Access to Benefits

Between the Categorical Imperative and Solidarity

Prof. Pablo Requena
Pontificia Università Santa Croce

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"More work is needed"

Philippines Manila Research Ethics Board

- 193 protocols
- 2012-2017

Jimenez EB, Virtudazo JMP, Torres CE, Bernabe R dlC. Availability of post-trial access in clinical trials: a review of clinical trial protocols submitted to the research ethics board of the University of the Philippines Manila. *Curr Med Res Opin*. 2019;35(11):1849-1855

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"More work is needed"

Philippines Manila Research Ethics Board

- 193 protocols
- 2012-2017

"To date, none of the clinical trial protocols evaluated by UPMREB fully complied with ethical requirements for PTA"

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The ethical question

What moral obligations do study sponsors have regarding participants once the experimentation is concluded?

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Ethical question

What moral obligations do study sponsors have regarding participants once the experimentation is concluded?

- Is it obligatory to provide the research product if proven beneficial for patients, or is it merely optional?
- Who should ensure compliance?
- For how long should this access be guaranteed?

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Outline

1. Some data
2. Central ethical issue
3. Suggestions for the Declaration of Helsinki

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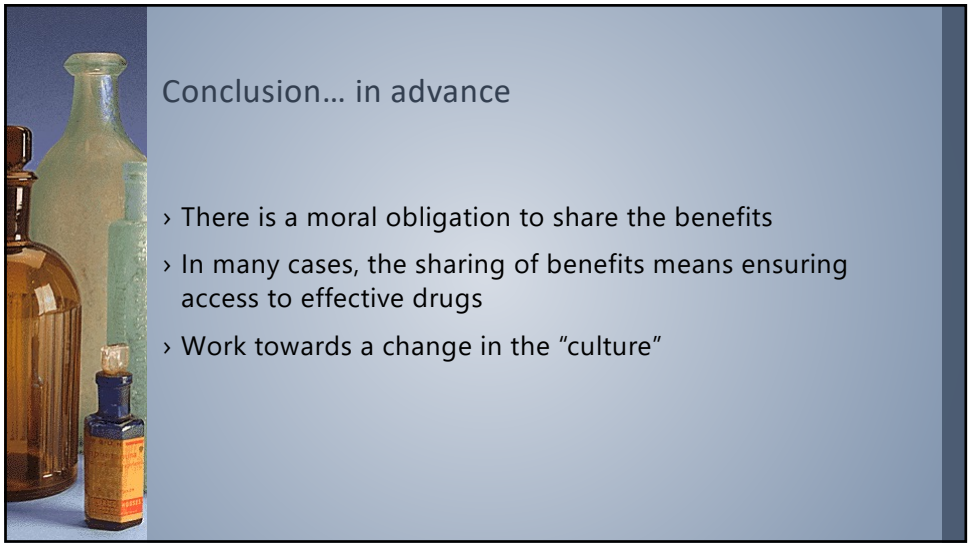
Conclusion… in advance
› There is a moral obligation to share the benefits
› In many cases, the sharing of benefits means ensuring access to effective drugs
› Work towards a change in the "culture"

