Early estimates of 2008-9 seasonal influenza vaccine effectiveness against A(H1N1)v outcomes

Results from a cohort study, Navarra, Spain

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EpiConcept
Navarra

- Region in Spain
  - 613,839 inhabitants
- Influenza surveillance
  - 532 GPs with computerised medical records
    ILI diagnosis
  - 76 sentinel GPs
    swab a systematic sample of ILI patients
    PCR, culture in 2 laboratories
- 2008-9
  - as part of I-MOVE, cohort study to measure seasonal influenza vaccine effectiveness (VE)
  - week 24, first cases of influenza A(H1N1)
Seasonal vaccine and risk of A(H1N1)v infection?

- Discordant results seasonal vaccine…
  - no effect?
    Australia [Kelly et al, Eurosurveillance 2009; 14(31)]
  - protective?
    Mexico [García-García et al, BMJ 2009; 339]
  - risk factor?
    Canada [Skowronski et al, submitted]
    Seasonal vaccination delayed until January 2010

Objective Navarra:
To measure effectiveness of 2008-9 seasonal influenza vaccine against A(H1N1)v related outcomes
Methods

• Study population
  – 585,158 people GPs´catchment population

• Outcomes
  – medically attended influenza-like illness (ILI)
  – laboratory confirmed A(H1N1)v infection (LAB)
  – all cause mortality (Deaths)

• Study design
  – cohort  (ILI, deaths)
  – nested case control (LAB)
Methods

• Covariates
  – sex
  – 5-year age group
  – district of residence
  – underlying chronic diseases
  – hospitalisations last 12 months
  – GP visits last 12 months
  – functional status
  – cohabiting with children
  – migrant

VE by
  - influenza period
  - age group
    < 65 yrs; ≥ 65 yrs

• Outcomes, exposure, covariates extracted from computerised medical records
Results
Incidence of ILI by week and periods of virus circulation
Navarra, 2008-9

Seasonal

H3N2

B

Transition

Pandemic

A(H1N1)v

ILI cases per 100,000 population

Weeks
Navarra population 613,839

Cohort 585,158

Unvaccinated 490,735

Vaccinated 94,423 (16%)

Cohort

0-14 yrs: 83,232
15-64 yrs: 401,533
≥65 yrs: 100,393

Unvaccinated

0-14 yrs: 3,100 (3.7%)
15-64 yrs: 28,397 (7.1%)
≥65 yrs: 94,423 (62.7%)
Results

Early pandemic phase (week 24 - 35)

- Outcomes
  - 2228 ILI
  - 245 swabs => 97 positive to A(H1N1)v
  - 847 deaths, 691 in ≥ 65 years

- Adjusted VE (95% CI)
  - ILI all age groups - 13% (-35 - 5)
  - LAB all age groups -18% (-289 - 52)
  - Deaths in < 65 years -15% (-74 – 33)
  - Deaths in ≥65 years 22% (8 - 23)
Adjusted VE against all deaths by influenza period and age group
Navarre 2008-9

< 65 yrs

≥ 65 yrs

VE %
Adjusted VE against all deaths ≥65 years, by influenza period and age group
Navarra 2008-9
Discussion

VE in early phase of pandemic

- No effect against ILI, A(H1N1)v LAB
  - negative point estimates, but small effects
  - ILI, non-specific outcome
  - LAB, small sample size
  - outcomes influenced by health-seeking behaviour
    - indication bias?
Discussion
VE in pandemic period

• All cause mortality
  – not influenced by health-seeking behaviour

• VE against deaths in < 65 years: no effect

• VE against deaths 65-84 years
  - observed in periods of influenza circulation
  - not observed in transition period
  - overestimated due to healthy vaccinee effect /frailty bias?
  no possibility to compare to pre-influenza season
Conclusions

• Navarra cohort GP database
  – timely estimates of seasonal VE against 2009 A(H1N1)v outcomes

• No evidence of seasonal vaccine as a risk factor for A(H1N1)v infection

• VE against deaths in 65 – 84 years
  – boosting of existing antibodies?
  – role of residual confounding?
Navarra, 2009-10

• Seasonal vaccination 2009
  – nearly finished
  – same target population as in 2008

• Pandemic vaccination
  – starting 16th November
  – different vaccines for different risk groups

• VE cohort study
  – I-MOVE
  – early, repeated pandemic / seasonal VE
  – more swabs to increase precision of LAB outcome
Acknowledgments

- GPs sentinel network in Navarra
- EpiConcept
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Background slides
Influenza vaccination programme in Navarra 2008-9

• Influenza vaccine for
  – ≥ 60 years
  – < 60 years with co-morbidity or risk factors
  – health care workers, other professions, institutionalised population

• Vaccination
  – from 13/10/2008 to 15/11/2008
  – 118,000 doses (19% of population)
Vaccination coverage
in non-institutionalised population
by age groups, Navarra, 2008-9 season

%
Swabs positive to influenza and proportion positive, by week and virus
Navarra, 2008-9
Results

Early pandemic phase (week 24 - 35)

• ILI Adjusted VE (95% CI)
  – ILI all age groups -13% (-35 - 5)
  • < 65 years -18% (-142 - 2)
  • ≥ 65 years 21% (-34 - 53)

  – LAB all age groups -18% (-289 - 52)
  • < 65 years -11% (-299 - 58)
  • ≥ 65 years -34% (-1483 - 88)
Adjusted influenza VE against all deaths in ≥ 65 years, by 3 week period, Navarra 2008-9

VE %

H3N2 week 47-8
B week 9-15
Transition week 16-23
Pandemic week 24 -

Weeks
Adjusted VE against all deaths in >65 by chronic disease and age group
Navarre 2008-9

Models adjusted for sex, 5-year age groups, chronic diseases, number of visits to GP in last 12 months (3 categories), great dependence, cohabiting with children, migrant, district
Adjusted VE against all deaths ≥65 years, by influenza period and risk groups
Navarra 2008-9

Models adjusted for sex, 5-year age groups, chronic diseases, previous hospitalization, number of visits to GP in last 12 months (3 categories), great dependence, cohabiting with children, migrant, district
Adjusted VE against all deaths in ≥ 65 years by influenza period
Navarre 2008-9

Models adjusted for sex, 5-year age groups, chronic diseases, prior hospitalization, number of visits to GP in last 12 months (3 categories), great dependence, cohabiting with children, migrant., district
Adjusted VE against ILI by age group and by influenza period
Navarra 2008-9

< 65 yrs

> 65 yrs

VE %

47 to 8 (A/H3N2) 9 to 15 (B) 16 to 23 (transition) 24 to 35 (pandemic)

47 to 8 (A/H3N2) 9 to 15 (B) 16 to 23 (transition) 24 to 35 (pandemic)
• Adjustement
  – 5 year age group
  – Chronic disease
  – Hospitalisations
  – Number of GP visits in last 12 months
  – Great dependence
  – Cohabit ing with children
  – Migrant
  – District
Jackson 2006 cohort study, >64 yrs, all outcomes by influenza activity

VE (%) vs Outcome

- Preinfluenza
- Influenza
- After season

Outcomes:
- Death
- Cerebrovascular disease
- CHF
- IHD
- Influenza, Pneumonia
- Trauma injury
Crude – adjusted VE against all deaths by age group and influenza period, Navarra 2008-9

< 65 yrs

47 to 8 (A/H3N2) 9 to 15 (B) 24 to 35 (transition) (pandemic)

47 to 8 (A/H3N2) 9 to 15 (B) 16 to 23 (transition) (pandemic)

≥ 65 yrs