use In Belgium, it may also inspire other countries to do the same which would make comparisons in terms of health care use among people who use drugs on the European level possible.

I have no major remarks. I would like, however, make some suggestions that may improve the readability of the paper.
Thank you for your comments and suggestions. Please find below our reply to your suggestions.

Background

Line 45

* I am not sure what is men by the sentence "Data are focusing… redemption sin pharmacies".

The sentence has changed and has been added to the previous sentence: “An example of such a database is the Danish Registry of Medicinal Product Statistics which contains information for the entire Danish population since 1994 about age, sex and municipality of the drug user, quantity of and expenditures for prescribed drugs, the practice code of the prescriber and the practice code of the dispensing pharmacy”.

Lines 48-49

* This sentence seems in contradiction with the next sentence which mentions that "other EU countries also developed databases following an integrated approach"

Indeed. “Also” was deleted to emphasis the difference: “At the same time other EU countries developed databases following an integrated approach, characterized by the collection of information on patients’ socio-demographics and prescribed drugs as well as all other types of health care events.”

Line 90

The use of health services by instead of

Thank you for your suggestion. This has been adapted.

Methods/Design

Lines 98-99

* Please explain briefly the case definition by Antoine and colleagues

Thank you for your suggestion. We have tried to clarify and to give a point-by-point explanation of the case definition used by Antoine and colleagues (lines 98-122):
“Cases were selected based on patients’ first registration in the TDI-database between 01/01/2011 and 31/12/2014, following the case definition used by Antoine and colleagues for the Belgian TDI registration (protocol 2.0) [1]: in TDI information is collected (a) on every treatment episode (b) started by a person (c) in a treatment center (d) for his or her alcohol or illicit drug use.

(a) An episode is defined as the period between the start of the treatment, which is the first face-to-face contact between a professional and the patient, and the end of activities in the context of the program prescribed. In outpatient settings this end of the episode occurs when the patient stops attending treatment for a period longer than six months, whereas in inpatient settings, it is defined as the moment when the patient leaves the center and no further admission is foreseen. However, data only show an image at the start of the episode and no information is available about the duration of the episode. Patients also have the right to refuse registration. If in the period 2011 to 2014 patients were admitted to treatment more than once, data from the start of the first episode were used for the current linkage. Since some patients were in treatment before 2011, this means that this first episode does not necessarily correspond to the first treatment ever, nor does it mean that there have not been any other treatment episodes afterwards. Treatment is defined as any activity targeting a person with substance use problems directly in order to obtain results in terms of reducing or eliminating these problems.

(b) The registration concerns all individuals without any restriction, with the only condition that the patient should have had a face-to-face contact with a care giver for his or her substance use problem.

(c) Activities have to take place in a treatment center, which is defined as a facility or practitioner providing treatment for drug or alcohol addiction. It can be an outpatient or inpatient service, either specialized in addiction treatment or included in larger scale facilities targeting different groups of people, and sometimes but not always recognized within a convention of authorities such as the National Institute for Health and Disability Insurance (NIHDI) [1].

(d) Drug types that are registered are opioids, cocaine/crack, stimulants other than cocaine, hypnotics and sedatives, hallucinogens, volatile inhalants, cannabis and alcohol, and their subcategories.”

Lines 101-104

* By giving the definition of an episode the reader might get the impression that episodes are registered while in fact - at least that is how I understand it - only the start of an episode is
registered and no information is available about the duration of the episode. This should be mentioned explicitly.

This is a good observation. We have put it explicitly on lines 106-108: “However, data only show an image at the start of the episode and no information is available about the duration of the episode. About the kind of treatment that is provided to the patient, only information about reimbursed services and medication is available.”

Line 110-117
* This piece of information is partly repeated in the section "Registration and collection of variables" and could be moved entirely to that section.

Thank you for your suggestion. We have moved it and rephrased it to get it in line with the rest of the text.

Lines 118-147
* Perhaps a new subtitle can be inserted since this section is not really about case definition anymore.

Thank you for your suggestion. We have added “Linkage procedure TDI-IMA”

Line 158
* "the fact that the patient was already in treatment for substance use disorders before" might be replaced by "history of previous treatment for substance use disorders"

Thank you for your suggestion. We have replaced the sentence.

