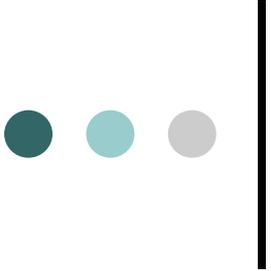


Screening in the genomic age: Implications for programs and policy-making

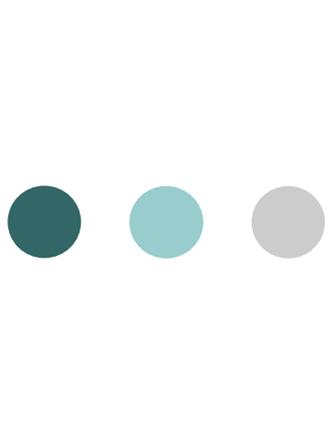
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VHPB Meeting, 18-19 March 2010, Budapest, Hungary



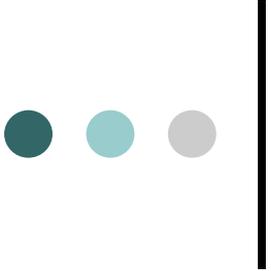
Overview

- **Section 1**
 - Classic and emerging screening criteria
- **Section 2**
 - Perennial challenges in policy-making
- **Section 3**
 - Hepatitis screening recommendations
- **Section 4**
 - Decision guide for population screening



Section 1

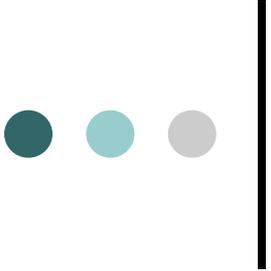
Classic and emerging screening criteria



How to decide whether or not to introduce screening?

- Due to the complexity involved in screening policy-making, many advocate the use of criteria
 - The Wilson and Jungner criteria have long been considered the gold standard

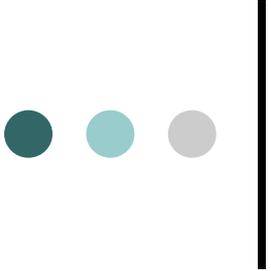
http://whqlibdoc.who.int/php/WHO_PHP_34.pdf



Classic criteria (1968)

Box 1. **Wilson and Jungner classic screening criteria**¹

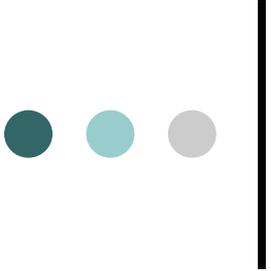
1. The condition sought should be an important health problem.
2. There should be an accepted treatment for patients with recognized disease.
3. Facilities for diagnosis and treatment should be available.
4. There should be a recognizable latent or early symptomatic stage.
5. There should be a suitable test or examination.
6. The test should be acceptable to the population.
7. The natural history of the condition, including development from latent to declared disease, should be adequately understood.
8. There should be an agreed policy on whom to treat as patients.
9. The cost of case-finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole.
10. Case-finding should be a continuing process and not a “once and for all” project.



Changing times

- A growing number of approaches to screening policy-making exist based on many different sets of criteria
 - Most are variations of classic criteria
 - New criteria reflect emerging trends
 - Non-paternalism
 - Evidence-based decisions
 - Results based management

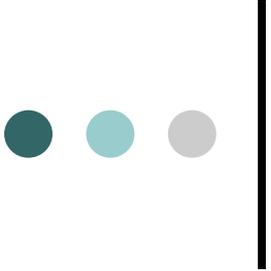
<http://www.who.int/bulletin/volumes/86/4/07-050112.pdf>



Emerging criteria over 40 years

Box 2. **Synthesis of emerging screening criteria proposed over the past 40 years**

- The screening programme should respond to a recognized need.
- The objectives of screening should be defined at the outset.
- There should be a defined target population.
- There should be scientific evidence of screening programme effectiveness.
- The programme should integrate education, testing, clinical services and programme management.
- There should be quality assurance, with mechanisms to minimize potential risks of screening.
- The programme should ensure informed choice, confidentiality and respect for autonomy.
- The programme should promote equity and access to screening for the entire target population.
- Programme evaluation should be planned from the outset.
- The overall benefits of screening should outweigh the harm.

