Author's response to reviews

Title: Overview and evaluation of 15 years of Creutzfeldt-Jakob disease surveillance in Belgium, 1998-2012.

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Author's response to reviews: see over
Public Health & Surveillance

SUBJECT: Revision of manuscript entitled “Overview and evaluation of 15 years of Creutzfeldt-Jakob disease surveillance in Belgium, 1998-2012.”

Dear Editor,

On behalf of all co-authors, I have the pleasure to submit the revised version of the manuscript previously entitled “Evaluation indicates that the Belgian Creutzfeldt-Jakob disease surveillance meets its objectives but can be optimized” with the new title “Overview and evaluation of 15 years of Creutzfeldt-Jakob disease surveillance in Belgium, 1998-2012” for publication in BMC Neurology.

Please find the point-by-point responses to the concerns raised by the reviewers at the end of this letter.

We sincerely hope that this revised manuscript will be accepted for publication in BMC Neurology.

Yours sincerely,
Amber Litzroth, Patrick Cras, Bart De Vil, Sophie Quoilin
Point-by-point responses to the concerns raised by the reviewers:

**Reviewer: André Karch**

Major compulsory revisions

1. As pointed out in my original review and supported by Prof. Yamada's comment 4, I do not think that the conclusion of this article is correct as I don't see any evidence that a vCJD case could be captured. There has never been one in Belgium, none of the neurologists there have seen one before and even then only a limited proportion would refer the case to the surveillance system. I think that you pointed out very nicely that the system is capable of finding trends in CJD incidence. Why not be more critical about the second aim? It doesn't change the quality of research you did, but on the other hand - at least I think - the manuscript cannot be accepted with this conclusion as it stands as it is not true.

We agree that too much importance is given to the self-reported referral of vCJD cases of 89%. This is not 100% and moreover, we should be cautious with interpreting survey results.

We have modified the title, abstract, discussion and conclusions:


Line 55-56: “However, we do not have sufficient evidence to conclude that the system meets its second objective of detecting vCJD cases arising in Belgium”.

Line 278-284: “Among those neurologist that responded to the survey, the vast majority (89%) would refer suspect vCJD cases to a reference centre or contact a reference centre. Moreover, the younger age of vCJD patients and the longer disease duration would render detection of vCJD cases by the surveillance system more likely, even if the neurologist does not contact the reference centre immediately. However, based on this evaluation, we cannot exclude the possibility that a vCJD case arising in Belgium remains undetected. Therefore, we do not have sufficient evidence to conclude that the surveillance system meets its second main objective of detecting vCJD cases arising in Belgium.”

Line 319-321: “Although self-reported referral behaviour of the Belgian neurologists indicates that vCJD cases are likely to be captured by the surveillance system, this evaluation does not give the necessary evidence that the system meets its second objective of capturing vCJD cases.”

2. **Confidence intervals for ORs need to be added. Again, you should specify that your OR for age is the OR per year increase in age.**

Confidence intervals are added:

Line 45: OR=0.95, 95% CI 0.92-0.98, p=0.001
Line 200-202: “The odds of undergoing an autopsy significantly decreased with every one year increase in age (OR 0.97, 95% CI 0.94-0.99, p=0.01). Only the effect of age was significant in the multivariable analysis (OR 0.97, 95% CI 0.94-0.99, p=0.01)”

Line 208-211: “and the odds of capture significantly decreased with every year increase in age (OR 0.95, 95% CI 0.92-0.98, p=0.001). Only the effect of age remained significant in the multivariable analysis (OR 0.95, 95% CI 0.92-0.98, p=0.001).

We specified that the OR is per year increase:

Line 45-46: “The odds of capture significantly decreased with every one-year increase in age (OR=0.95, 95% CI 0.92-0.98, p=0.001).”

Line 163: “The effect of a one-year increase in age on the…”

Line 199-201: “The odds of undergoing an autopsy significantly decreased with every one-year increase in age (OR 0.97, 95% CI 0.94-0.99, p=0.01).”

Line 208-210: “We detected a significant difference between the provinces (p=0.023) and the odds of capture significantly decreased with every one-year increase in age (OR 0.95, 95% CI 0.92-0.98, p=0.001).”

Minor essential revisions:
1. 27 sentences in a row in the Methods section start with "We.." (separated by 3 sentences starting with "For..., we").

   We modified the phrasing in methods, see lines 95-168

2. lines 187 and 190: familial history of CJD is described to show both a significant upward and downward trend

   We deleted the second on, it was a mistake.

Line 188-191: “For 1998-2012, a significant downward trend in annual completeness was observed in the following variables: symptoms at onset (p=0.004), EEG result (p=0.023) and familial history of CJD (p=0.004). For 1998-2012, a significant upward trend in annual completeness was observed in the following variables: date of birth (p=0.034) and date of death (p=0.028).”