How do we know that a medicine is safe during pregnancy or breastfeeding?

Katie Bunge, M.D.

University of Pittsburgh School of Medicine

Magee-Womens Hospital of UPMC

Ensuring Safe HIV Prevention Methods for Pregnant and Breastfeeding Women

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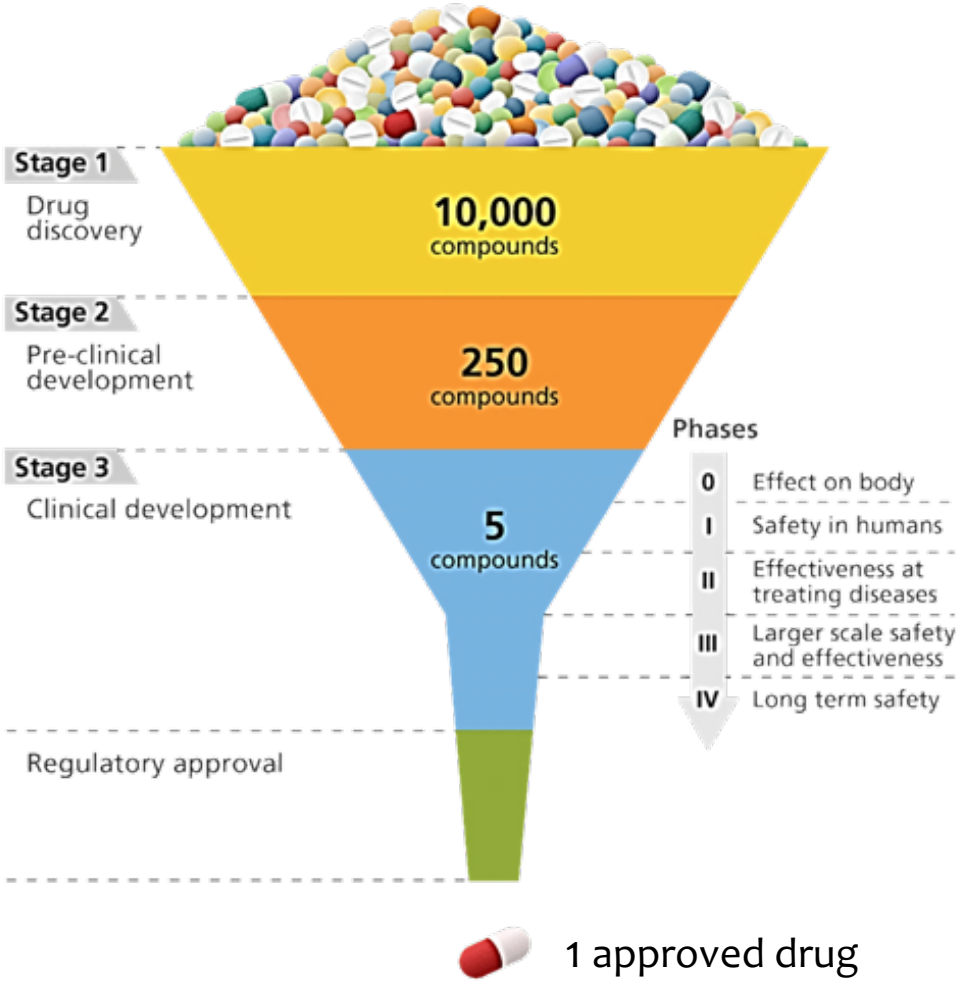
First, where do medicines come from?



- The answer is somewhat complicated
- The process begins with laboratory and animal studies, then studies in people – it can take 10 years or more
- Of 10,000 or so potential compounds, very few make it all the way through the process to become an approved drug

