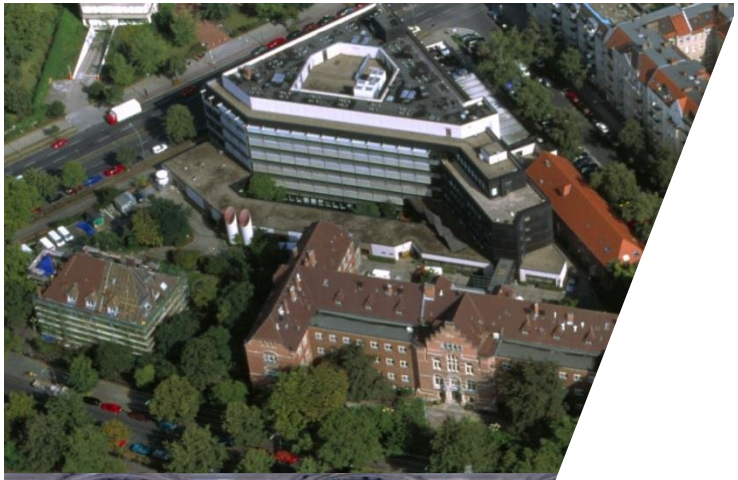

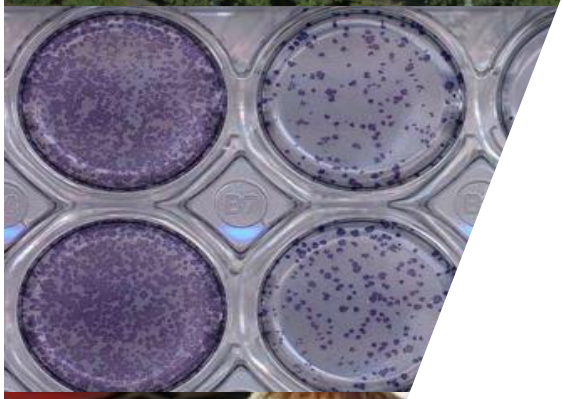

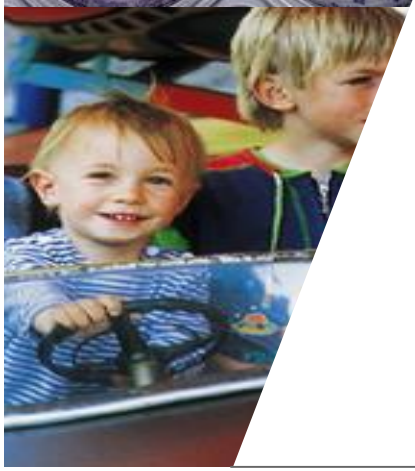

ROBERT KOCH INSTITUT

How are new vaccines implemented in vaccination programs – NITAGs

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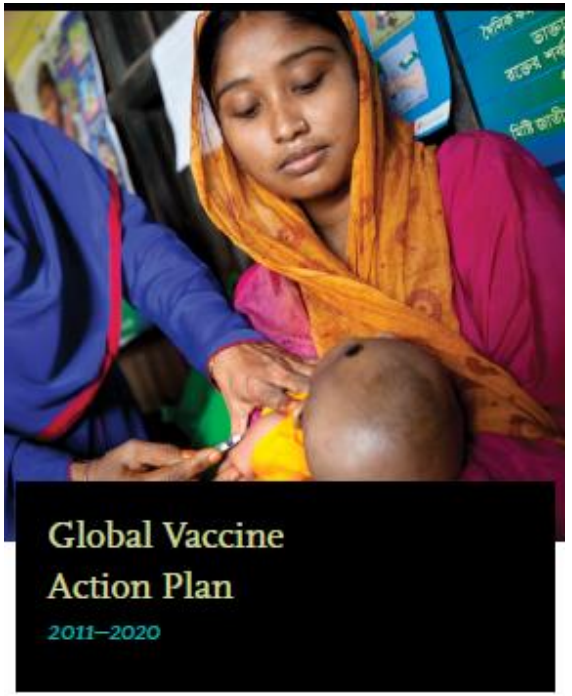
Content

- What is a NITAG?
- Key issues when deciding on vaccine introduction
- NITAGs in the EU/EEA
  - role & characteristics
  - working procedures & decision-making
- Conclusions