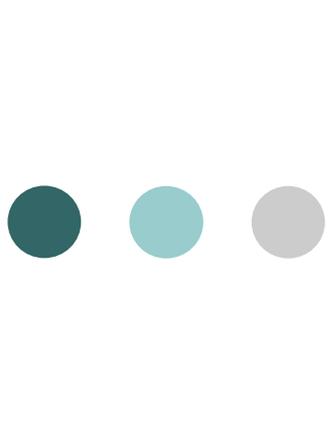


Screening policy-making is an iterative process

- Cannot be reduced to a list of 10 criteria
- Requires the consideration of:
 - Multiple issues
 - Multiple perspectives
 - Multiple types of evidence
- Ethical considerations are inherently embedded into the decisions made

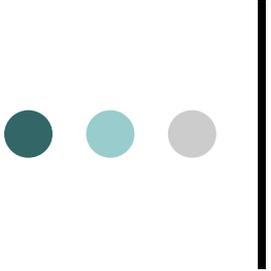


Perennial challenges in screening policy-making



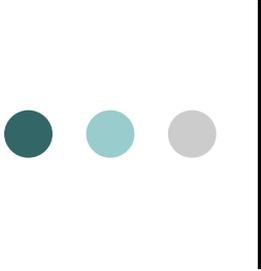
Section 2

Perennial challenges in policy-making



Screening policy-making raises many complex questions

1. Does screening provide an added benefit?
2. Do the benefits outweigh the harms?
3. Can the benefits be realized in this context?
4. Is screening worth the opportunity costs?
5. Which perspectives are used to decide?
6. What evidence is needed to decide?

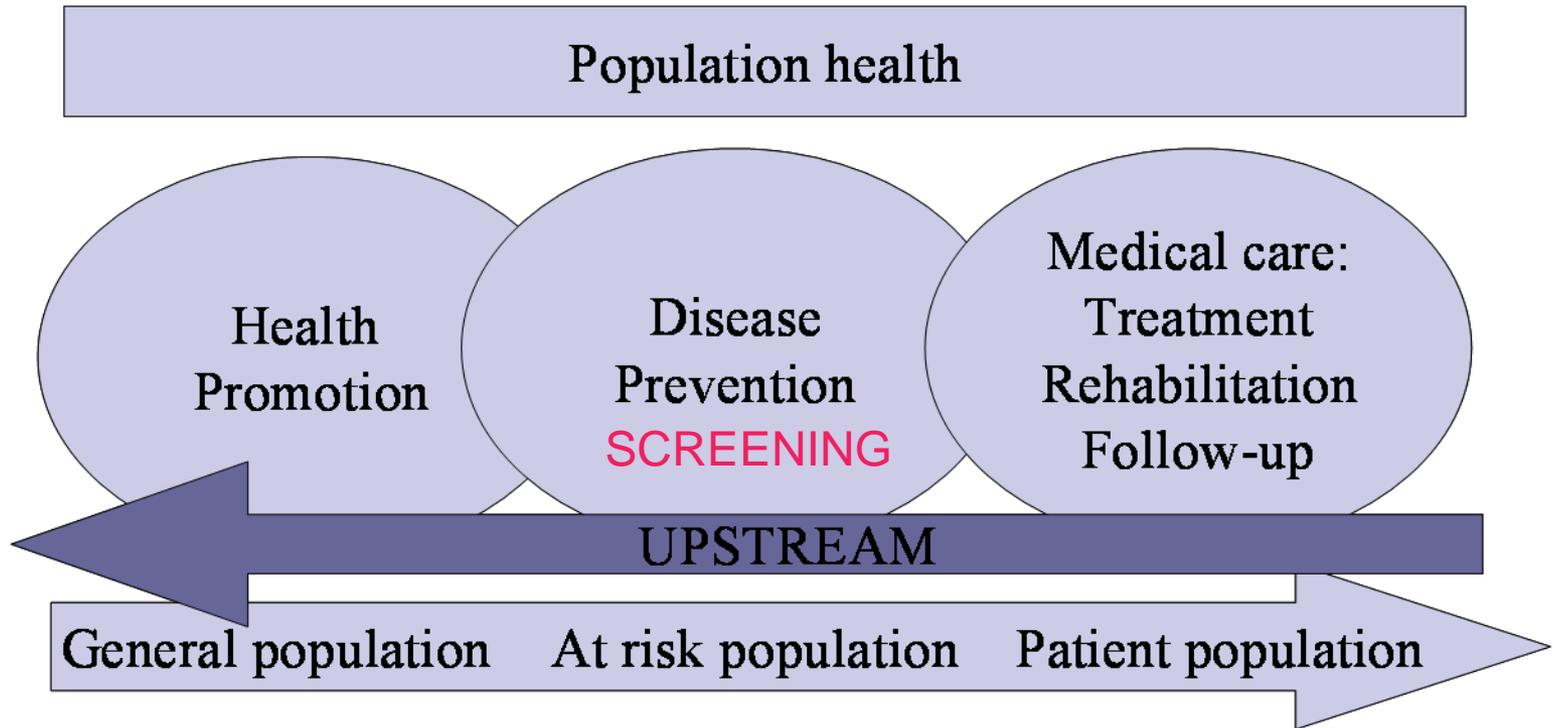


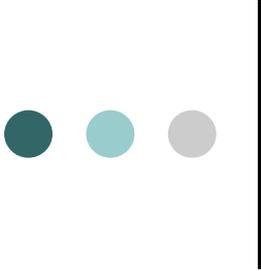
1. Does screening provide an added benefit?

