



## Impact of serogroup A meningococcal conjugate vaccine for Africa

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### Abstract

The introduction of a serogroup A meningococcal conjugate vaccine in the African meningitis belt has been a remarkable success. Meningitis due to the serogroup A meningococcus, previously responsible for most epidemics, has fallen by 99% in vaccinated countries. Success must, however, not distract from the continuing burden of meningitis in this region of Africa. The number of all meningitis epidemics at health district level has fallen by 60% following vaccination, but epidemics due to other meningococcal serogroups continue and may be increasing. The introduction of low cost multivalent conjugate vaccines must be given high public health priority.

### Main text

The development, introduction and roll-out of a serogroup A meningococcal conjugate vaccine (MenAfriVac<sup>R</sup>) across sub-Saharan Africa through the Meningitis Vaccine Project was a remarkable achievement: remarkable for the rapidity of vaccine development, remarkable for the short time from clinical trials to regulatory approval and to public health use, remarkable for the low cost of a high quality vaccine, remarkable for the funding and support for the vaccination program given by many individuals, organizations and governments in and out of Africa, and remarkable for the drive of the program leadership(1-7). The rollout that started in Burkina Faso in 2010(8) reached over 270 million people aged 1 -29 years by 2017(1). Vaccine

acceptability was high, such that vaccine coverage was, with few exceptions, well above 90% as measured both by administrative coverage estimates and specific coverage surveys(8).

So, after seven years, what has been the impact of the vaccination program? Burkina Faso, a country at the center of the meningitis belt with universally good quality surveillance, saw an immediate fall in meningitis incidence(9), and serogroup A meningitis cases fell to very low levels as the rollout progressed across the meningitis belt(10). Although these data were highly encouraging, vaccine effectiveness was important to demonstrate as MenAfriVac<sup>R</sup> was licensed based on data from clinical trials showing safety and high immunogenicity(1, 8), but without evidence of effectiveness. The most convincing evidence of effectiveness to date has come from Chad where the vaccination program was introduced region by region over two years during a nationwide epidemic of serogroup A meningococcal meningitis. Incidence of meningitis fell immediately following introduction in one region while remaining high in the rest of the country, and the epidemic stopped after vaccination in the rest of the country(11). A recently published analysis of surveillance data in nine countries estimated vaccine impact on serogroup A meningitis as leading to a 99% reduction of disease in fully vaccinated countries(12).

Further evidence of effectiveness come from studies of vaccine impact on carriage prevalence. In Burkina Faso repeated cross sectional carriage surveys documented a fall in carriage of serogroup A meningococci from 0.39% before vaccination to 0% in the three week to 13 month period afterwards(13), and in Chad a similar reduction in carriage was seen from 0.75% before to 0.02% four to six months after vaccination(11). Repeated surveys in Burkina Faso showed

that carriage of serogroup A remained very low, suggesting an important additional benefit of herd protection(14).

As the new vaccine was targeted at the predominant strain responsible for devastating meningitis epidemics, communication messaging and publications generated around introduction of the new vaccine may have led to an expectation among public and public health professionals that meningitis epidemics would be eliminated(4, 9, 15). However, there was never a prospect that a monovalent vaccine could stop epidemics from meningococcal strains not covered by the vaccine or from other bacteria. Meningitis epidemics due to serogroup W continued and a new serogroup C clone emerged in Nigeria and Niger which caused epidemics from 2013 to 2017(16-18). Whilst an analysis of disease trends estimated an important 60% reduction both in overall meningitis incidence and in the number of district level epidemics following the MenAfriVac<sup>R</sup> roll out, an increased trend was seen in confirmed meningitis due to other meningococcal serogroups(12). There was no change in the incidence of pneumococcal meningitis, at a time when pneumococcal conjugate vaccines were only just being introduced in these countries.

Could an abrupt and sustained fall in carriage of serogroup A meningococci in the meningitis belt lead to an increased risk of meningitis from other pathogenic strains? WHO expert groups in 2015 and 2017 concluded that there was no evidence of capsule switching or of serogroup replacement as serogroup A carriage outside epidemics was usually absent or at very low levels before introduction of MenAfriVac<sup>R</sup>, serogroup distribution fluctuated markedly before vaccination, and the serogroup C outbreak strain in Nigeria and Niger is a novel clone unrelated

to circulating serogroup A strains(19, 20). They also acknowledged that the factors driving epidemics and the evolution of pathogenic strains were not fully understood. Although pharyngeal carriage of serogroup A is normally at low level outside epidemics, rapid transmission clearly occurs during large scale epidemics. Could an absence of serogroup A strains in the epidemic season give other meningococcal strains more opportunity to cause epidemics? With an elevated level of immunity to serogroup A polysaccharide after vaccination, one might expect a lowering of immunity to sub-capsular antigens that were previously circulating on serogroup A meningococci. If some of these antigens cross-reacted with subcapsular antigens in other serogroups, could this lead to a rise in meningitis due to these other serogroups? Irrespective of the underlying mechanism, the risk of meningitis due to other serogroups appears to be increasing, a trend that must be carefully monitored.

Introduction of a serogroup A meningococcal conjugate vaccine for Africa has been a massive public health success with virtual elimination of serogroup A meningitis and of serogroup A epidemics. It is essential to maintain the drive for countries to introduce MenAfriVac<sup>R</sup> into the national childhood immunization program to avoid the predicted resurgence of serogroup A meningitis(1, 21). However, this program has not seen the end of meningitis epidemics in Africa. More than 25,000 suspected cases of meningitis reported each year from 2015 to 2017(20). The Meningitis Research Foundation initiated a meeting at Wilton Park, UK in May 2017 to develop a global action plan for meningitis by 2030(22). WHO supports this plan that needs broad engagement by policy makers and funders. Alongside advocacy to reduce costs of

existing conjugate vaccines, the development and introduction of affordable multivalent meningococcal conjugate vaccines must be assured and prioritized.

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