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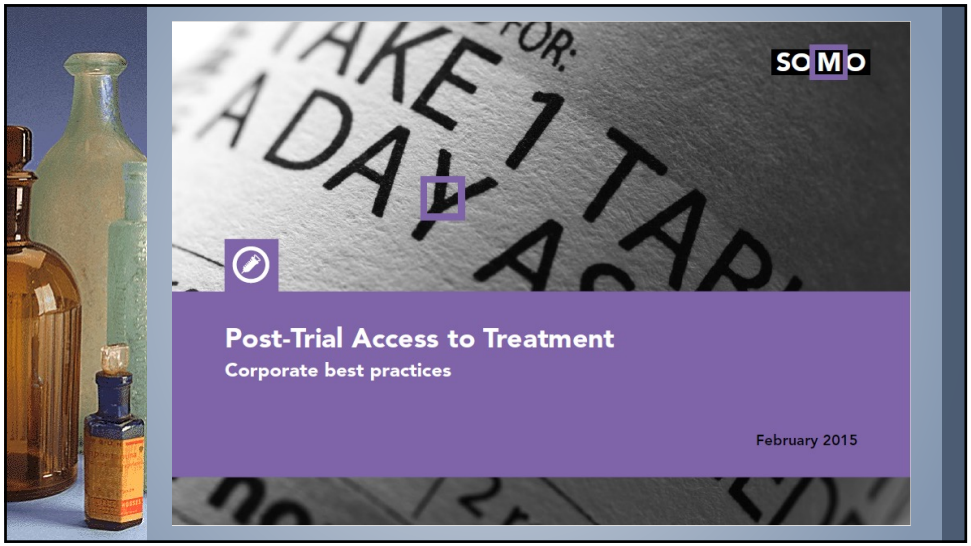
SOMO
Post-Trial Access to Treatment
Corporate best practices
February 2015

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1. Some data

- Major pharmaceutical companies
- Difficulty in collecting good examples of PTA
- Confirms the exceptional nature of PTA

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European Journal of Clinical Pharmacology (2018) 74:1001–1010
https://doi.org/10.1007/s00228-018-2474-9

CLINICAL TRIAL

The patient's safety and access to experimental drugs after the termination of clinical trials: regulations and trends

Ricardo Eccard da Silva[1,2] · Angélica Amorim Amato[2] · Thiago do Rego Sousa[3] · Marta Rodrigues de Carvalho[4] · Maria Rita Carvalho Garbi Novaes[2,4]

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- European Clinical Trials Register (EUCTR): 2014
- 1624 studies in 21 countries

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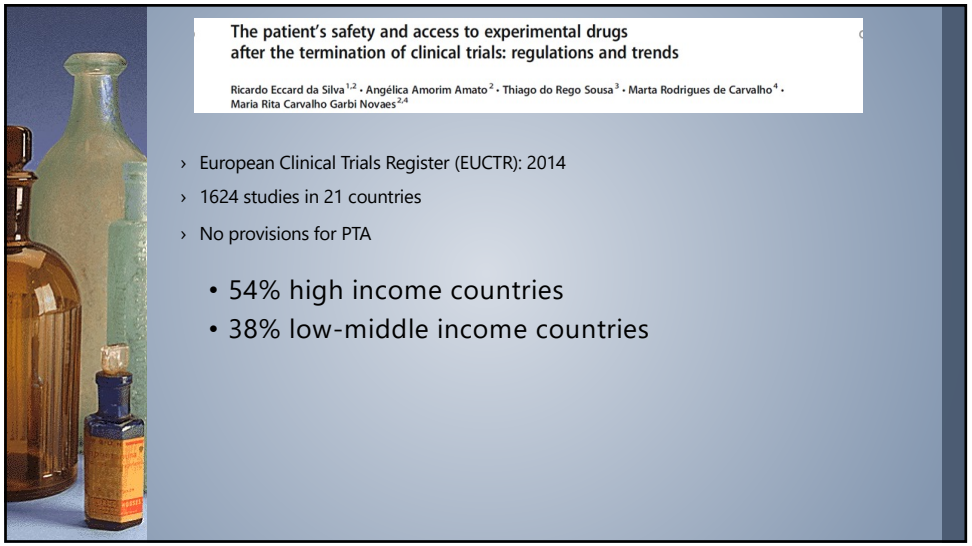
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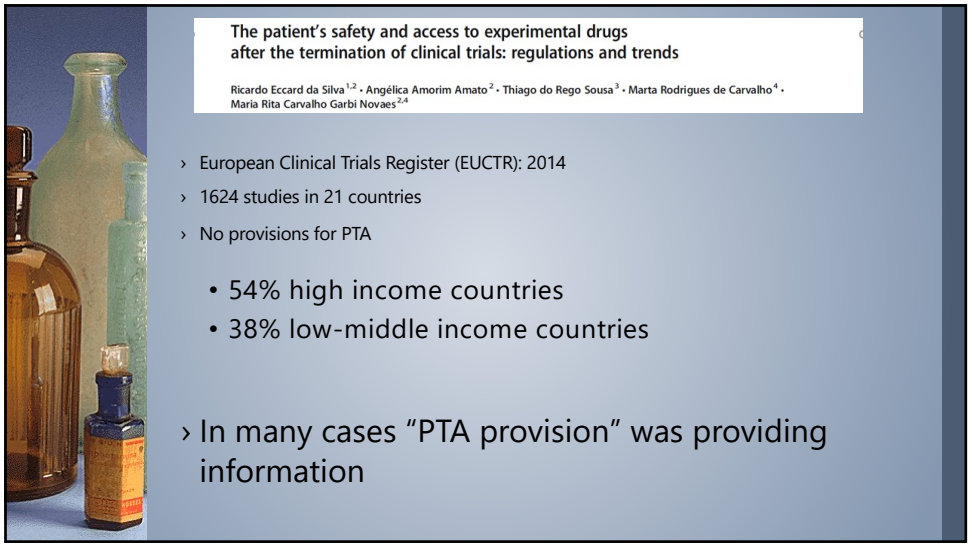
› 1624 studies in 21 countries
› No provisions for PTA
• 54% high income countries
• 38% low-middle income countries

