Reviewer’s report

Title: The healthcare costs of intoxicated patients who survive ICU admission are higher than non-intoxicated ICU patients: A retrospective study combining healthcare insurance data and data from a Dutch national quality registry

Version: 1 Date: 16 Dec 2018

Reviewer: Yves Chaput

Reviewer's report:

The authors have made substantial changes to the manuscript and answered the vast majority of the queries that I had submitted to them.

I have but a few remaining comments left concerning this manuscript. These are however all MINOR points that the authors can look at and see if they wish to integrate into their manuscript. I have divided them into 2 categories, the first are follow-up minor points to the major points raised at my first review.

The second category contains style and grammar suggestions. In this latter case I have included the line numbers and a short phrase that the authors can look at and compare to what they have written. If they feel the changes beneficial then they can include them into their revised manuscript. If not, then they can discard them.

MINOR FOLLOW-UP POINTS:

BACKGROUND SECTION

I would put the phrase beginning with "Depending on region and healthcare system it is estimated… " (line 63, page 1) following the second phrase of the Background section (that ending with "…three times higher than…"). I would then change to another paragraph beginning with " The majority of intoxications …. That would both introduce the ICU and the concept of intoxicated patients in the ICU in the 1st paragraph.

As an example:

It has been suggested that ICU-survivors often suffer from long-term sequelae that may significantly increase health care costs to society [1]. Indeed, it has been shown that over a 2-year period, patients admitted to the ICU with sepsis have monthly healthcare expenditures three times higher than prior to their ICU admission [1,2]. Depending on region and healthcare system
it is estimated that between 2.7 and 40% of patients seen in the emergency room are subsequently admitted to the ICU and between 65.3.4 to 14% of ICU admissions are admitted for intoxications [7-9].

The majority of intoxications …

METHODS SECTION

Not to be too anal but is VEKTIS a government run reimbursement program? For instance, do Dutch citizens pay out of pocket for medical treatment and obtain reimbursement via VEKTIS? If this is the case then it would be useful to mention it this section.

GRAMMAR AND STYLE MINOR POINTS:

BACKGROUND SECTION

None. This section as been extensively re written.

METHODS SECTION

Line 80 "The NICE registry is a national quality registry in which all Dutch ICUs participate and collect clinical, demographic, physiologic, and outcome data from all admitted patients."

Line 85, "We combined data from the NICE registry and the insurance claims database..."

Line 86, "Health insurance is obligatory for all Dutch citizens and 99% have private healthcare insurance."

Line 99, "This population-based control group was weighted on the combination of the variables gender, age and socio-economic."

Line 119, "The latter was matched 1:1 with patients in the combined database who were admitted to the ICU for reasons other than intoxication (the so-called "ICU population").

Line 123, "The intoxication population was matched 1:1 with people in the combined database not admitted to the ICU."

Line 128, "Health care costs are related to chronic conditions requiring pharmacological and other medical treatments."
Line 129, "We determined the underlying medical conditions present at admission to the ICU from the APACHE IV severity of illness model. Additionally we looked at proxies for underlying medical conditions and concomitant diseases from the Vektis database. For example, patients with reimbursed costs for diabetic medications were attributed a diabetes comorbidity (see additional files, table e2). Costs per day were analyzed in relation to the number of underlying medical conditions, as described previously [2]."

Line 154, "As healthcare costs per day alive were skewed to the right the natural logarithm of the healthcare costs per day alive was used."

Line 166, "Additionally, for all three-study populations we created subgroups based on the number of chronic medical conditions."

RESULTS SECTION

Line 182, "The final dataset included 2591 patients admitted to the ICU for intoxication. These 2591 patients had 2968 ICU admissions in 2013. Intoxication was the underlying reason for 95.8% (n=2843) of admissions whereas 4.2% (n=125) were admitted for reasons other than an intoxication."

Line 186, phrase beginning with "In total, 14…" is difficult to decipher and should be clarified.

Line 188, "Finally, 2591 control persons were matched 1:1 with the intoxication population."

Line 192, "Supplementary file (Figure e1) illustrates survival curves for the intoxication, ICU and control population"

Line 194, "The healthcare costs…of the intoxication group survivors were…compared to the ICU group survivors…and to the control group survivors". (or "population" rather than "group", whatever the authors prefer)

Line 199, "..compared to those of the ICU population" (same with line 201).

Line 203, " Those within the intoxication group surviving all three years who were intoxicated with "sedatives" had the…during the total study period"

Lines 207 / 208, "Fifty-three percent (1389/2591) of patients in the intoxication group had one or more underlying medical conditions at the time of their ICU admission, compared to 40.3% (1038/2577) in the ICU group. Approximately 19% (489/2591) of those in the control group had one or more medical condition."

Line 215 "The costs per day alive …number of underlying medical conditions…"

Line 217, "…costs per day alive in relation to the number…"
DISCUSSION

Line 238, "More than 60% had been treated by a psychiatrist..." Is this accurate? Were they actively treated or had they been "assessed" or "seen" by a psychiatrist in the 90 days prior? Those are 2 different things.

Line 239, "After hospital discharge...approximately 12% were transferred to a ...". (I'm not quite certain you can start a phrase with "And").

Line 240, "This suggests that a proportion of healthcare costs are...acute care setting."

Line 241, "One of the few studies that assessed patients 6-months beyond discharge...cost/effectiveness ratio, defined as the cost of..."

Line 245, "...health care quality of life (HRQoL), then..."

Line 249, "...a small study of Dutch survivors..."

Line 252, "...cost/effectiveness ratio of Dutch patients surviving an ICU admission for an acute intoxication (may?) be poorer..." The word "will" is emphatic, as if the hypothesis is actually a fact.

Line 254, "We have shown that the healthcare ... were high(er)..."

Lines 258-260, Not quite certain what the meaning of these phrases is. My interpretation is: In this latter study the Simplified....whereas the APACHE IV model was used in the present study". Is this correct?

Line 260, "... compared to the SAPS II model,

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes
Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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