How to measure impact of rotavirus vaccination: Opportunities for synergies across Nordic countries?

Elmira Flem
Department of Vaccines
Norwegian Institute of Public Health

Nordic Vaccine Meeting
April 23-25, 2014
Outline

• Rotavirus disease and economic burden
• Rotavirus vaccine introduction story
• Planned post-introduction activities
• Thoughts on synergies across Nordic countries
Rotavirus Disease in Norway

• RV accounts for around 60% of AGE hospitalisations\(^1\)
• Annually among children under 5 years:
  – 900-1000 hospitalisations
  – 7 200 outpatient visits
  – 29 000 home care episodes
• Median age 18 months and 60% are 6-23 months old
• Low mortality
• Predominant genotypes\(^2\): G1 (53%), G9 (16%), G3 (13%)

Rotavirus Seasonality, Norwegian Patient Registry, 1999-2004

Year
No. hospitalizations
Rotavirus
Viral
Unspecified etiology

1999 2000 2001 2002 2003 2004

No. hospitalizations
0 60 120 180 240 300

Rotavirus
Viral
Unspecified etiology

Year
1999 2000 2001 2002 2003 2004

Rotavirus
Viral
Unspecified etiology
Economic Evaluation of Rotavirus Vaccination, Norway

- Markov model-based cost-utility analysis, 2009*
- Both vaccines are assessed
  - Threshold of 500 000 NOK per QALY
- ICER from health care perspective:
  - Rotarix 687,500 NOK & Rotateq 762,000 NOK
- Vaccination unlikely to be cost-effective from health care perspective but likely from societal perspective

New Vaccine Introduction: Norway

• NIPH has advisory role on immunization
• Specially convened expert group for each new vaccine
• Recommendations provided to Ministry of Health and Care Services
• Funding decision taken by the government
• Vaccine procurement and follow-up done by NIPH
Rotavirus Vaccine Introduction

- **December 2011**: Positive recommendation by the expert group
- Additional advice sought from the National Council for Priority Setting in Health Care
- **June 2012**: Negative recommendation
- **October 2013**: Funding allocated from 2014
- Implementation scheduled for autumn 2014
Vaccine Impact & Effectiveness

• What do we know by now?
  – Effectiveness above 90% in Europe, USA, Australia against rotavirus hospitalizations and ED visits
  – Vaccination confers herd or indirect protection
  – Important to continue strain surveillance
Available Tools

• WHO/IVB/08.16, 2009
  – Generic Protocol for Monitoring Impact of Rotavirus Vaccination on Gastroenteritis Disease Burden and Viral Strains

• ECDC technical documents, 2013
  – Generic protocol for retrospective cohort studies
  – Generic protocol for retrospective case control studies
  – Generic protocol to assess impact
Which endpoints/outcomes to measure to assess VE & VI?

1. Laboratory-confirmed rotavirus gastroenteritis (RVGE)

2. All-cause acute gastroenteritis (AGE)
   - Associated with hospitalization, outpatient visit or death, all age groups

3. Breakthrough infections if any

4. Specific rotavirus serotypes

5. Economic outcomes
Planned Follow-up in Norway

• Mandatory notification for laboratory confirmed RVGE to Norwegian surveillance system for communicable diseases (MSIS)
  – Used for all vaccine-preventable diseases
  – Requires revision of legal framework
• National laboratory surveillance
  – Voluntary lab network reporting monthly # RV-positive samples since 1990s
  – Include # tests performed and method used
• Establish rotavirus reference laboratory at NIPH
Special Studies: Active Rotavirus Surveillance

• In place since January 2014
  – Includes 4 largest hospitals in Norway
  – Enrollment of inpatients and ED patients with AGE
  – Bulk stool and rectal swabs obtained and tested for rotavirus and other enteric viruses
  – Clinical and economical data collected during hospital stay and follow-up ca. 1 week after discharge

• Primary endpoints:
  – Incidence of RVGE-related hospitalizations and ED visits
Special Studies: Vaccine Effectiveness

- Prospective hospital-based case-control study

- **Cases:**
  - Children age-eligible for vaccination hospitalised with AGE and tested RV-positive

- **Controls:**
  - Children with AGE testing RV-negative
  - Children selected from Norwegian Immunisation Registry (SYSVAK)

- Data linkage using SYSVAK and several other health registers
Vaccine Effectiveness: Objectives

• Estimate effectiveness of RV vaccines against:
  – laboratory-confirmed RV hospitalization  AND
  – hospitalization associated with all-cause gastroenteritis in children <5 years of age
  – effectiveness of incomplete series of RV vaccines
  – serotype-specific effectiveness

• Identify risk factors for poor vaccine performance if observed
Special Studies: Vaccine Impact

- Estimate incidence and assess national trends of AGE and RVGE-hospitalizations, ED and outpatient visits before and after vaccine introduction
- Norwegian Patient Registry (NPR)
  - all hospitalizations since 1990
- Norwegian Health Economics Administration (HELFO)
  - health reimbursements from GPs and EDs
- Person-identifiable data available since 2007/2006
- ICD-10 and ICPC-2 codes
- High data completeness
Special Studies: Economic Evaluation

• Update cost estimates of RV hospitalizations, ED and outpatient visits
• Collection of cost data during ongoing active hospital surveillance
• Update cost-effectiveness estimates by using:
  – novel dynamic modeling approach*
  – "real-world" data on vaccine impact and coverage

Why should we join forces?

• Important to provide data at regional level:
  – vaccination-program specific effectiveness
  – long-term protection
  – extent of herd immunity
  – strain replacement and serotype-specific VE
  – risk factors
  – safety (vaccine-attributable IS risk in Europe)

• Difficult to address these questions by individual countries
Current status in Nordic countries

• National program: Finland and Norway
• Regional introductions: Sweden
• Pending decision: Denmark and Iceland?
• Strengths:
  – Similar disease epidemiology
  – Relatively similar health care systems
  – Existing research infrastructure
• Are there opportunities for synergies???