11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› In many cases "PTA provision" was providing information

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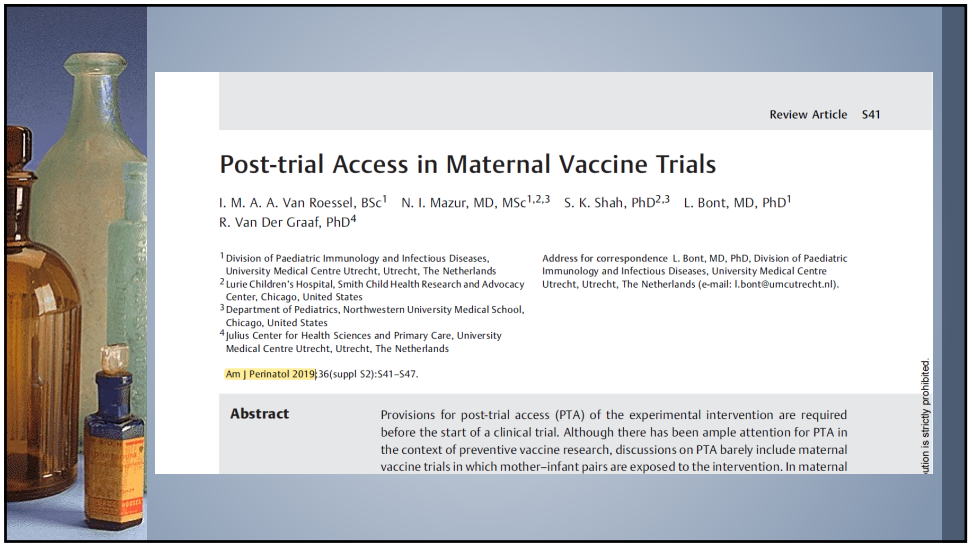
Review Article S41
Post-trial Access in Maternal Vaccine Trials
I. M. A. A. Van Roessel, BSc[1] N. I. Mazur, MD, MSc[1,2,3] S. K. Shah, PhD[2,3] L. Bont, MD, PhD[1]
R. Van Der Graaf, PhD[4]
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[4] Julius Center for Health Sciences and Primary Care, University Medical Centre Utrecht, Utrecht, The Netherlands
Address for correspondence L. Bont, MD, PhD, Division of Paediatric Immunology and Infectious Diseases, University Medical Centre Utrecht, Utrecht, The Netherlands (e-mail: l.bont@umcutrecht.nl).
Am J Perinatol 2019;36(suppl S2):S41–S47.
Abstract
Provisions for post-trial access (PTA) of the experimental intervention are required before the start of a clinical trial. Although there has been ample attention for PTA in the context of preventive vaccine research, discussions on PTA barely include maternal vaccine trials in which mother–infant pairs are exposed to the intervention. In maternal
ution is strictly prohibited

