Ethical issues related to vaccine development and immunization programmes

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Outline

• Milestones in medical ethics
• General ethical principles
• Ethical issues at each stage of the vaccine product life cycle
• Ethical issues related to the use of vaccines in immunization programs
Milestones in ethics
Medical ethics

Deals with duties of the physicians in general

- **400 BC** – Hippocratic Oath
  - *First do not harm, ensure patient confidentiality and no conflict of interest*

- **9th Century** – Ishaq bin Ali Rahawi: Conduct of a physician


- **1949** – WMA-International code of Medical Ethics (revised 1968, 1983, 2006)
  - *Physician shall act in the patient’s best interest*

http://www.wma.net/en/30publications/10policies/g1/index.html
Milestones in ethics (continued)

Research ethics

• 1947 – The **Nuremberg Code** is a set of 10 ethical principles for human experimentation elaborated as a result of the Nuremberg trials at the end of World War II*
  
  – *The voluntary consent of human subjects is absolutely essential.*

*http://ori.dhhs.gov/education/products/RCRintro/c03/b1c3.html

Milestones in ethics (continued)
Research ethics

• 1964 – **The Declaration of Helsinki** is a set of ethical principles for medical research involving human subjects developed for the medical community by the World Medical Association (WMA). Regarded as the cornerstone document of human research ethics.
  - Initially: 12 paragraphs – 2008: 35 paragraphs
  - *It is the duty of physicians who participate in medical research to protect the life, health, dignity, integrity, right to self-determination, privacy, and confidentiality of personal information of research subjects.*

http://www.wma.net/en/30publications/10policies/b3/
Milestones in ethics (continued)
Research ethics

• 1979 - The US **Belmont Report** (by the American Commission for the Protection of Human Subjects) develops guidelines to be followed to assure that such research is conducted in accordance with the ethical principles
  - *Respect for persons, beneficence, and justice*
  - *Applications of these principles to conduct research requires careful consideration of informed consent, risk-benefit assessment and selection of subjects of research*

http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.html
Milestones in ethics (continued)

Research ethics


  - *Respect for persons, beneficience, non maleficence and justice*
  
  - *Develops issues such as informed consent, standards for external review, recruitment of participants, …*

  - Currently under revision to include conflict of interest; research using the internet; epidemiological research close to or overlapping with biomedical – and to integrate changes in the Declaration of Helsinki and other relevant documents

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Milestones in ethics (continued)

Research ethics

• 2000 – **UNAIDS** Ethical considerations in biomedical HIV prevention trials – Revised 2007, 2010 - Additional guidance point added in 2012
  
  - *Ethics applied to HIV vaccine trials in humans, including recruitment of participants, informed consent, standard of care, …*

Milestones in ethics (continued)

Public health ethics

• 2002 – American Public Health Society - Principles of the Ethical Practice of Public Health highlight the ethical principles that follow from the distinctive characteristics of public health.

- Humans are inherently social and interdependent.

http://www.apha.org/NR/rdonlyres/1CED3CEA-287E-4185-9CBD-BD405FC60856/0/ethicsbrochure.pdf
Milestones in ethics (continued)
Public health ethics

2007 - **British Nuffield Council of Bioethics: Public Health: Ethical Issues** addresses the complex questions about the relationship between the state and the individuals and organisations that are affected by its policies.

- **One chapter devoted to infectious diseases, including vaccination**
- **State intervention is primarily warranted where an individual’s actions affect others**
- **Importance of reducing health inequalities**
- **Any policy, including a policy to ‘do nothing’, implies value judgements about what is or is not good for people, and requires justification**

General ethical principles

Health interventions must be in accordance with

• Justice
  – Ensure fair spread of benefits and risks among parties (distributive justice)
  – Ensure that resources should be allocated fairly –
  – Give special attention to vulnerable groups
General ethical principles

Health interventions must be in accordance with

- **Justice**
  - Ensure fair spread of benefits and risks among parties (distributive justice)
  - Ensure that resources are allocated fairly
  - Give special attention to vulnerable groups