- Classical benefits:
 - Early diagnosis and treatment leading to reductions in morbidity and mortality
- Expanding notions of benefit:
 - More informed reproductive choices
 - Shorter diagnostic odyssey (controversial)
- Added benefit as compared to:
 - The status quo (e.g. routine clinical care)
 - Other screening strategies (e.g. other target)
 - Non-screening alternatives (e.g. 1° prevention)

Screening is just one strategy among many

- Strategies for improving population health

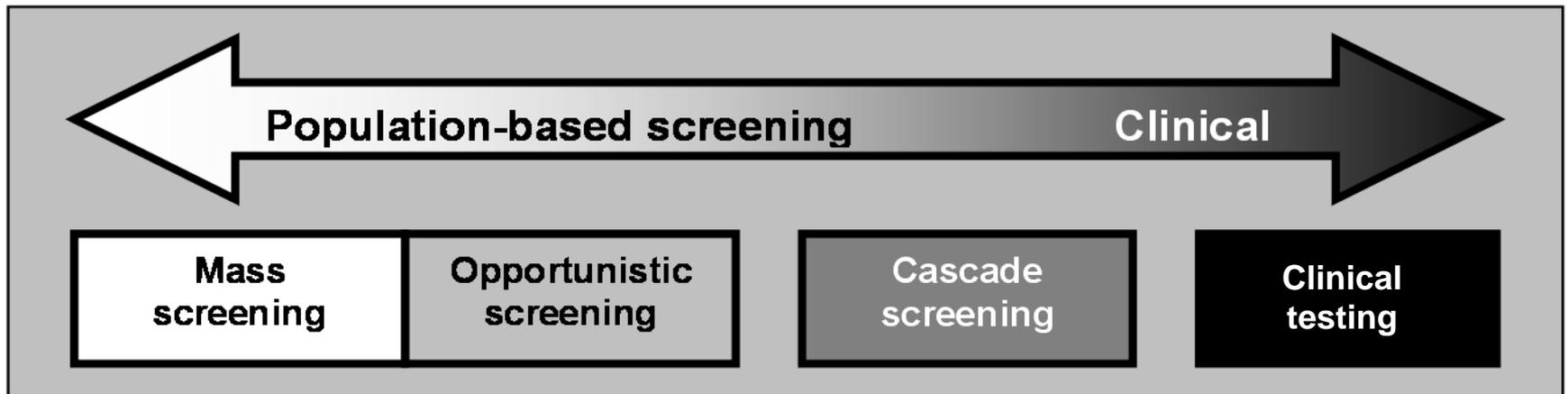




2. Do the benefits of screening outweigh the harms?

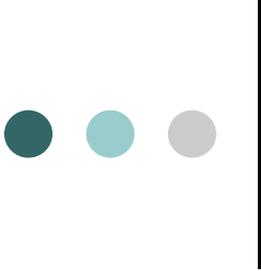
- Beware of over-estimating the benefits (NNS)
 - Lead time bias, length bias, etc.
- Beware of under-estimating the harms (NNH)
 - Labelling individuals or groups
 - Interventions often not benign
 - No perfect screening test
 - False positives: anxiety, unnecessary follow-up, cost
 - False negatives: missed diagnosis, false reassurance
- Balancing benefits versus harms
 - Unlike testing in a clinical context:
 - Can accept greater risk due to greater potential benefit
 - Screening involves soliciting people who are “well”:
 - Precautionary principle – first do no harm

The optimal balance depends on the screening continuum



Low risk populations are often unaware they could be affected and are more likely to have false positive test results thus greater caution is needed

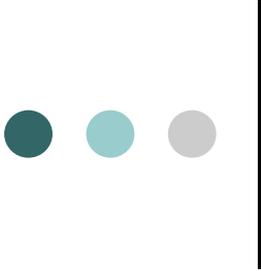
High risk populations may accept a more modest balance of benefits vs. harms since they are at risk or already have symptoms and thus have a greater chance of benefit



3. Can the benefits be realized in this context?

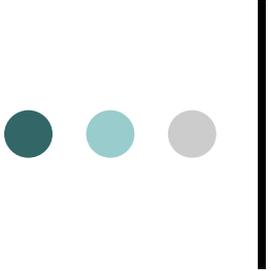
- “In theory, screening is an admirable method of combating disease ... [but] in practice, there are snags... The central idea of early disease detection and treatment is essentially simple. However, the path to its successful achievement (on the one hand, bringing to treatment those with previously undetected disease, and, on the other, avoiding harm to those persons not in need of treatment) is far from simple though sometimes it may appear deceptively easy.”