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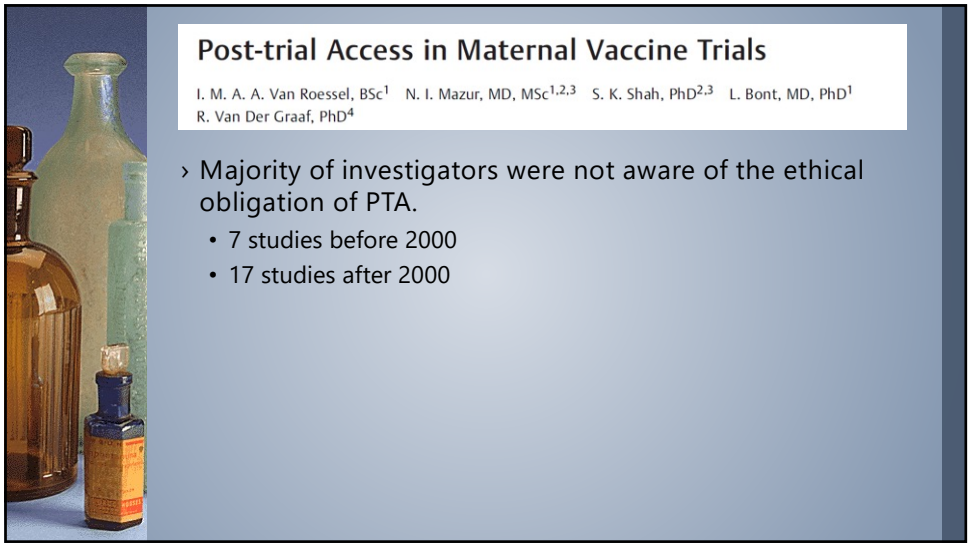
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• 7 studies before 2000
• 17 studies after 2000

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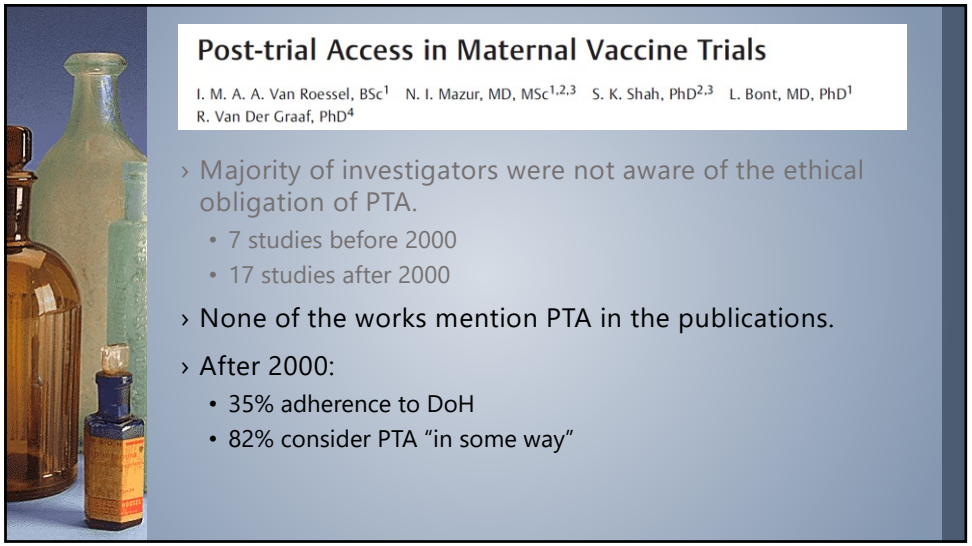
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R. Van Der Graaf, PhD[4]
› Majority of investigators were not aware of the ethical obligation of PTA.
• 7 studies before 2000
• 17 studies after 2000
› None of the works mention PTA in the publications.
› After 2000:
• 35% adherence to DoH
• 82% consider PTA "in some way"