- **Autonomy**
  - Respect individual freedom of thought and action
  - Protect persons with impaired or diminished autonomy
General ethical principles

Health interventions must be in accordance with

• Beneficence/ altruism/ solidarity
  - Maximize benefits
  - Contribute to welfare of others
General ethical principles

Health interventions must be in accordance with:

• **Beneficence (altruism/ solidarity)**
  - Maximize benefits
  - Contribute to welfare of others

• **Non-maleficence**
  - First do not harm
  - Minimize potential harms
  - Avoid using an intervention that is unsafe or ineffective
Ethical issues in the life-cycle of a vaccine

Preclinical

Design & execution of research involving human subjects

Exploratory & Preclinical stage

Phase I

Phase II

Phase III

Regulatory approval

Vaccine introduction & Phase IV

Introduction of vaccines in various settings - best market/most needed?

Ethics of animal research

Human research ethics

Conflicts of interest

Public health ethics
Ethical principles for public health immunisation programs

- Benefits
- Risks
- Effectiveness
- Equity and justice
- Autonomy
- Reciprocity
- Trust
Benefits

• Vaccination is a preventive intervention
• The program should benefit the individual and the community
• Disease burden should be sufficient, in terms of severity and frequency, to ethically justify the risk and expense of the programme
• The benefit is provisional (future) and exposure may never occur
• The benefit can be indirect eg in the case of maternal immunization aiming to protect the infant
• Increasing number of vaccines protect against more diseases, but may also pose increased risk
Risks

• All vaccines present a risk to the individual, although minimal
• Acceptable risk is low/very low in healthy individuals/children. No established accepted benefit-risk ratio - varies according to epidemiological situation
• Risk is born by the individual and its family while benefit accrues to the community
• Program organizers should train vaccinators to handle vaccine reactions to minimize risks
• New vaccines must be introduced in an organized manner. Program organizers should monitor for AEFIs through timely reporting of adverse events to ensure the program is as safe as possible
• Should safety issues arise – routines for investigation of individual cases and initiation of studies well established
Effectiveness

- Program organizers should monitor vaccination coverage and vaccine effectiveness and should halt or alter the program if it is or becomes ineffective (unsafe)
- Data protection laws may hamper classical and modern epidemiology, in particular data linkage
- To facilitate compliance with data protection laws and not delay studies general IRB pre-approvals to conduct studies will facilitate
- Comparative effectiveness trials may be needed using vaccines targeted at the same disease
- Sufficient funding for scientifically sound monitoring is essential
Vaccine data safety surveillance using data linkage - comparison of opt-in and opt-out parental consent

Vaccine assessment using linked data working group (VALID)
South Australia, Australia

Randomised controlled trial comparing the two policies
- opt-in 21%
- opt-out 96%

Conclusion and suggestion: A waiver of consent for data linkage studies are needed for data linkage studies meeting all appropriate criteria and should be granted by ethics committees

*Berry et al J Med Ethics 2012, 38 (10):619-625*
Shared responsibilities between stakeholders - interactions in the post licensure era

- Regulatory agencies stipulate post-marketing surveillance in risk management plans
- Vaccine manufacturers are dependent on regulatory agencies, public health and/or academia for support on microbiological surveillance, safety monitoring and effectiveness
- Interactions hampered by public health needs for independence
- Solution?
- Increasing difficulties in the tendering processes with a series of court trials challenging the tendering process and delaying the immunisation programs
Equity and justice

- Also vulnerable and disadvantaged groups should be targeted
- Great variability between countries/regions within countries which vaccines are offered (vary between 9-16 vaccines)
- The program should be cost-effective in comparison with competing health-care interventions
- Availability of very different vaccines for the same disease may raise ethical problems which challenge conventional cost-effectiveness considerations of the value of vaccines and introduce other values such as public trust
- Examples of that is oral polio vaccines that are cheaper than inactivated polio vaccines, both are highly effective in eradicating polio. OPV is preferred in developing countries, largely because of cost, however, one in every 2.4 million doses of OPV causes VAPP
Autonomy

• Vaccine recipients and the parents/care takers of children or adults not competent to make their own decision should be given sufficient information to make autonomous, informed decisions about the risks and benefits of immunisation – compulsory immunisation infringes autonomy

• How much should Public Health actively promote vaccine programs?

