Is vaccine development responsive to population disease burden?

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Background

- US notifiable infectious diseases represent a significant disease burden in the US population.
- Prophylactic vaccines for infectious diseases can be powerful tools to reduce population disease burden.
- Most US notifiable infectious diseases do not yet have recommended vaccines.

Objectives

- Examine whether there have been efforts toward vaccine development for notifiable infectious diseases that do not yet have recommended vaccines.
- Test whether vaccine development effort is greater for diseases with greater burden.

Methods

Notifiable diseases: From 1996-2000 CDC annual summaries, we identified 16 high-incident infectious diseases with no recommended vaccines. These are: ehrlichiosis, Rocky Mountain spotted fever, listeriosis, legionellosis, malaria, Streptococcus A, cryptosporidiosis, hepatitis C, E. coli-related enteritis, tuberculosis, shigellosis, syphilis, salmonellosis, HIV-AIDS, gonorrhea, and chlamydia (in order of increasing incidence).

Disease burden: Measures of incidence and deaths for each disease were obtained from CDC Summaries of Notifiable Diseases and the National Center for Health Statistics. Case-fatality rates for each disease were calculated by dividing deaths by incident cases. Distributions were skewed, so burden measures were assigned ranks for analysis, with higher ranks assigned to larger numbers.

Vaccine development: We used data for the years 2001-2011 from a proprietary global database of pharmaceutical development to build three measures of vaccine development effort for each disease: (1) any or no vaccine development effort; (2) number of candidate vaccines attempted; and (3) total number of years of development across all vaccine candidates. Distributions were skewed, so vaccine candidate measures were assigned ranks for analysis, with higher ranks assigned to larger numbers.

Analyses: Logistic regression was used to predict any or no vaccine development from ranked measures of burden. Spearman rank correlations were used to assess relationships between ranked measures of burden and ranked measures of vaccine candidate development. All analyses were conducted in Stata 11.

Results

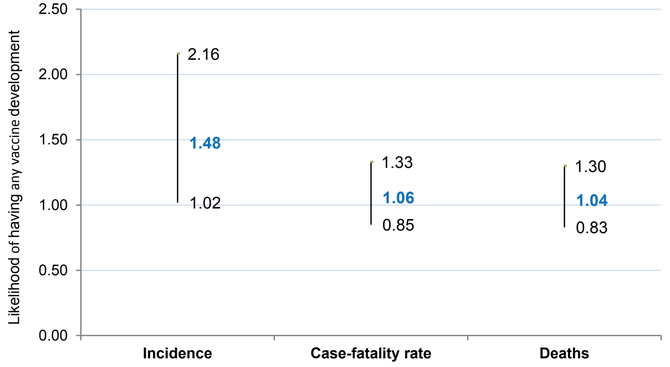
Principal measures of interest:

- Mean annual incidence ranged from 427 (ehrlichiosis) to 597,758 (chlamydia).
- Deaths ranged from 0 (chlamydia, ehrlichiosis) to 12,543 (HIV-AIDS).
- Case-fatality rates ranged from 0 (chlamydia, ehrlichiosis) to .31 (HIV-AIDS).
- Vaccine candidates in development:
  - Six diseases had no vaccine candidates in development (in order of increasing incidence, these are ehrlichiosis, Rocky Mountain spotted fever, listeriosis, legionellosis, cryptosporidiosis, and syphilis).
  - Among diseases with vaccine candidates in development, the number of vaccine candidates ranged from 3 (salmonellosis and gonorrhea) to 152 (HIV-AIDS)
  - Among diseases with vaccine candidates in development, years of development ranged from 4 (salmonellosis) to 537 (HIV-AIDS).

Association of vaccine development with measures of interest:

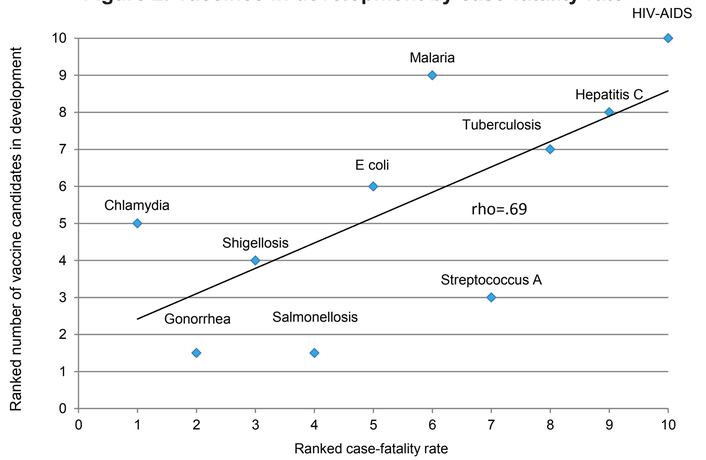
- Having any vaccine development was associated with higher incidence (OR=1.48, 95% CI=(1.02, 2.16)), but not with case-fatality rate or deaths.
- Case-fatality rate was significantly associated (rho=.69; p=.03) with ranked number of candidate vaccines (Figure 2), but not with years of development.
- Incidence and deaths were not associated with number of vaccine candidates or years of development.

Figure 1. Association of any vaccine development with disease burden: Odds ratios and confidence intervals



Results (cont.)

Figure 2. Vaccines in development by case-fatality rate



Notes: Non-integer values for ranks of vaccines in development are shown where there were rank ties. Greater numbers of vaccines in development and higher case-fatality rates have higher ranks.

Discussion

- Vaccine development effort is greater for diseases with higher disease burden.
- Higher incidence was associated with having vaccine development. Diseases without measurable development effort are unlikely to have recommended vaccines available soon.
- Higher case-fatality rate was associated with more vaccines in development.
- Limitations to this study include the small number of notifiable diseases examined and the large disease burden outside the list of notifiable diseases.

Conclusions

- Vaccine development effort may be triggered by high case incidence and may be more intense for diseases with higher case-fatality rates.
- To encourage greater vaccine development for diseases with little or no vaccine development effort, public health and research communities may need to provide targeted incentives.