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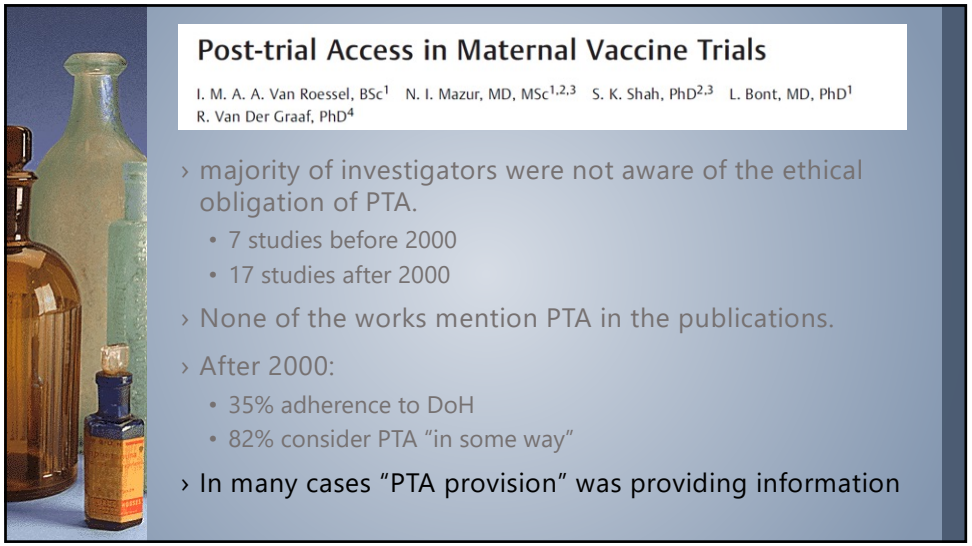
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Research

Availability and affordability of new medicines in Latin American countries where pivotal clinical trials were conducted

Núria Homedes[a] & Antonio Ugalde[b]

Objective To assess whether new pharmaceutical products approved by the United States Food and Drug Administration (FDA) in 2011 and 2012 were registered, commercialized and sold at affordable prices in the Latin American countries where they were tested.
Methods We obtained a list of new molecular entities (new pharmaceutical products) approved by the FDA in 2011 and 2012. FDA medical reviews indicated the countries where pivotal clinical trials had been conducted. The registration status of the products was obtained from pharmaceutical registers; pharmaceutical companies confirmed their availability in national markets and local pricing observatories provided the price of medicines in retail pharmacies. Affordability was assessed as the cost of a course of treatment as a proportion of monthly income. Information on safety and efficacy was gathered from independent drug bulletins.
Findings Of an expected 114 registrations, if the 33 products had been registered in all the countries where tested, only 68 (60%) were completed. Eight products were registered and commercialized in all countries but 10 had not been registered in any of the countries. With one exception, products for which we obtained pricing information ($n = 18$) cost more than the monthly minimum wage in all countries and 12 products cost at least five times the monthly minimum wage.
Conclusion Many pharmaceutical products tested in Latin America are unavailable and/or unaffordable to most of the population. Ethical review committees should consider the local affordability and therapeutic relevance of new products as additional criteria for the approval of clinical trials. Finally, clinical trials have opportunity costs that need to be assessed.