Global Vaccine Action Plan



Six strategic objectives

1. All countries commit to immunization as a priority

   INDICATOR:
   -Domestic expenditure for immunization per person targeted
   -Presence of an independent technical advisory group that meets defined criteria

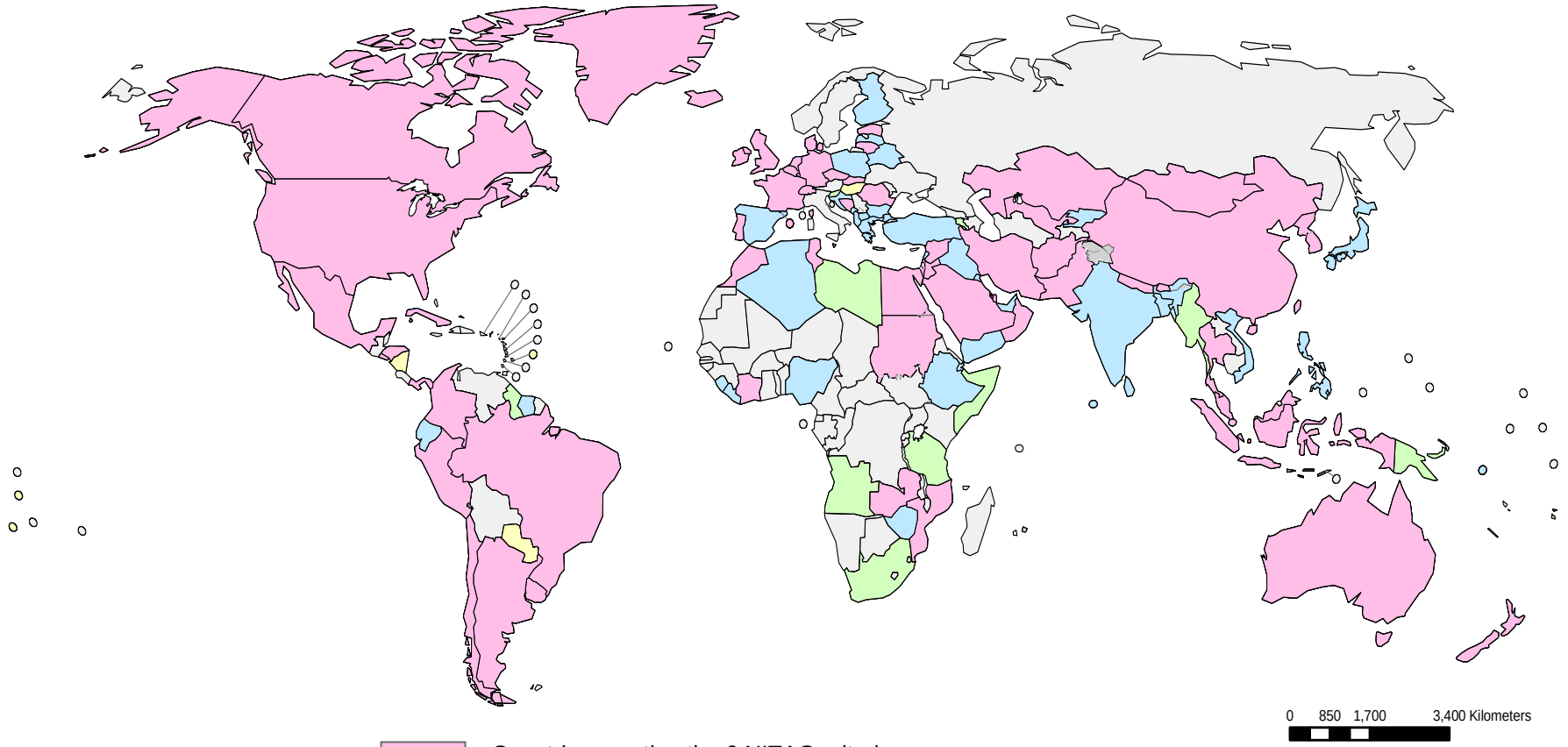
2. Individuals and communities understand the values of vaccines and demand immunization

3. ....