- Wilson and Jungner, 1968



No screening without a screening program

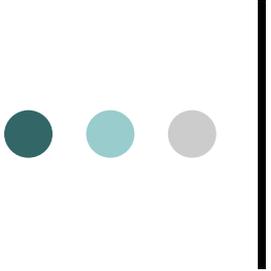
- Screening is more than just a test
- 3 coordinated levels:
 - Program management
 - Oversight, resource management, service organization, monitoring outcomes, etc.
 - Clinical services
 - Education, recruitment, informed consent, offer of screening, non-directive counselling, offer of intervention, follow-up, etc.
 - Laboratory testing
 - Analytical validity, clinical validity, quality assurance, data storage, confidentiality, etc.



Implications can vary widely

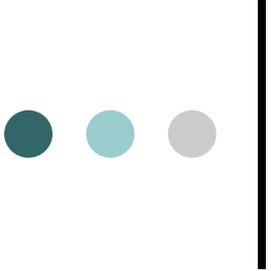
- Implications of screening depend on:
 - The health condition
 - The test(s) used
 - The timing of testing
 - The intervention(s)
 - The target population
 - The screening program
 - The implementation context

Changing any one of these parameters
can lead to very different outcomes



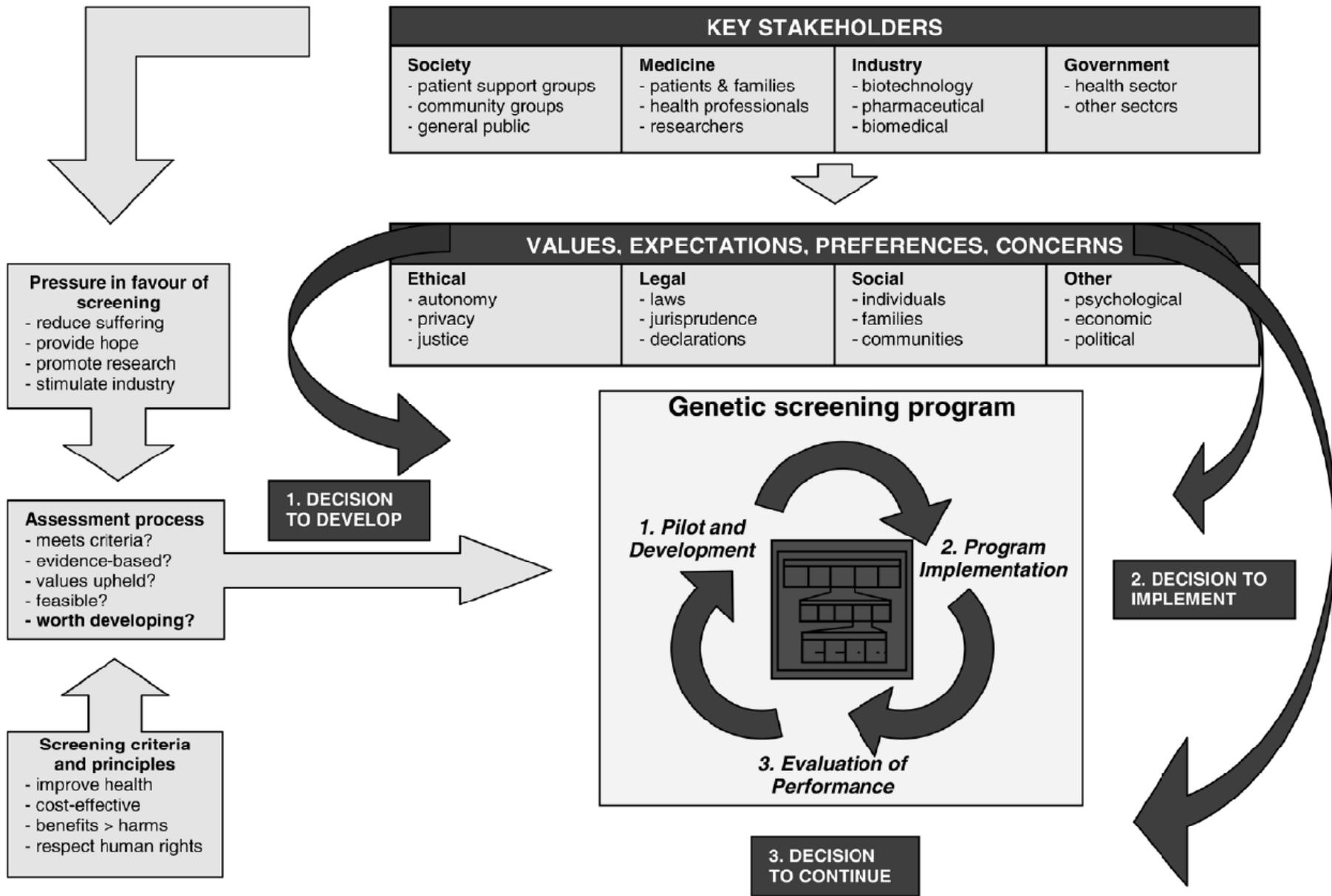
4. Is screening worth the opportunity costs?