Bull World Health Organ 2015;93:674–683 | doi: http://dx.doi.org/10.2471/BLT.14.151290

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Research

Availability and affordability of new medicines in Latin American countries where pivotal clinical trials were conducted

Núria Homedes[a] & Antonio Ugalde[b]

- 2011-2012
- 33 products in US market; 8 in all Latin-American countries
- Only 1 product had a price lower than the country's monthly minimum wage

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developing world bioethics

Developing World Bioethics ISSN 1471-8731 (print); 1471-8847 (online)
Volume 9 Number 2 2009 pp 65–73

doi:10.1111/j.1471-8847.2008.00228.x

INTERNATIONAL RESEARCH AND JUST SHARING OF BENEFITS IN MEXICO

RICARDO PÁEZ AND JAVIER E. GARCÍA DE ALBA

Keywords
international research,
justice,
Mexico,
sharing of benefits,
social context

ABSTRACT
International research enrolling human subjects has raised an ethical concern regarding the just distribution of benefits between the countries that design the research and the host communities. Although several universal declarations have expressed this concern, a gap between theory and practice continues to exist, as well as a significant divergence between the design of the research protocol and the social context where it will be implemented. Although institutional review boards have made a valuable effort to evaluate international research, their sensitivity to the just sharing of research benefits as well as their attention to the social context must be evaluated. This article analyzes the distribution of benefits in a review of international research in Mexico and produces an ethical reflection based on the results.

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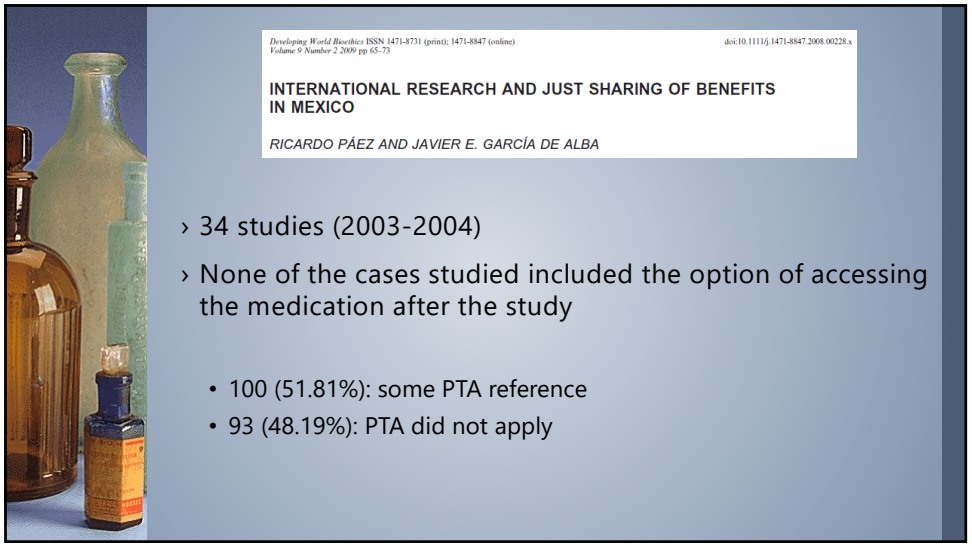

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INTERNATIONAL RESEARCH AND JUST SHARING OF BENEFITS IN MEXICO

RICARDO PÁEZ AND JAVIER E. GARCÍA DE ALBA

- 34 studies (2003-2004)
- None of the cases studied included the option of accessing the medication after the study
  - 100 (51.81%): some PTA reference
  - 93 (48.19%): PTA did not apply

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INTERNATIONAL RESEARCH AND JUST SHARING OF BENEFITS IN MEXICO

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What did they understand by PTA?

