Reviewer’s report

Title: Central European Vaccination Advisory Group (CEVAG) guidance statement on recommendations for influenza vaccination in children

Version: 1 Date: 4 March 2010

Reviewer: Catherine WEIL-OLIVIER

Reviewer’s report:

some majors points should be taken in account:
- in the description of burden:

  Bhat's paper describes 153 deaths (around 2/3 before 5 yrs of age; the 0.88/100 000 incidence is for the under 6 months of age and not a global result.

  "children < 6 ms of age": serious complications such as acute otitis media poccur in children under 5 years of age but not specifically in children < 6 months (usually, otitis media is rare in this infant age group)

  "typical symptoms of early...": Silvennoinen’s paper describes ambulatory children <13 yrs of age with 78% of them with rhinitis

laboratory (culture, PCR) confirmation should be distinguished from rapid tests at bed side and their benefit for early and improved diagnosis in order to overcome the underdiagnosis which indeed exists

number of registered cases: replace by notified cases

distinguish in underreporting ambulatory care and hospitalisation the former being more difficult.

distinguish also by age group: it is admitted that clinical diagnosis in children over 5 yrs of age is similar to the one in adults: around 70% during epidemics

"it has been shown that only 28% of children with lab confirmed...": this is the sentence from the summary of the article: "Few children who had laboratory-confirmed influenza were given a diagnosis of influenza by the treating physician in the inpatient (28 percent) or outpatient (17 percent) settings" which does not mean the same

however even among school age children (clinical) diagnosis is well below 50% overall : the exact formulation is "sensitivity of the clinical diagnosis of influenza was 38% and the positive predictive value was 32%" in Peltola's paper.

in young children, the clinical presentation of influenza related illness can consist of.....might not be attributed to influenza "in absence of laboratory confirmation".

- discussion on "seasonal" influenza vaccination:
for the logic of presentation, it should be preferable to present the vaccines (TIV) and what is known so far in children before considering the vaccination strategy

a lot of statements and few strong data to support them: to reinforce the ideas, it would be preferable to add some scientific data upon immunogenicity, and protective efficacy/effectiveness and by age groups. The vagueness of "children" contributes to a weakness of discussion especially when speaking of herd immunity/indirect benefit: demonstrated only when school aged children are (largely) vaccinated

as only TIV are available all through Europe (it should be pointed out that vaccines are the same for adults and children, though not evaluated yearly in children under 18 yrs), the discussion should start with what is known so far with TIV in children by age groups and the caveats (limitations, lacks...): please note than any data under 2 years of age should appear in this paper if known: otherwise this lack should be pointed out.

for TIV: it should appear
- recommended for children aged 6 months to 8 yrs (included)
- the (minimum 4 weeks) interval between the two doses in primovaccination
- the half dose in children < 36 months of age
- the need for yearly booster

one speaks of vaccine "strain" more than vaccine virus

then the future: adjuvanted inactivated injectable vaccines and LAIV

to note: LAIV has been demonstrated to be efficient in the following 2nd season even with a drifted strain (Belshe)

please note that depending on the circulating strain, vaccine efficacy may or may not be demonstrated against H1N1, H3N2 or B: thus it cannot be extrapolated from the RCT's a constance of efficacy over any seasonal flu.

both LAIV and MF59 adjuvanted vaccine would be of interest in "the ability of an influenza vaccine to trigger an immune response against drifted viruses not in the vaccine formulation" so please to reorder this part of the discussion would clarify those points.

for US recommendations: in 2003 there was an encouragement when feasible converted in a recommendation on year 2004 (but no "reverting back"

there is some confusion between vaccines and recommendations / strategies which are spoken on different occasions in this paper: a restructuration of this part would improve greatly the readability

the statement "the efficacy of influenza vaccines in children has been shown in several studies" needs to be backed by strong references

end of page 10: what is the significance of numbers in brackets?
emphasize the fact there is no vaccine for children < 6 ms and only very few (if any!) studies published demonstrating an indirect benefit for this age group the Zaman study was in pregnant mothers and tropical country) 

I would not speak of pregnant mothers in this paper 

this draft should focus on seasonal flu vaccination. if speaking of pandemic strains (and corresponding vaccines) it should be to show the benefit of scientific knowledge which may omprove influenza seasonal vaccines in the future. A strong clarification of ideas is needed on page 12 & 13 if the Authors want to keep this §

page 13: coverages rates should appear as a caveat and presumably are in high risk groups children (?) many other European data (Spain, France) have been published on this topic. 

health workers: use preferably "health care professionals"

in the US the rate of children receiving the 2 doses of primary series is (very) low < 20% (MMWR): if a recommendation were to be taken: there is a strong need to have some wording on how to trigger it and maintain it through the years (a lack in this draft)

the background of a routine recommendation should be summarized: burden (USA, MMWR), indirect costs (Finland, Heikinnen), others?

tolerance: risk of Guillain Barre post vaccine should be related to the risk post flu disease (5-10 fold higher depending on the surveys)

**Level of interest:** An article of limited interest

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

no