6 indicators of a well-functioning NITAG

1. Formal, written terms of reference
2. Legislative mandate (Ministerial decree)
3. At least 5 areas of expertise represented
4. Agenda distributed ahead of meetings
5. Declaration of no conflict of interest
6. Regular meetings (at least twice yearly)

National Immunization Technical Advisory Groups (NITAGs) in 2012 by WHO regions



Data Source: Joint Reporting Form, 2012

Map production: Immunization Vaccines and Biologicals, (IVB), World Health Organization

Date of slide: 17 October 2013

What is a NITAG?

- A body of national experts that provides technical and scientific guidance to the government (ministry of health and/or the NIP) on immunization policy, norms, and practices
- As a scientific advisory group, the NITAG ideally should be independent from the government

What should a NITAG do?

- Conduct the best possible review of scientific evidence
- Bring credibility through expertise, minimizing pressure from outside interest groups, and eliminating real or apparent personal conflicts of interest

From vaccine licensure to recommendation

Licensure

= is the vaccine safe and effective for the intended use?

Product-specific

1) safety
2) potency (incl. efficacy, immunogenicity)
3) purity

Recommendation

= how to best make use of the available vaccines in a given population (public health)

Additional aspects, e.g.

1) local disease incidence / severity / epidemiology
2) potential indirect effects
3) cost-effectiveness
4) best schedule/target group. Implementation aspects

Vaccine introduction decisions

Decisions involves trade-off between likely benefits and downsides (risks), both at individual and population level

- Likely benefits: e.g.
  - reduction in number of cases, hospitalizations, deaths
  - protection of unvaccinated persons (by herd effects)
  - decreased costs in the healthcare system
  - elimination of a disease

- Likely downsides: e.g.
  - adverse events following immunization
  - negative population-level effects (e.g. shift in age distribution, serotype replacements)
  - program costs

Challenges in introduction decisions

- Dynamic / more complex vaccine market
  - new vaccines / technologies available or in the pipeline
  - different product profiles (efficacy, safety, valency)
  - limited financial resources
  - busy vaccination schedules (prioritization necessary)
  - often target mild/common or severe/rare diseases
- Data issues
  - several key aspects only known after widespread use
  - how much evidence is needed?
- Implementation issues
  - public acceptance
  - new target groups (challenge for communication)

Systematic approach needed for vaccine introduction decisions

- helps to improve quality of the recommendation
- reduces anticipated or actual arbitrariness
- improves transparency
  - → facilitates critical appraisal
  - → builds trust
- contributes to acceptance of recommendation in the professional community and the public
- helps to compare recommendations endorsed by different countries / states

Immunization programs in the EU/EEA

- Considerable differences in vaccination schedules in EU countries
- Differences exist in
  - number of vaccines included in the National Immunization Program (NIP)
  - number of vaccine doses
  - target age-groups
- E.g. in the 29 EU/EEA member states, between 4 and 16 (median 11) vaccines are recommended to adults

(Kanitz et al. Vaccine 2012)

Decision-making process

- Different driving forces
  - NIP, country decision-makers, international organizations, academic community, physician societies, private sector
- Each country has its own mechanism for an informed decision-making process

Objectives

- To better understand in EU member states
  - the qualities and processes within NITAGs
  - factors considered and processes for the inclusion of vaccines in NIPs
- To identify reasons for the differences in NIPs in EU member states
- To identify potential modes and synergies for future collaborations

VENICE (Vaccine European New Integrated Collaboration Effort)

- Established in 2006

- Initially, network of nominated gatekeepers from all 28 EU member states and 3 EEA countries,
  - since 2015 transition into formal ECDC network with National Focal Points VPD as contact persons

- "VENICE III" started in 2013
  - 5 work packages
  - work package 5: "Development of a roadmap for potential collaborations between NITAG-related institutions"

Survey method & response

- 2 surveys (2013 and 2014)

  Nohynek et al. CMI 2013 // Takla et al. EuroSurveill 2015

- Via VENICE gatekeepers:
  for each EU/EEA country identification of one NITAG member or other NITAG-involved expert

- Response: 28/30 countries
  - Hungary and Luxemburg did not participate

Description of NITAGs in the EU, 2014

- 26/28 (93%) with NITAG or equivalent expert group
  - No NITAG: Norway & Sweden