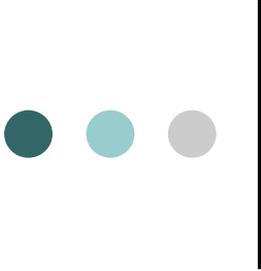
- Often entails large and expensive programs
- Requires time and \$\$ in planning to
 - Realize added benefits
 - Minimize potential harms
- High risk rather than population approach
- Does not act on upstream determinants
- Must compete for scarce resources with
 - Other prevention strategies
 - Other health priorities
 - Other non-health priorities



5. Which perspectives are used to decide whether to screen?

- Policy decisions are subject to many competing pressures and ultimately involve a value judgement which must integrate the best evidence and local contextual factors, as well as balancing the different needs and perspectives of:
 - Individuals and families at risk
 - The target population
 - Society at large

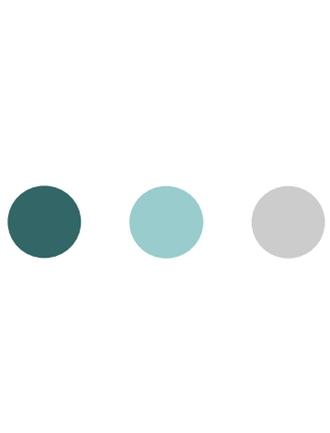




6. What evidence is needed to decide whether to screen?

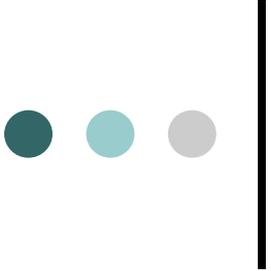
- Synthesize multiple types of evidence:
 - Data on expected benefits
 - Data on potential harms
 - Data on opportunity costs
- Requires critical appraisal of the research literature as well as consultations with:
 - The target population
 - Experts in the field
 - Clinical, laboratory, public health, administration, ethicists, jurists, economists, etc.
 - +/- wider public debate

“Absence of evidence is not evidence of absence”
- Altman



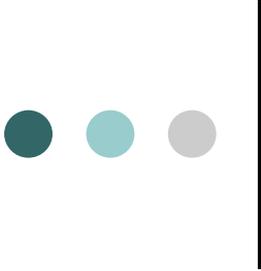
Section 3

Hepatitis screening recommendations



Continuum of strategies for the prevention of hepatitis

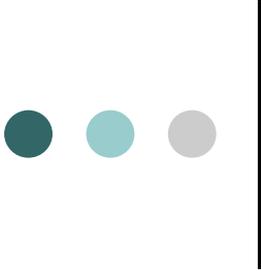
- Primary prevention
 - Vaccination programs
 - Judicious processing of donated blood products
 - Harm reduction programs for IV drug users
 - Education on safe sex practices
- Secondary prevention
 - Screening pregnant women and post-exposure prophylaxis of newborns with HBsAg+ mothers
- Tertiary prevention
 - Medical management to reduce complications



Evidence-based screening recommendations 2004

- US Preventive Services Task Force:
 - Strongly recommends screening for hepatitis B virus (HBV) infection in pregnant women at their first prenatal visit (**Grade A**)
 - *good evidence that screening improves health outcomes and benefits substantially outweigh harms*
 - Recommends against routinely screening the general asymptomatic population for chronic hepatitis B virus infection (**Grade D**)
 - *at least fair evidence that screening is ineffective or that harms outweigh benefits*

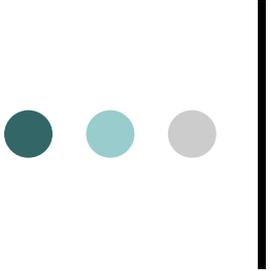
<http://www.ahrq.gov/clinic/3rduspstf/hepbscr/hepbrs.pdf>



