Background

• Previous review of the burden of rubella and Congenital Rubella Syndrome (CRS) in developing countries was conducted for 1996 (Cutts and Vynnycky)

• Total numbers of CRS cases in 1996: 110,000 (95% range: 14,000-308,000)

• Number of countries outside Europe which had not introduced rubella-containing vaccine:

  1996: 126 (~2/3 developing countries)
  2008: 67
Overview of the study

Aims

• To estimate the annual burden of CRS during 2000-2008, for the 193 WHO member states, six WHO regions and globally

• To revise previous estimates for 1996 to include countries which had already included rubella vaccination

Literature search

16 databases searched; studies excluded if they were conducted among biased populations e.g. Health-care workers, refugees, samples collected among individuals suspected to have rubella

Modelling methods

Depended on whether the setting had introduced rubella vaccine by 2000
Examples of the variable quality of available datasets

Ethiopia (females), 1994
(Cutts et al, 2000)

Nigeria ,?
(Bukbuk et al, 2002)

Brazil - Mato Groso du Sul, 2002-3
(Figuero-Filho et al, 2007)

Niger, ?
(Develoux et al, 1991)
Data for populations in which rubella-containing vaccine had not been introduced by 2000

- 31 datasets available on the age-specific proportion of individuals seronegative for rubella
- 20 countries covered by the data:
  - 14 African countries
  - 8 datasets from India, 2 from Pakistan and Yemen

(NB: ~67 countries had not yet introduced rubella vaccine by 2000)
Methods for populations in which rubella-containing vaccine had not been introduced

- A catalytic model was fitted to the data to estimate the force of infection (rate at which susceptible individuals are infected) among children and adults.

General structure of a catalytic model:

- Where possible, the sensitivity of the antibody test was also estimated.
Examples of typical datasets

Congo, ? (Yala at al, 1991)

Pakistan, ? (Iqbal and Bokhari, 1997)

India (Lucknow), 1972-3 (in Seth, 1985)

Kenya, 1996-9 (Shulman, unpublished)
Force of infection estimates for those aged ≥13 years for the available datasets in countries in which rubella-containing vaccine had not been introduced by 2000
Methods for unvaccinated populations – equations for the CRS incidence

- CRS incidence per 100,000 live births in a given age range
  \[ \text{Proportion susceptible in that age range} \times \text{Risk of infection during 16 weeks} \times 0.65 \times 100,000 \]

- Risk that a child is born with CRS = 65% if infection occurs during the first 3 months of pregnancy.

- If multiple data sources were available, CRS incidence taken as the average obtained for each data set.

- If no serological data: CRS incidence taken as the regional average.

- Number of new CRS cases each year among pregnant women in a given age range
  \[ \text{Age-specific CRS incidence per live birth} \times \text{numbers of births} \]
Estimates of the incidence of CRS in populations in which rubella-containing vaccine had not been introduced by 2000

No. of CRS cases per 100,000 live births

Study setting

AFRO

EMRO

SEARO
Limitations of estimates for populations in which rubella-containing vaccine has not been introduced

• Only 33% of serological studies are from the 1990s/2000; year of study is unknown for 33% of available datasets

• Data are available from only 20 out of the 67 countries that had not introduced rubella-containing vaccine

• Sampling methods are sometimes unclear

• Data quality is sometimes very poor e.g. few datapoints, large confidence intervals, test quality is unclear

• etc
1. Use a model to describe the transmission of rubella among males and females in the given setting before the introduction of vaccination

2. Incorporate reported vaccine coverage over time in the model
General structure of the transmission model

end of year

newborns

Susceptible[0] → Pre-Infectious [0] → Infectious[0] → Immune[0]
General structure of the transmission model

- Susceptible[0] → Pre-Infectious[0] → Infectious[0] → Immune[0]
- Susceptible[74] → Pre-Infectious[74] → Infectious[74] → Immune[74]

End of year
An example of the predicted force of rubella infection over time in England for 2000-2008, using the transmission model.
Methods for populations in which rubella-containing vaccine has been introduced by 2000-2007

1. Use a model to describe the transmission of rubella among males and females in the given setting before the introduction of vaccination

2. Incorporate reported vaccine coverage over time in the model

3. Calculate the CRS incidence per 100,000 livebirths in a given age range for each year, using the formula:
   \[ \text{Incidence} = \frac{\text{Proportion susceptible in a given age range}}{\text{Risk of infection during 16 weeks}} \times 0.65 \times 100,000 \]

   Use observed proportion seronegative if available, or model predictions
Predictions of the incidence of CRS in 2000 and 2008 in Europe

Number of CRS cases per 100,000 live births

Country
Average incidence of CRS per 100,000 live births, 2008

Source: Vynnycky, Adams et al (in preparation)
Average number of CRS cases born in 2008

Source: Vynnycky, Adams et al (in preparation)
Estimates of the global burden of CRS, 2000-2008

[Graph showing the number of CRS cases globally and regionally for 2000 and 2008.]
Estimates of the global burden of CRS, 1996-2008

Number of CRS cases

Region

AFR | AMR | EMR | EURO | SEAR | WPR | Worldwide

1996 | 2000 | 2008

0 50000 100000 150000 200000 250000 300000

Health Protection Agency
Conclusions

• Average global burden of CRS has remained relatively unchanged since 2000 with 112,000 cases per year; very wide range: 16,000-300,000

• Average global burden has decreased slightly since 1996 (~120,000 cases born worldwide, in 1996; 110,000 in countries which had not yet introduced rubella vaccine)
Conclusions

• The average burden may have increased in African, SE Asian countries due increased numbers of births over time

• Burden remains the highest in countries which have not yet introduced vaccination

• The burden has declined in countries which did introduce adequate vaccination

• Further adequate serological studies are needed to improve the reliability of the estimates
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