1. Existence of standard care outside the trial
2. No provision of the study drug after the trial
3. Unknown benefit due to the experimental nature of the study
4. The drug is available on the market or will be manufactured
5. Access to the study drug during the study

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1. Some data: conclusions

PTA is rarely considered today

- High percentage of protocols:
  - Do not consider PTA
  - State that it does not apply in their case
  - Mention types of PTA that contradict what is present in ethics
- In the majority of cases, PTA is limited to sharing information
- Unclear policy in many pharmaceutical companies

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2. Central moral question

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2. Central moral question

Belmont Report (1978)

"research should not unduly involve persons from groups unlikely to be among the beneficiaries of subsequent applications of the research" (Part B, 3. Justice)

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2. Central moral question

› A matter of justice

› The debate about "exploitation"

› "Addressing Exploitation: Reasonable Availability Versus Fair Benefits" (Ezequiel Emmanuele, 2008)

› Not every lack of PTA constituted exploitation

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2. Central moral question

"Hierarchy" in morality:

1. Injustice as "exploitation"
2. Injustice that does not entail "exploitation"
3. No "real" injustice

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2. Central moral question

The culture or vision driving the experimentation

› Primarily profit-driven

› Strong solidarity dimension

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2. Central moral question

The culture or vision driving the experimentation

› Primarily profit-driven

› Strong solidarity dimension

Justice is necessary but it is not sufficient

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3. Suggestions
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WMA DECLARATION OF HELSINKI – ETHICAL PRINCIPLES
FOR MEDICAL RESEARCH INVOLVING HUMAN SUBJECTS

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One more difficulty: rule for *most* or *all* cases…
• Challenging for law
• "Impossible" for ethics

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Normative ethics vs. Virtue ethics

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22. The design and performance of each research study involving human subjects must be clearly described and justified in a research protocol.
(…)
In clinical trials, the protocol must also describe appropriate arrangements for post-trial.

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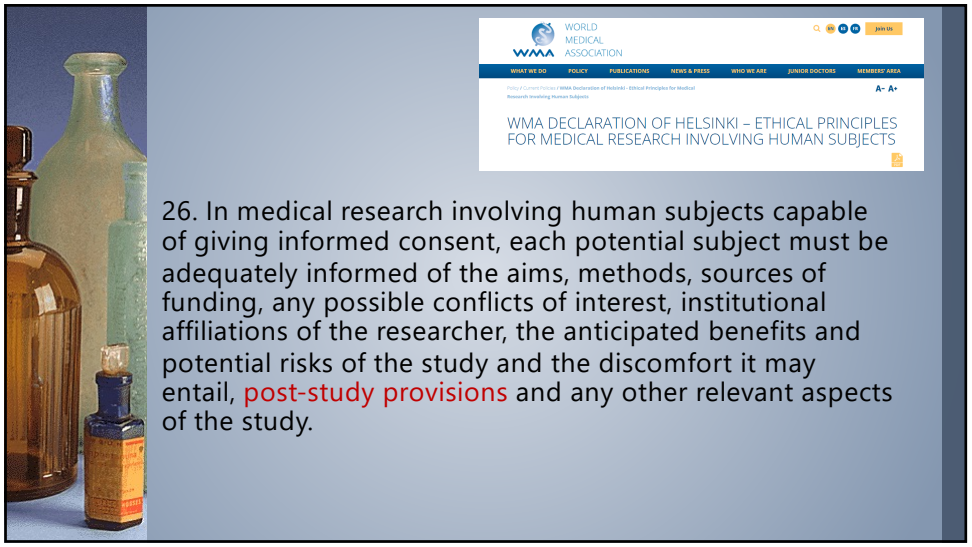
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26. In medical research involving human subjects capable of giving informed consent, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail, post-study provisions and any other relevant aspects of the study.

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Post-Trial Provisions
34. In advance of a clinical trial, sponsors, researchers and host country governments should make provisions for post-trial access for all participants who still need an intervention identified as beneficial in the trial. This information must also be disclosed to participants during the informed consent process.