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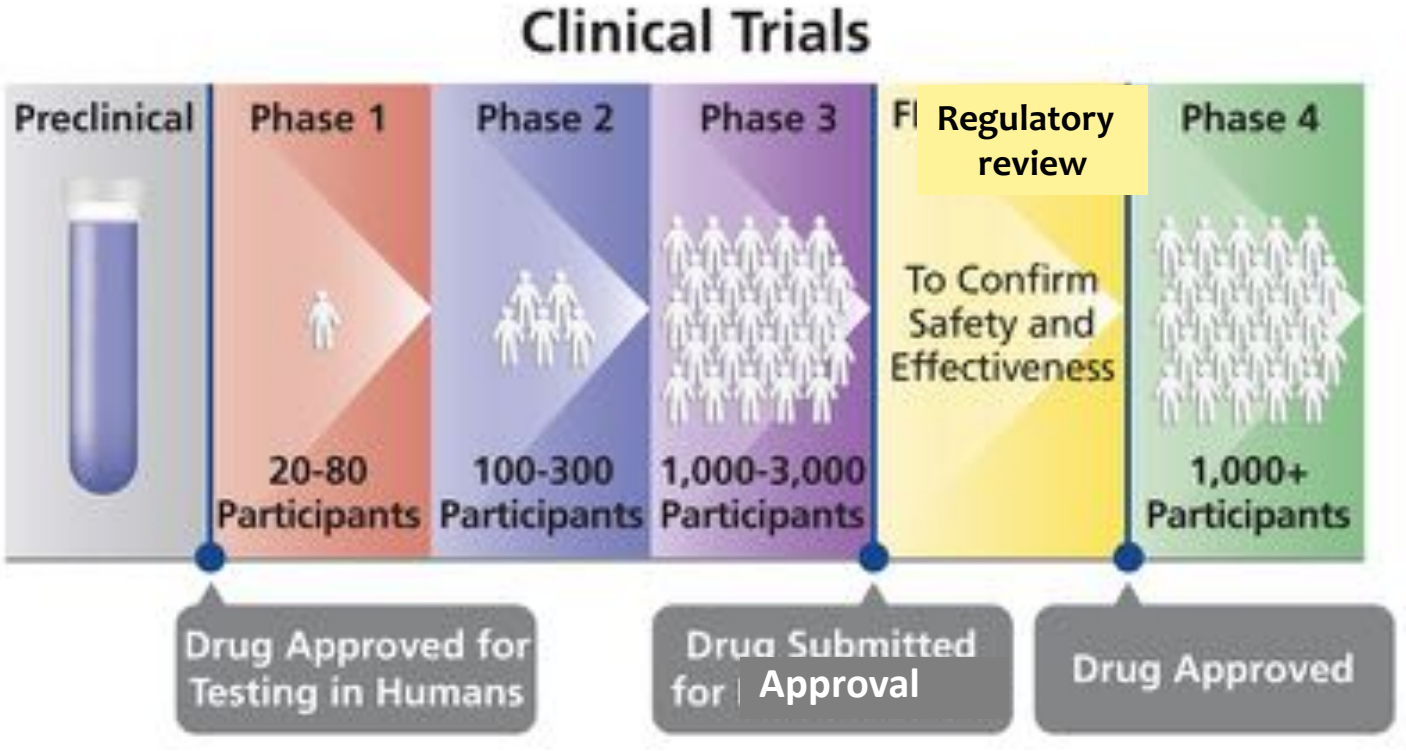
How is a drug determined to be safe and effective in people?

- First, Phase I studies look at safety in a very small number of people
- If there are no concerns, studies will be conducted in a larger number of people, with safety still a primary concern.
- Larger (Phase III) studies are conducted to determine whether the product works as it is intended to (effectiveness)



How do drugs get approved?

- If a drug is found to be safe and effective, the company that makes the drug will compile everything there is to know about that drug
  - Results of laboratory studies
  - Results of animal studies
  - Results of clinical studies in people
- A drug regulatory agency will decide whether or not to approve the drug based on its review of all this information.

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Can anyone take part in a clinical research study?

- Researchers are very particular about who can participate in a clinical trial
- Each study has its own rules about who can – or cannot participate – called eligibility criteria.
  - May be based on age, gender, medical condition, etc.
- Safety is the number one concern

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What about pregnant or breastfeeding women?

- Most clinical trials, particularly of new drugs, exclude pregnant and breastfeeding women.
- Women who enroll often must use contraception, and if fall pregnant, stop study product
- Why?
  - To protect the developing fetus or baby from potential harm

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The approval decision is based on data, but…

- If pregnant and breastfeeding women could not participate in any of the clinical trials, there won't be any information about the drug in these populations.
- There will be lots of information about these kinds of people….

- Because there were lots of people like them in the trials…
- And very few people, if any, like her….

Approval will not apply to pregnant and breastfeeding women

- This means that a drug that is approved will be "contraindicated" in women during pregnancy and breastfeeding
- Contraindicated means that the drug should not be used because there is concern that it may cause harm

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But what if a woman who is pregnant or breastfeeding needs medicine?

- Her care provider must make a decision ….

"Can I assume it will be safe and effective in women who ***ARE*** pregnant or breastfeeding…?"

"This is what I know about this drug in animals…"

"It was safe in women who were NOT pregnant or breastfeeding…"

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But what if a woman who is pregnant or breastfeeding needs medicine?

- What's the risk?
  - Don't know for certain the drug will be safe for the mom, or that it will work in the same way
  - Don't know for certain that the drug will be safe for the baby

(sound familiar?)

How do we know that a drug is safe during pregnancy and breastfeeding?

Two approaches:

1. Follow pregnancy outcomes after product is released via registries

2. Intentionally study the safety of these prevention products in pregnancy and breastfeeding

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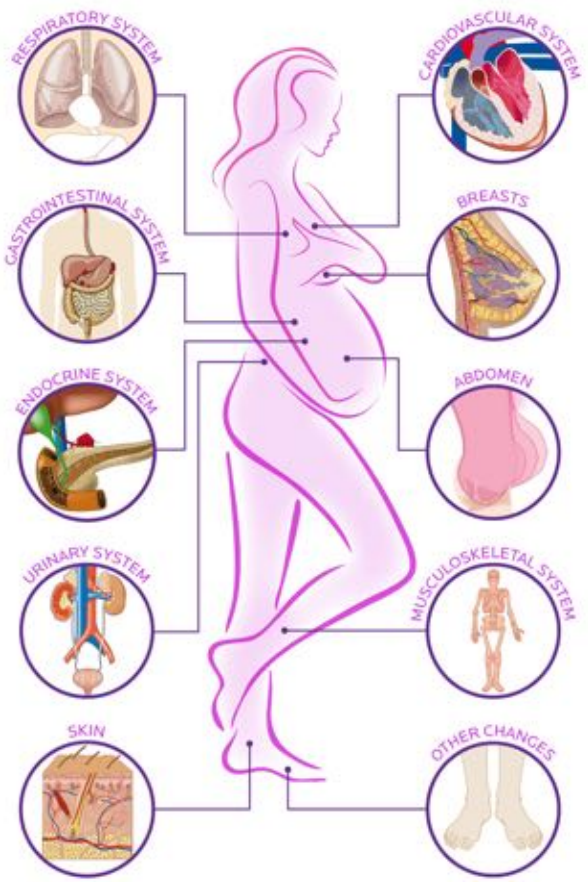
The story of antiretroviral (ARV) drugs

- Of 31 approved ARVs, it was on average 5 years AFTER approval before any pregnancy data was collected
  - No data in 3/7 drugs approved since 2010
- Big unknowns, particularly for newer drugs:
  - Does the drug get absorbed in the body of a pregnancy women in the same way?
  - Is the drug safe to use during pregnancy and breastfeeding?
  - Does the drug affect development of the baby (fetus) if taken during pregnancy?
  - Is it safe to use during breastfeeding?

Why we should study drugs in pregnancy rather than leave safety to chance



- The body undergoes many changes during pregnancy
- A drug may work differently in a woman who's pregnant
- It may pass to the placenta and cause harm to the developing fetus or put the pregnancy (mother/fetus) at risk
- Fear of unknown risks may cause women to forgo taking a medication that would benefit them and/or their fetus

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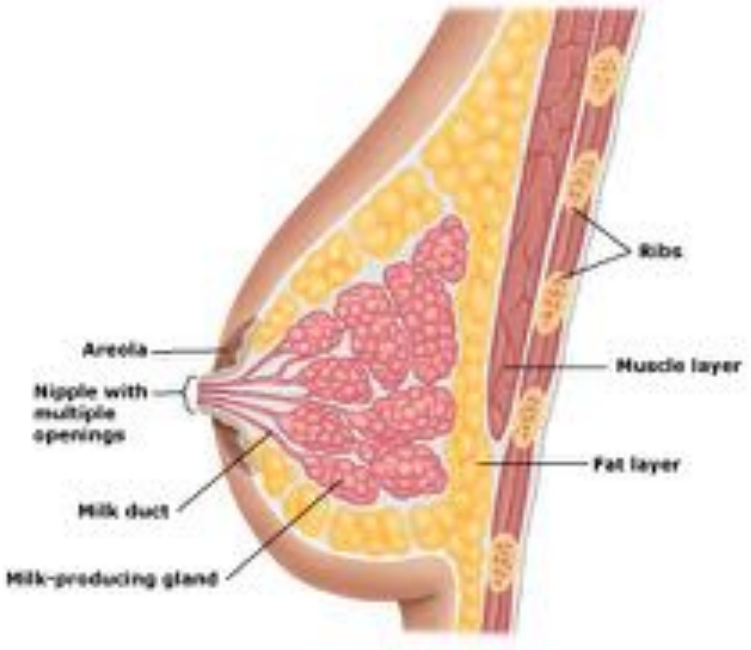
Why we should study drugs in breastfeeding women rather than leave safety to chance

- The body undergoes many changes during breastfeeding
- Certain drugs may or may not
  - Impact milk supply
  - pass into breastmilk
  - be orally absorbed by the infant
  - have adverse effects on the infant
- If risks of medication are unknown, some mothers may stop breastfeeding, potentially depriving infant of benefits of breast milk and introducing more risk to the infant than the drug would have



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Studying **treatment** drugs in pregnancy

- May be easier to justify <u>intentionally</u> exposing pregnant women to a study product because of therapeutic benefit

Starting with a population needing treatment

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The balance has shifted for **prevention**

- Unique challenge to PREVENTION trials in pregnancy

Starting with a healthy population

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What's the difference between learning about safety in a clinical trial vs in the real world?

- If there is a safety problem, in the real world there's potential to do harm to many more women and babies because there is less monitoring and many more women could be using the drug
- In a trial setting, study staff can closely monitor each woman and stop the drug if there is any suggestion of harm
- In the real world, there's not that kind of woman by woman control or oversight of what is happening to her and her pregnancy -- Potentially putting many more women and babies at risk

But what if a woman who is pregnant or breastfeeding needs medication?

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Summary

- Many experts and ethicists agree that pregnant and breastfeeding women deserve to be included in clinical trials of potentially beneficial drugs
  - Mothers benefit, Infants benefit, Clinicians benefit, Science benefits
- Women may be pregnant or breastfeeding for a significant portion of their lifespan
- Pregnancy and breastfeeding represent periods of high HIV risk
- Preventing HIV infection in the mother also protects the baby

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Questions?