• How much accurate but sometimes scary information can and should public health provide?*

• Mandatory immunisation is common not only in the childhood immunisation programs but also for health care workers although exempts for philosophical reasons are provided

*http://www.euronews.com/2012/03/26/eliminating-measles-personal-stories/
## Mandatory vs recommended programmes in Europe*

<table>
<thead>
<tr>
<th>Vaccination</th>
<th>Vaccine offered</th>
<th>Recommended (RA or RR)</th>
<th>Mandatory (MA or MR)</th>
<th>Mixed</th>
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<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
<td></td>
</tr>
<tr>
<td>Diphtheria</td>
<td>29 100.0%</td>
<td>16 55.2%</td>
<td>11 37.9%</td>
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<td>16 55.2%</td>
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<tr>
<td>Hep B</td>
<td>29 100.0%</td>
<td>17 58.6%</td>
<td>10 34.5%</td>
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<tr>
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<td>8 27.6%</td>
<td></td>
</tr>
<tr>
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<td>29 100.0%</td>
<td>21 72.4%</td>
<td>8 27.6%</td>
<td></td>
</tr>
<tr>
<td>Men C</td>
<td>22 75.9%</td>
<td>22 100.0%</td>
<td></td>
<td></td>
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<tr>
<td>PNC</td>
<td>28 96.6%</td>
<td>23 82.1%</td>
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<td>1 3.6%</td>
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<tr>
<td>Varicella</td>
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<td>19 95.0%</td>
<td>1 5.0%</td>
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<tr>
<td>Flu</td>
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<td>28 96.6%</td>
<td></td>
<td>1 3.4%</td>
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<tr>
<td>BCG</td>
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<td>15 65.2%</td>
<td>7 30.4%</td>
<td>1 4.3%</td>
</tr>
<tr>
<td>Hep A</td>
<td>25 86.2%</td>
<td>22 88.0%</td>
<td>2 8.0%</td>
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<td>22 95.7%</td>
<td>1 4.3%</td>
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</tr>
</tbody>
</table>

*ECDC VENICE network Eurosurveillance 2012 May 31; 17(22).
Should vaccines be mandatory for health care workers?

- Measles, rubella, hepatitis b, varicella, influenza etc?
- Are available vaccines safe?
- Are available vaccines effective? Preventing transmission between community & HCW and between patients & HCWs?
- Would a mandatory policy enhance patient safety?
- Is there an ethical basis for such a policy?
- Is such a policy cost-saving? If not, is it justifiable anyway?
- Are adequate and scientifically sound alternatives available?

Reciprocity

• People who suffer rare, serious complications of public health immunisation programs should receive adequate medical care and there is a strong ethical argument that governments should have no-fault compensation schemes.

• At least 20 countries have implemented compensation schemes.

• How comparable are these schemes? Across regions? Across continents?

• Do the schemes provide life-long compensation if needed?

*Kelly et al Med J Aust 2011
Trust

- Public health immunisation programs depend on mutual trust, which may be threatened by many circumstances. Measures to improve public consultation regarding decisions about public health immunisation programs will improve their ethical status.

- Pandemics present a different set of problems as people then commonly demand vaccines that are in short supply.

- Behaving ethically in a disaster may shift the balance toward what is best for the community as a whole.
Conclusion

• Finding a balance between the public good, protection of the vulnerable, and deference to individual rights remains a key challenge for vaccine policy, particularly as vaccine safety fears persist and vaccination programs continue to expand.

• The evaluation of ethical issues demands a dialogue about ethics among all relevant stakeholders, informed by the best available evidence of analysis.

• Attention to ethical issues will be essential to the continued success of global vaccination programs in advancing and promoting public health.
Thank you for your attention