Line 159
* "and" should be a comma

Thank you for your suggestion. This has been adapted.
Data are collected in three different ways, as explained on the IMA-website (http://www.aimima.be/Data-Gezondheidszorgen?lang=nl) under the heading “Hoe worden de gegevens gezondheidszorgen verzameld?”: at the counter of the health insurance agency, through third parties such as hospitals, groups of nurses, homes for elderly, or together with pharmaceutical data.

Analysis and reporting

Lines 200-201

* I believe this information should be moved to the section where linkage is described

Thank you for your suggestion. The sentence has moved to lines 130-131.

Lines 231-233

* I don't find this information in table 2.

It has been explained more in detail in lines 253-257: “By applying the aforementioned matching criteria, to each person in TDI four comparators were matched. However, the number of comparators is not exactly four times the number of cases. Indeed, as shown in table 2 there are 30,905 people in treatment for substance use disorders, but only 122,142 unique comparators, meaning that as a result of the stringent matching criteria 1,478 comparators have been linked to more than one case.”

Discussion

Lines 243-245

* Please add a reference

Thank you for your suggestion. We have added two references.

Line 249 and elsewhere
* The term "people who use drugs" (PWUD) is preferable to "drug users"

Thank you for your suggestion. “Drug users” has been changed to “PWUD” throughout the whole manuscript.

Line 250
* "needs" should be "conditions" of "diseases".

Thank you for your suggestion. This has been adapted.

Line 254
* risk of infections instead of "on"

Thank you for your suggestion. This has been adapted.

Line 279-280
* plus prescribed but not reimbursed drugs eg benzodiazepines

Thank you for your suggestion. This has been adapted.

Reviewer #2: certain writing patterns need review of the manuscript by the authors for example in the background section, page 4 line 47 of the manuscript instead of "(e.g. Torstensson et al. [3])." the brackets can be removed and written as "e.g. Torstensson et al. [3]"

Thank you for your suggestion. We have removed the brackets.

Reviewer #3: The paper looks interesting, but requires further copy editing before it can be published.

The authors could improve the quality of the paper by addressing following in the revised version of the paper.

Thank you for your comments and suggestions. Please find below our reply to your suggestions.
1. "Case definition" should be elaborated in the paper instead of referring the reader to other sources. Specific limitation with the current definition and how the authors operationalized the case definition in the current study should be articulated. The constructs of "episode" and "treatment" as explained in the paper are not clear and leaves the reader with some confusion. These should be clearly explained.

Thank you for your suggestion. We have tried to clarify and to give a point-by-point explanation of the case definition used by Antoine and colleagues (lines 98-122):

“Cases were selected based on patients’ first registration in the TDI-database between 01/01/2011 and 31/12/2014, following the case definition used by Antoine and colleagues for the Belgian TDI registration (protocol 2.0) [1]: in TDI information is collected (a) on every treatment episode (b) started by a person (c) in a treatment center (d) for his or her alcohol or illicit drug use.

(a) An episode is defined as the period between the start of the treatment, which is the first face-to-face contact between a professional and the patient, and the end of activities in the context of the program prescribed. In outpatient settings this end of the episode occurs when the patient stops attending treatment for a period longer than six months, whereas in inpatient settings, it is defined as the moment when the patient leaves the center and no further admission is foreseen. However, data only show an image at the start of the episode and no information is available about the duration of the episode. Patients also have the right to refuse registration. If in the period 2011 to 2014 patients were admitted to treatment more than once, data from the start of the first episode were used for the current linkage. Since some patients were in treatment before 2011, this means that this first episode does not necessarily correspond to the first treatment ever, nor does it mean that there have not been any other treatment episodes afterwards. Treatment is defined as any activity targeting a person with substance use problems directly in order to obtain results in terms of reducing or eliminating these problems.

(b) The registration concerns all individuals without any restriction, with the only condition that the patient should have had a face-to-face contact with a care giver for his or her substance use problem.

