Early prevention of pertussis is key reply

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Early prevention of pertussis is key

In the conclusion of their interesting Article, Daan Barug and colleagues state that their data "support a start of pertussis vaccination at age 3 months instead of 2 months in the case of timely administration of maternal Tdap [tetanus, diphtheria, and acellular pertussis] vaccination".[1] Although this might be true for pertussis vaccination per se, unfortunately no stand-alone pertussis vaccine is broadly available.[2] In fact, in this study from the Netherlands, all infants received a diphtheria, tetanus, and pertussis-inactivated poliomyelitis-*Haemophilus influenzae* type b-hepatitis B six-in-one vaccine. Postponing the first dose from 2 months to 3 months might be disadvantageous for optimal protection against diseases other than pertussis—for example, invasive *Haemophilus influenzae* type b infection. Moreover, the measurable blunting of the immune response against pertussis vaccine antigens is not different when the immunisation series in infants whose mothers were immunised in pregnancy is delayed to age 3 months compared with age 2 months, as the authors themselves correctly point out by citing studies from the UK and Belgium.[3-5] Therefore, early protection against pertussis, diphtheria, tetanus, poliomyelitis, hepatitis B, and *Haemophilus influenzae* type b is still a valid option in the era of immunisation of pregnant women against pertussis.

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Authors' reply

We agree with Ulrich Heininger that when altering the primary infant vaccination schedule for the six-in-one diphtheria, tetanus, and pertussis-inactivated poliomyelitis-*Haemophilus influenzae* type b-hepatitis B (DTaP-IPV-Hib-HepB) vaccine from a dose at ages 2, 3, and 4 months to a reduced dose schedule (with doses at ages 3 and 5 months) in cases of timely maternal tetanus, diphtheria, and acellular pertussis (Tdap) vaccination during pregnancy in babies born full-term, one needs to take into account not only protection against pertussis[1] but also against the other diseases.

We investigated potential disadvantages of a reduced-dose schedule for optimal protection against diseases other than pertussis, particularly *Haemophilus influenzae* type b (Hib) infections. In the Netherlands, vaccination against Hib was introduced in 1993. From 1995–98, when a 3, 4, and 5 months primary vaccination schedule for DTaP-IPV-Hib was used, a mean of five Hib cases per year was observed in infants younger than 1 year. A mean of five Hib cases per year was also observed in the period after 1999, when a months 2, 3, and 4 schedule was used.[2] Only six cases of Hib were reported for infants aged between 2 months and 3 months in the period between 2010 and 2017. One must weigh the potential extra cases that can occur between 2 months and 3 months of age against the benefits of one fewer dose of DTaP-IPV-Hib-HepB for all children born full-term to mothers vaccinated during pregnancy and of the first vaccination occurring at an older age. Of course, invasive Hib cases should be closely monitored after this vaccination schedule switch. High vaccine effectiveness has been observed against confirmed invasive Hib disease, both following two and three primary doses.[3] There is no reason to believe that the effectiveness of the Hib vaccine will be lower after the schedule change.

We previously described higher antibody concentrations for most pneumococcal serotypes following a months 3 and 5 schedule compared with a months 2, 3, and 4 schedule for the 13-valent pneumococcal conjugate vaccine (PCV).[4] PCVs are given simultaneously with the DTaP-IPV-Hib-HepB combination vaccine. A later start of the first vaccination and a longer interval between vaccine doses improves priming and antibody concentrations, with less potential for interference from maternal antibodies.[5] We could not compare blunting after first vaccinations at age 3 months versus age 2 months but, if anything, we would expect less blunting with a first vaccination at an older age. Although we admit that early protection against pertussis, diphtheria, tetanus, poliomyelitis, hepatitis B, and Hib remains a valid option in the era of immunising pregnant women against pertussis, we favour a reduced-dose schedule with a later start when feasible.

We declare no competing interests.

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Low prevalence of antibodies against pertussis in pregnant women in Italy

See **Online** for appendix

This online publication has been corrected. The corrected version first appeared at thelancet.com/infection on July 24, 2019

We read with great interest the Article by Daan Braug and colleagues[1] on the results of the maternal pertussis vaccination trial and its effects on the immune response of infants in the Netherlands.

Since 2016, recommendations for maternal immunisation against pertussis have been introduced in Italy, within the National Vaccination Plan 2016–18 and 2017–19,[2] with a dose of tetanus, diphtheria, and acellular pertussis (TdaP) vaccine given during the third trimester of pregnancy, ideally during the 28th week. To date, no data on coverage of pertussis vaccination in pregnant women have been published by the Italian Ministry of Health.

For **Italian Ministry of Health vaccination** website see www.salute.gov.it/portale/vaccinazioni/homeVaccinazioni.jsp

To generate data on the level of immunity against pertussis in pregnant women, we did a serological study to determine the prevalence of antibodies against *Bordetella pertussis* among pregnant women in Apulia, a large Italian region.

195 serum samples were anonymously collected in compliance with Italian ethical law from pregnant women aged 20–46 years (mean 33·6 years [SD 4·6]) in the province of Bari between 2016 and 2017 as part of routine pregnancy medical checks. Samples were tested for IgG against *B pertussis* by use of SERION ELISA classic *Bordetella pertussis* IgG commercial kit (Virion\Serion, Würzburg, Germany). Results below the limit of quantification (10–1000 IU/mL) were considered with an arbitrary value of half the lower limit (5 IU/mL). IgG pertussis titers of 50 IU/mL or higher were regarded as positive by the manufacturer. 77·4% (95% CI 71·0–82·8) of samples had antibody concentrations below 50 IU/mL, and 26·7% (20·9–33·3) had antibody concentrations below the limit of quantification. No significant differences were noted between age groups (appendix).

These findings are consistent with studies done in Italy among pregnant and postpartum women in 2015–18, with very few or no women who had received Tdap during pregnancy,[3,4] and only a third were willing to be vaccinated if recommended by their health-care provider.[3] Adherence to the recommendation seems to be hampered by concerns regarding immunisation safety, poor information, and lack of professional engagement by physicians and health-care providers,[3,4] highlighting the need for vast information and education interventions on the benefits and safety of pertussis vaccination during pregnancy. Because, in Italy, children are given their primary vaccination with the Tdap vaccine at ages 3, 5, and 11 months, a minimal effect on immune response to pertussis vaccination in infants whose mothers have been vaccinated during pregnancy should occur, according to the results of Barug and colleagues.[1]

We declare no competing interests.

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High-income countries and latent tuberculosis infection screening for migrants

I would like to correct a claim in the Comment by Eskild Petersen and colleagues[1] on latent tuberculosis infection (LTBI) strategies. The authors state that "all high-income countries now have proactive latent tuberculosis infection screening and treatment programs for all new migrants and refugees".[1] However, the literature shows that this claim is incorrect.

A review by Kunst and colleagues[2] illustrated that policies on the screening of refugees and migrants in Europe (a continent with many high-income countries) are diverse, and screening for LTBI is rarely done.

Another review[3] on effectiveness and cost-effectiveness of LTBI screening programmes for migrants living in the European Union/European