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Lessons can be learnt from this study

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EDITOR—The paper by Kristensen et al describes improved survival in infants in Guinea-Bissau who received measles or BCG vaccines but increased mortality in those who received diphtheria, tetanus, and pertussis vaccine.¹ At the request of the World Health Organization we visited Guinea-Bissau during 8–15 October 2000 to review this study.

We found the methods to be as described in the paper. As data collection is continuing, we were able to accompany the field staff on several visits. We reviewed the data management procedures and found them to be in order. While several potential sources of bias could be hypothesised we were not able to identify any that could invalidate the study. This is a single study, which was not originally designed to address this issue, and the methodological weaknesses have been highlighted in the accompanying editorial and commentary.^{1 2} By its characteristics and its surprising findings this study should provoke substantial further investigation of the subject. Although these results should not be used as a basis for changing national or global vaccination policy, they demand an immediate response. The first response from the WHO was to seek out data from other developing countries that may be used to address this question, and this is happening.

Other studies may not show the same findings in relation to diphtheria, tetanus, and pertussis vaccine, in which case the particular circumstances in Guinea-Bissau should be considered. At the time of the study 25–30% of all children died before their 5th birthday, most from malaria or pneumonia, although this has not been well studied. Data from other places with high mortality and intense malaria transmission will therefore be particularly interesting.

Regardless of the outcome of the ongoing investigations, the work in Guinea-Bissau highlights the importance of considering the overall impact of vaccines on children's health. Thus the finding that measles and BCG vaccines seem to improve survival beyond what can be attributed to the prevention of the specific diseases is particularly good news that should stimulate similar studies in other areas.

Broader lessons can be learnt from this study. Public health research to support public health interventions is not a luxury but a necessity. Up till now, the overall impact of routine childhood vaccines on survival in places with high mortality has not yet been evaluated systematically. We should learn from this omission and ensure that all public health interventions are underpinned by the appropriate public health research, both experimental and observational, to ensure that they are both safe and efficacious.

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WHO responds to Guinea-Bissau report

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EDITOR—The paper by Kristensen et al challenges the safety of diphtheria, tetanus, and pertussis vaccine, one of the principal vaccines used by national immunisation programmes.¹ The authors shared their results with the World Health Organization before publication, and they cooperated in allowing the organisation to review the field sites in Guinea-Bissau and the data bank in Copenhagen.

The Global Advisory Committee on Vaccine Safety of the WHO, an independent group of experts in drug safety, vaccine science, and epidemiology that advises the Department of Vaccines and Biologicals of the organisation, has closely considered the reported findings and conclusions of the paper. It has found that numerous and serious deficiencies in the paper did not allow it to reach the same definitive conclusions reached by the authors. In particular, it found that the reported observations are incomplete and do not tally, no systematic effort has been made to address the likelihood of bias introduced by the method of data collection, and categorical inferences have been drawn from data that are either not significant or critically dependent on a very small number of results that might equally be explained by chance. In addition, the probability of the results being distorted by confounding factors has not been adequately addressed. The analysis was data driven and not based on a priori generation of a hypothesis, which makes interpretation of significance values and confidence limits problematic. The conclusions of this paper need to be scrutinised to the same extent as adverse events previously mistakenly attributed to diphtheria, tetanus, and pertussis vaccine.