(c) Activities have to take place in a treatment center, which is defined as a facility or practitioner providing treatment for drug or alcohol addiction. It can be an outpatient or inpatient service, either specialized in addiction treatment or included in larger scale facilities targeting different groups of people, and sometimes but not always recognized within a convention of authorities such as the National Institute for Health and Disability Insurance (NIHDI) [1].
(d) Drug types that are registered are opioids, cocaine/crack, stimulants other than cocaine, hypnotics and sedatives, hallucinogens, volatile inhalants, cannabis and alcohol, and their subcategories.”

2. The authors mention the use of "a deterministic algorithm" to link TDI and IMA database. It will be helpful to the reader if the authors could explain this algorithm and specifically what it seeks to achieve (in a more broad sense) and why it is described as deterministic, and particularly which causal framework it is meant as deterministic? The authors also mention another algorithm in the same section, but it is not clear if this is also deterministic as previously described. The latter algorithm needs further explanation.

“Deterministic” stands for a linkage where we are sure that records with the same identification number in both the TDI and IMA database correspond to the same person. It is the opposite of a “probabilistic” linkage, where the linkage depends on certain characteristics of the person (such as sex and first letter of the surname), and where it is not 100% sure that records refer to the same person. We used a deterministic linkage based on the national identification number, which is unique for every Belgian citizen and for other people living in Belgium with social security rights (as explained in lines 126-127). However, we have removed the term “deterministic algorithm” since it might be confusing. Instead, we have explained more in detail the difference between the linkage of the TDI and IMA-database (which was done at random) and the matching with a group of comparators.

It reads now (lines 127-130): “The TDI-database was linked to the IMA-database for the period between 01/01/2008 and 31/12/2017, based on the national identification number (NIN) of the patient. This number is unique for every Belgian citizen and for other people living in Belgium with social security rights. It is used in TDI to avoid double counting over several treatment episodes and over different treatment centers. In TDI, the NIN was encrypted for the linkage by a trusted third party, eHealth. In IMA, the NIN was encrypted twice by a trusted third party, the Crossroads Bank for Social Security (CBSS). The linkage procedure has been established in line with all relevant national privacy rules [2].”

3. The study appears to apply matched case control study, but did not explain the rationale for using following matching variables: sex, age, and place of residence. Importantly, who were these groups matched on and what were their background characteristics? So after matching on the selected variables, how many subjects were available for analysis? It is not clear from the paper the "unit of analysis’ applied in making inference for discussion. This has to be explained in-depth.
Thank you for your suggestion. Indeed, this might have been confusing. We have explained more in detail the reasons why we have chosen these matching variables (lines 143-151): “For every patient included in the TDI-database four comparators were drawn at random from the clients of the seven Belgian health insurance companies [3]. Cases and comparators were matched on sex, age and place of residence [4]. Sex and gender were used as basic matching variables. The matching on municipality was related to both the underlying regional differences in health care regulation and health care availability (with for instance geographically different access to specialized medical health care for substance use disorders) as well as socio-economical differences between patients in the different regions of Belgium. As a result, this matching procedure allows adjusting for confounders and at the same time it created a “comparative” group that is similar to the patients in TDI who are mainly men (71.8%) with an average age of 39.8 years [5].”

Indeed, each record in TDI was matched at random on age, sex and place of residence to four records in IMA. However, since data are retrospective as well as prospective from the moment of matching, i.e. from the moment patients started treatment, we cannot use the term case control study. The matching only created a “comparative” group that is similar to the patients in TDI. The number of subjects available for analysis is mentioned in table 1 in the column with header ‘TDI-IMA linkage records’. However, the number of comparators is not exactly four times the number of cases. Indeed, as shown in table 2 there are 30,905 people in treatment for substance use disorders, but only 122,142 unique comparators, meaning that as a result of the stringent matching criteria 1,478 comparators have been linked to more than one case. This is explained in lines 253-257.

4. The data linkage procedure is not clear, and authors need to explain how the linkage is related or different from the algorithm used.

We hope we have answered this question when answering the second comment.

References


2. Commissie voor de bescherming van de persoonlijke levenssfeer: Beraadslaging nr. 15/033 van 19 mei 2015 met betrekking tot de mededeling van gecodeerde persoonsgegevens betreffende de gezondheid door het IMA en het TDI-register aan het Wetenschappelijk
Instituut Volksgezondheid in het kader van een wetenschappelijke studie (SCSZG/15/078). 2015.