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The "simplest" suggestion: substitute "should" with "must".
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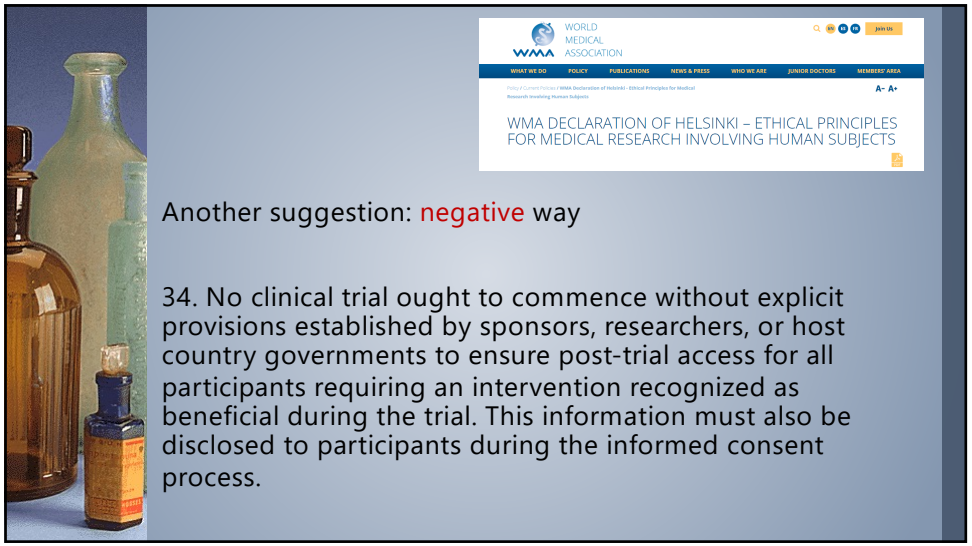
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Another suggestion: negative way
34. No clinical trial ought to commence without explicit provisions established by sponsors, researchers, or host country governments to ensure post-trial access for all participants requiring an intervention recognized as beneficial during the trial. This information must also be disclosed to participants during the informed consent process.

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Corollary
› No protocol should be approved for a country (or an area within the country) when an effective and necessary drug cannot be provided to research participants after the trial
› Ethics Review Committee

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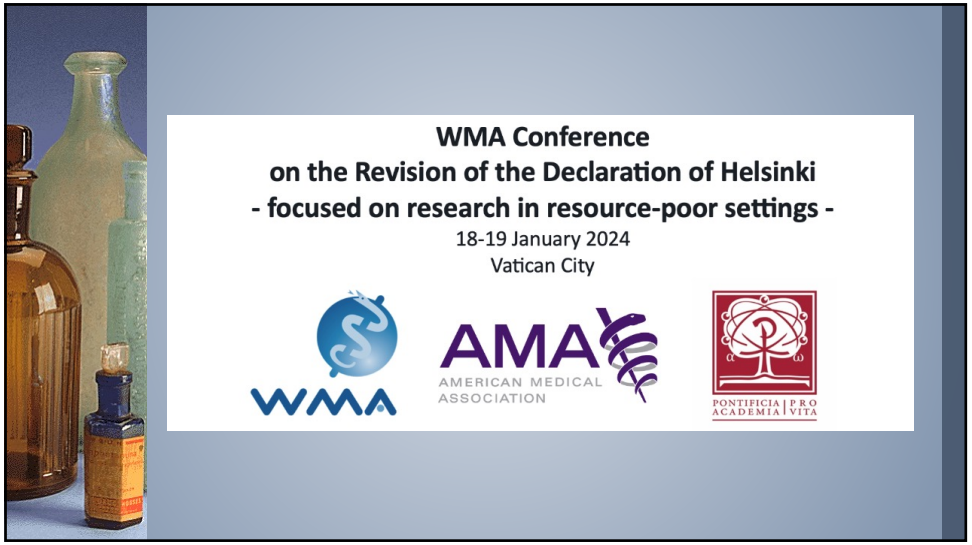
WMA Conference
on the Revision of the Declaration of Helsinki
- focused on research in resource-poor settings -
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