- Established

  >40 years: Germany, Luxembourg, Netherlands, UK

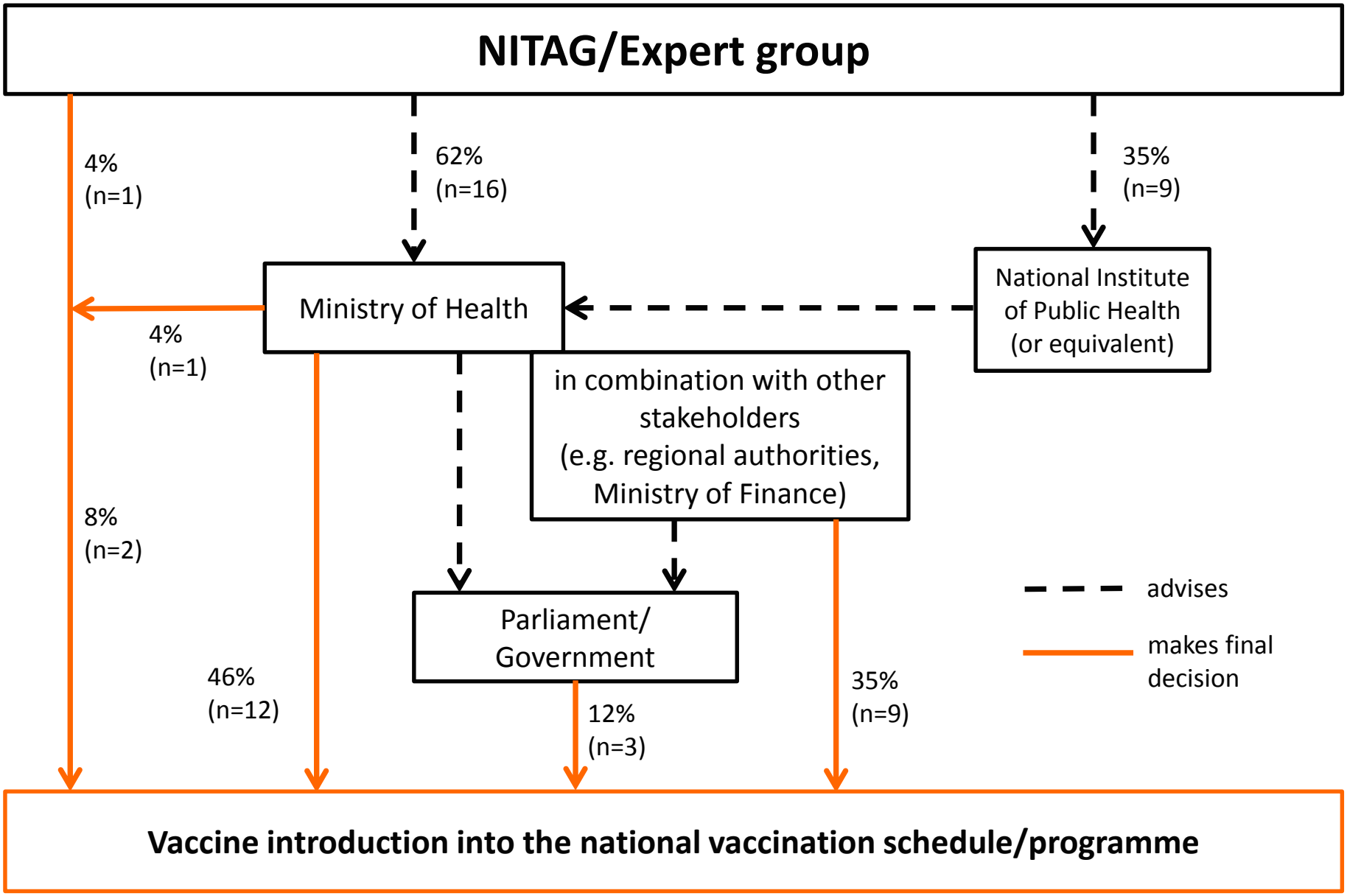
  <5 years: Czech Republic, Romania, Slovenia

- Number of NITAG members: 7-35 (median 14)
  - declaration of conflict of interest: 20 (77%)

Professional expertise of NITAG members (n=26 NITAGs in EU countries)

Field of expertise	Countries	Proportion
Epidemiologists	25	96%
Paediatricians	24	92%
Virologists/Microbiologists	17	77%
Immunologists	20	73%
Vaccinology experts	21	81%
Public health experts	21	81%
Health economists	5	19%
General practitioners	5	19%
Regulatory Authority on Medicines	3	12%