Rationale for Grade D

- The prevalence of HBV infection is low
- Routine vaccination has already reduced incidence significantly
- The majority of those infected do not develop chronic disease
- There is limited evidence on the effectiveness of interventions
- BOTTOM LINE:
 - No evidence that screening the general population improves outcomes for cirrhosis, hepatocellular carcinoma or mortality
- NOTWITHSTANDING NEW EVIDENCE:
 - Universal screening and immunization reduces chronic carrier state and new infection rate in children and adolescents, but studies from hyperendemic areas may not be generalizable

<http://www.ahrq.gov/clinic/3rduspstf/hepbscr/hepbup.pdf>

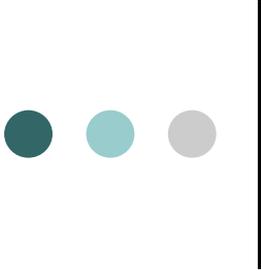


USPSTF conclusions

- Universal immunization is most effective
 - **Population approach**
 - Shift the entire population curve left
- There remains an adult and adolescent population at high risk for infection
 - **+/- High risk approach??**
 - Identify those at high risk (screening)
 - Offer individual protection

<http://www.ahrq.gov/clinic/3rduspstf/hepbscr/hepbrs.pdf>

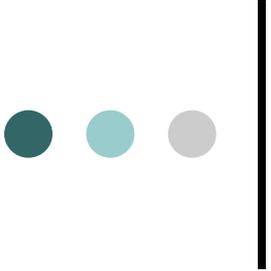
Rose G. Sick individuals and sick populations.
Int J Epidemiol 1985; 14: 32-38.



MMWR recommendations 2008

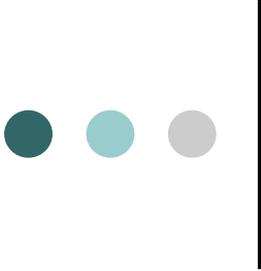
- Serologic testing for hepatitis B surface antigen (HBsAg) **has been recommended previously** for:
 - pregnant women
 - infants born to HBsAg-positive mothers,
 - household contacts and sex partners of HBV-infected,
 - persons who are the source of blood or body fluid exposures that might warrant postexposure prophylaxis (e.g., needlestick injury to health worker or assault),
 - born in countries with HBsAg prevalence of $\geq 8\%$, and
 - persons infected with human immunodeficiency virus

<http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5708a1.htm>



New – targeting additional high-risk groups

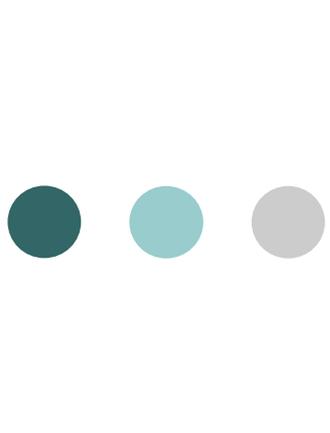
- Routine testing for HBsAg **is now also recommended for additional populations** with HBsAg prevalence of $\geq 2\%$:
 - born in regions with HBsAg prevalence of $\geq 2\%$,
 - men who have sex with men, and
 - injection-drug users



MMWR rationale for screening additional high-risk groups

- **Availability of interventions:**
 - Advances in treatment of hepatitis B and detection of liver cancer can reduce morbidity and mortality
- **Prevention of further transmission:**
 - Identification of infected persons also allows for primary prevention of ongoing HBV transmission
- **Some high risk groups meet screening criteria:**
 - serious health disorder
 - can be diagnosed before symptoms occur
 - reliable, inexpensive, and minimally invasive test
 - years of life to gain if intervention is initiated early
 - costs of screening are reasonable

