

**Why are we reviewing the evidence on  
non-specific effects (NSE) of vaccines on  
mortality in children < 5 years of age?**

**Update on the WG on NSE**

**T. Nolan**

**Chair of SAGE Working Group  
on NSE**

# Non- specific effects of vaccines

for which they are intended.

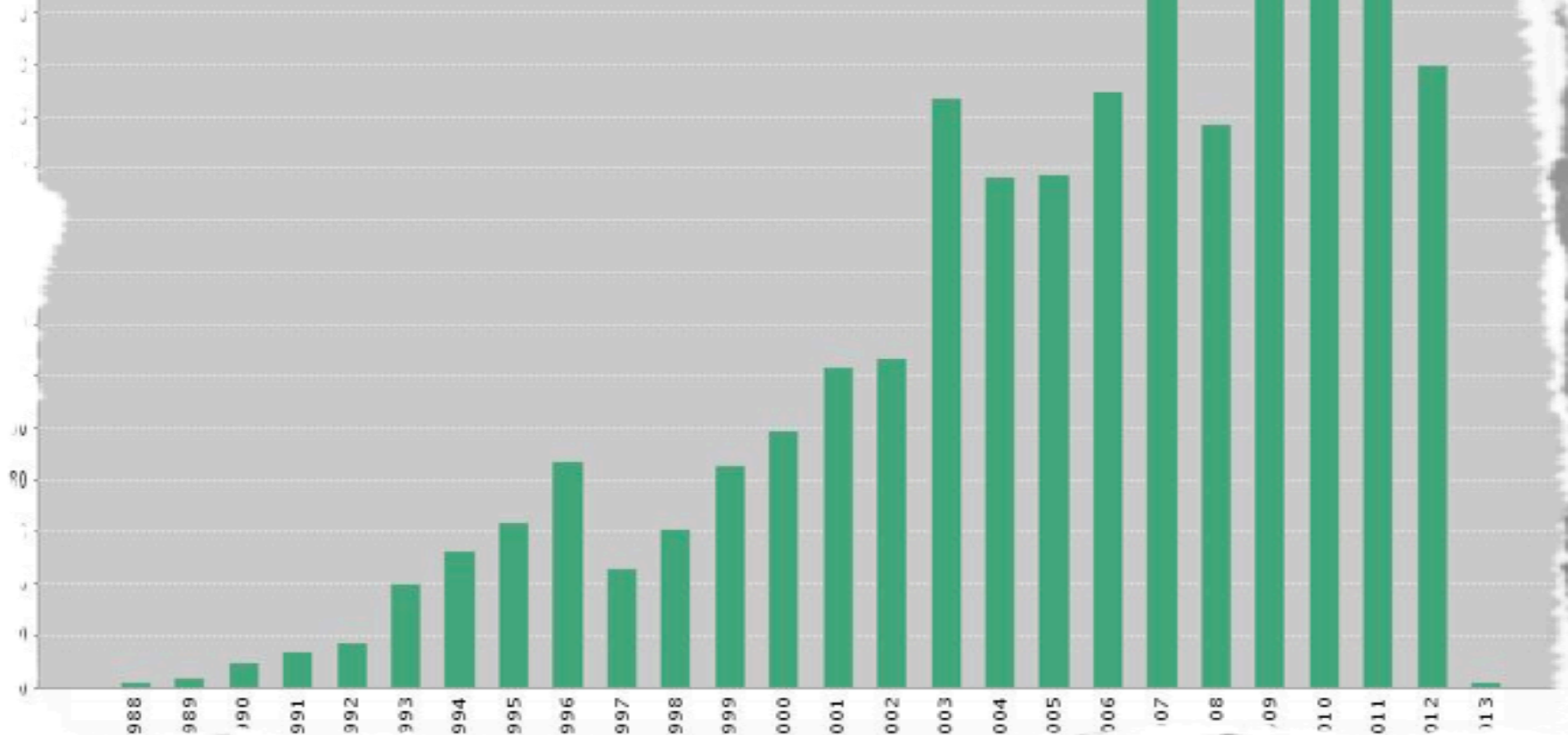
# Aaby P and vaccine, 1988-2012

Sum of the Times Cited : 3456

Sum of Times Cited without self-citations: 2376

Citing Articles : 1648

Citing Articles without self-citations: 1522



# **From the research conducted Aaby and colleagues have stated to have four main hypotheses:**

**(1) BCG vaccine reduces mortality** from infections other than tuberculosis until an inactivated vaccine is given

**(2) Measles vaccine reduces mortality** from infections other than measles until an inactivated vaccine is given; this effect may be stronger if the child still has maternal antibody when receiving measles vaccine.

**(3) Whole-cell diphtheria-tetanus-pertussis vaccine (DTP) increases mortality** from infections other than diphtheria, tetanus and pertussis until a live vaccine is given; this effect is stronger in females than in males

**(4) Live and killed vaccines may interact to produce good or bad non-specific effects** when given simultaneously or when the sequence is changed, and the effects may be modified by vitamin A

# WHO Global Advisory Committee on Vaccine Safety and NSE

YEAR	Summary of discussion
2000	Review Guinea Bissau data, concerns re-potential bias
2001	Descriptive review of 7 studies, selection bias noted Commissioned studies in 4 countries, reviewed study results
2003	Two task forces organized: epidemiology + effect on immune system
2004	Review results of task forces (included 17 studies), evidence does not support deleterious effect of DTP
2005	Workshop to address immunological mechanisms – live vaccines (innate immunity+ adaptative immune response)
2006	GACVS attend Danish National Research Foundation meeting
2007	Two independent workshops on methods held
2008	Review recent studies, concluded that statement should expand to other vaccines