Decision-making structure



Key factors considered by NITAGs for decision-making (n=22 NITAGs, 2013 survey)

Key factor	Proportion (%)	
Vaccine efficacy/effectiveness	**100**	Largely context-free aspects
Vaccine safety at population level	**100**	
Severity of disease	**100**	
Vaccine safety at individual level	92	
Method of vaccine administration	58	
Disease burden in neighboring country	29	
Disease burden in home country	**100**	Context-sensitive aspects (i.e. country specific)
Feasibility of recommendation	92	
Priority of vaccine related to other VPDs	84	
Results from **economic evaluations**	80	
Results from **mathematical modeling**	46	
Public perception about the disease	44	

NITAG evidence assessment (n=26)

	Number	%
Formal approach for evidence assessment (e.g. framework or standard operating procedures)	**20**	**77**
Use of systematic reviews in the recommendation development process is for NITAG/expert group		
-required	**15**	**58**
-optional	**11**	**42**
Usually/ often conducted/ if resources permit	10	38
Quality appraisal tools used for systematic reviews	5	19
GRADE methodology	4	15
Transmission modelling considered as part of the recommendation development process	**18**	**69**
Health economic evaluations considered s part of the recommendation development process	**20**	**77**

NITAG products

	Number	%
Background paper published with decision rationale	**13**	**50**
If yes, the document contains…		
-references of used literature	9	69
-narrative summary	8	62
-detailed results of systematic - reviews including meta-analysis	6	46
-other materials	6	46
-comprehensive background report (including all items above)	2	15

Views on collaboration

- 93% of respondents saw potential for collaboration / resource-sharing
- Interests in
  - sharing of experiences and work program / priority topics
  - joint conduct or sharing of systematic reviews for context-free aspects (vaccine efficacy/safety/impact)
  - sharing of (generic) models & epidemiological assessments
- Potential barriers
  - structural concerns
  - lack of funding / resources
  - language barriers & cultural differences

Conclusions (I)

- Majority of EU countries with NITAG
  - but other entity takes final decision on implementation
- Independent if a formal framework is in place or not, common key factors are considered
- Applied frameworks and extent of evidence review differ widely (resources / role of NITAG)
- Some factors weighted differently, e.g. role of health economics and transmission modelling

Conclusions (II)

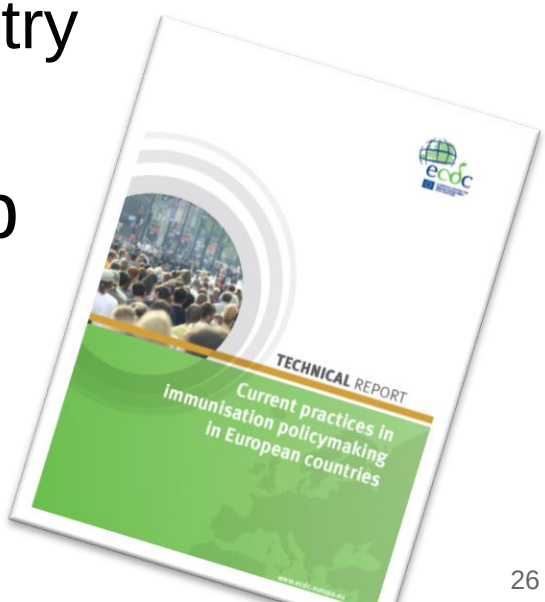
- Other reasons for NIP differences might include
  - historical development of NIPs
  - different vaccination systems / funding schemes
    - Centralized (e.g. UK, Finland, Netherland)
    - Decentralized (e.g. Germany, France)
    - Central/governmental procurement, tender systems
  - different local epidemiology & cost-effectiveness
  - local preferences & values (cultural differences?)
  - integration of schedule in the local health system (e.g. well-baby visits)

Conclusions (III)

- Duplication of efforts if every NITAG conducts own systematic reviews on the same key factors

- Vast majority sees potential for collaboration
  - scientific collaboration to support NITAG decisions, esp. exchanging experiences & on evidence review
  - decisions remains in the NITAG / country

- ECDC technical report and roadmap developed by VENICE consortium and discussed at a stakeholder meeting in Dec 2015



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