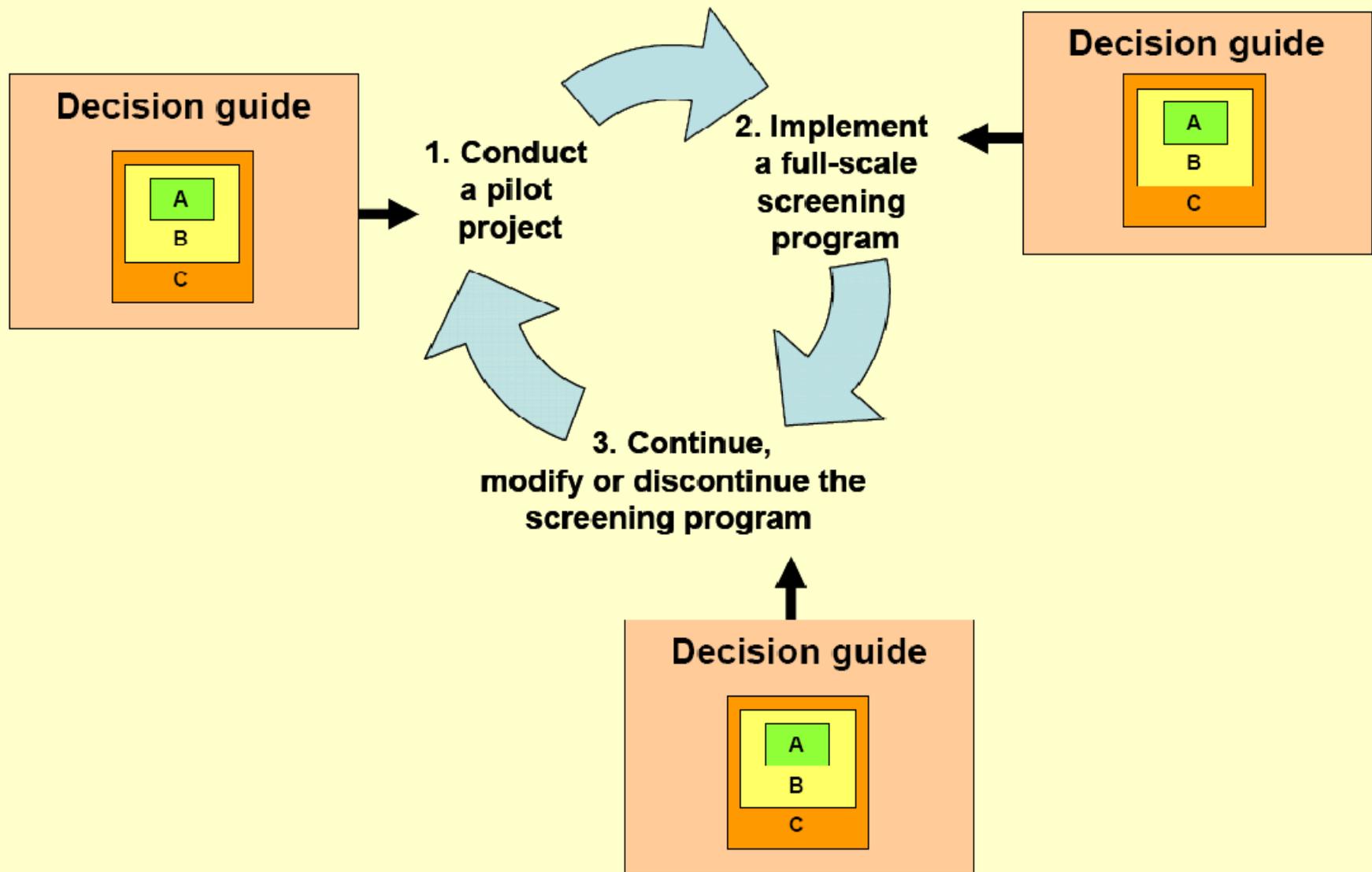
OPEN TO
FURTHER
DISCUSSION

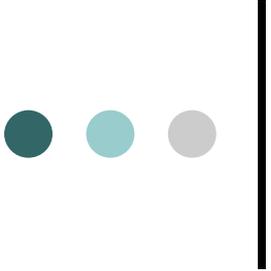


Section 4

Decision guide for population screening

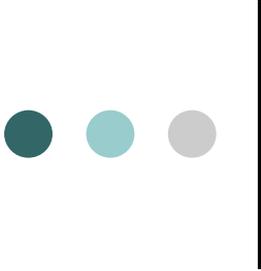
LIFE CYCLE OF A SCREENING PROGRAM





Multiple policy decisions

- Decision to:
 1. **Develop & pilot the screening strategy**
 - YES = Proceed to development and piloting
 - UNSURE = Gather further data and reconsider
 - NO = Abandon screening, prioritize alternative
 2. **Implement a full-scale program**
 - YES = Proceed to large-scale implementation
 - UNSURE = Gather further data and reconsider
 - NO = Abandon screening, prioritize alternative
 3. **Continue the screening program**
 - YES = Continue implementation unchanged
 - YES, BUT = Pilot modifications from evaluation
 - NO = Abandon screening, prioritize alternative



Multiple issues

- a) Added benefit outweighs harm?
- b) Realize net benefit in local context?
- c) Worth the opportunity cost?

Is there evidence of screening strategy efficacy and safety?

(i.e. could this screening strategy provide greater benefits than the status quo without creating undue harm?)