# **SAGE Meeting, Nov 2011**

## **Conclusions and Recommendations**

**Director IVB briefly described previous WHO actions regarding NSE and referred to recent publications on the topic**

**SAGE requested that the non-specific effects of vaccines be presented for review**

# **OVERALL AIM**

**To determine if the current data are indeed compelling enough to demand further careful investigation; and**

**if so, to define the path towards obtaining unequivocal data on these issues that would allow for rational, data-driven adjustments in vaccination policies—again, if warranted**

# TORs of the WG on NSE

The Working Group will specifically be asked to:

**Review and provide guidance on the protocol for two independent systematic reviews** on the evidence of selected vaccines on child survival/ deaths by all causes in children less than 5 years of age:

- epidemiological studies

- immunological factors

**Review the available evidence** that addresses the effect of BCG, DTP and measles-containing vaccines on survival/all-cause mortality in children less than five years of age and, the outcomes of the above mentioned reviews and related GRADE tables.

**Determine if the current evidence on non-specific effects of vaccines is sufficient to lead to adjustments in policy recommendations or to warrant further scientific investigation.**



# Composition of the WG on NSE

## **SAGE Members**

**Terry Nolan (Chair)**

**Zufiqar Bhutta**

**Kate O'Brien**

## **Experts**

**Christine Stabell Benn**

**Diane Griffin**

**Mike Brennan**

**Jaleela Sayed Jawad**

**Stephen Evans**

**Martin Mermikuwu**

**Paul Fine**

**Walter A. Orenstein**

**Brad Gessner**

**Dipika Sur**

# Timeline



July–Oct 2012

Nov 2012–April 2013

May– Sept 2013

Oct – Nov 2013

DRAFT Protocols + tools development  
Scope & questions of review

Scoping meeting  
Peer review protocol  
Systematic search

SAGE Working Group  
Questions for SAGE

Constitution of WG  
1<sup>st</sup> Teleconference WG  
Adjustments to protocol

Information report to  
SAGE

Data analysis – 1<sup>st</sup> Draft  
Review of findings  
+quality + bias  
GRADE conclusions

1<sup>st</sup> meeting of WG (Sept)  
1–2 day open meeting  
1–2 days closed session

Findings & conclusions  
Final report

GRADE conclusions  
Recs to SAGE

Presentation to SAGE