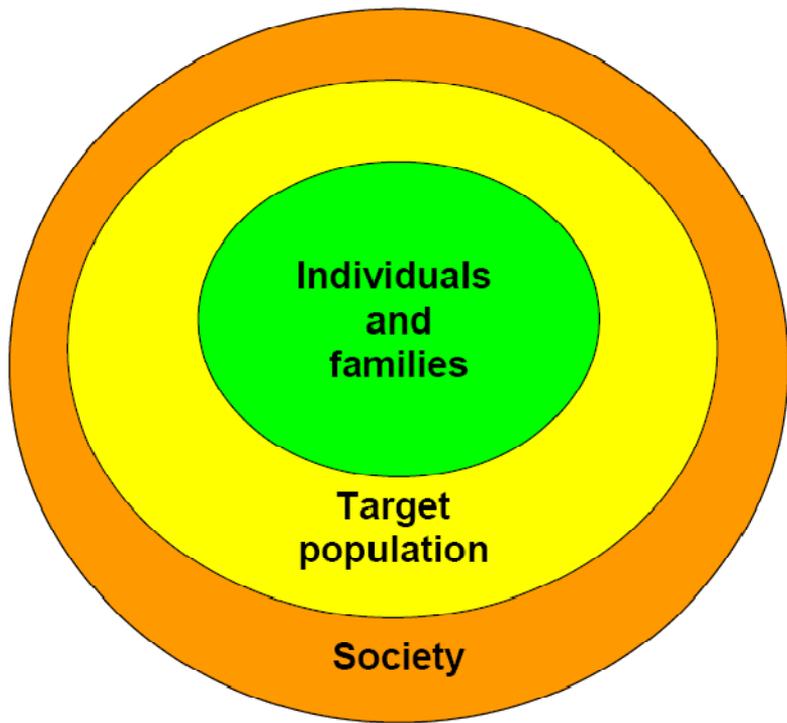
Will the screening program be effective and efficient in this implementation context?

(i.e. will the screening program be capable of realizing the benefits and minimizing the risks?)

Should the screening program be introduced in this jurisdiction?

(i.e. given multiple considerations, priorities and constraints, should screening be offered and funded?)

Multiple perspectives



Is there evidence of screening strategy efficacy and safety?

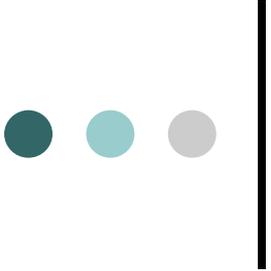
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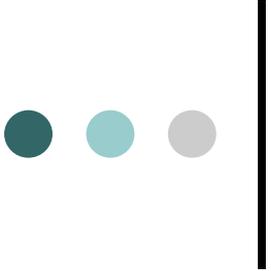
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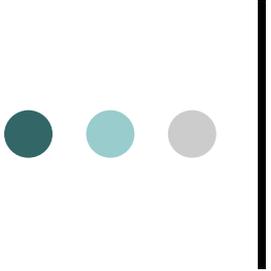
The process is the product

- The process of working through the large amount of evidence required to address each of the criteria makes apparent the tremendous complexity involved in screening policy decisions and allows different stakeholder groups to have a shared understanding



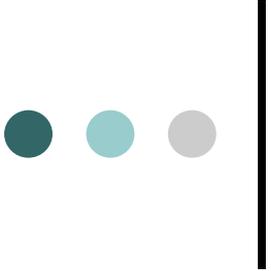
Neither good nor bad

- Screening as a strategy to prevent disease is neither good nor bad – it depends on:
 - how the screening program is developed and implemented,
 - whether an added benefit can be assured,
 - what safeguards are in place to minimize potential harms, and
 - whether the program is properly integrated into a wider continuum of services



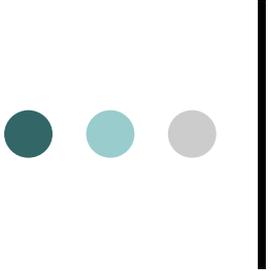
Fair process

- Using the decision guide to **make explicit the many advantages and disadvantages of screening**, as well as the potential opportunity costs, makes ultimate political decisions more transparent and allows decisions to be revisited as the knowledge base evolves



Not yet published

- Please see decision guide attached
 - Confidential
 - Please do not circulate



Suggested citations

- Andermann A, Blancquaert I, Beauchamp S, Déry V. Revisiting Wilson and Jungner in the genomic age: A review of screening criteria over the past 40 years. *Bulletin of the World Health Organization* 2008; 86(4): 1-3.
- Andermann A, Blancquaert I, Beauchamp S, Costea I. Guiding policy decisions for genetic screening: Developing a systematic and transparent approach. *Public Health Genomics* 2009 (DOI: 10.1159/000272898). Epub ahead of print.
- Andermann A, Blancquaert I, Déry V. Genetic screening: A conceptual framework for programs and policy-making. *Journal of Health Services Research and Policy*. Forthcoming.
- Andermann A, Blancquaert I. Genetic screening: A primer for primary care. *Canadian Family Physician*. Forthcoming.