Moving from an idea to a research question.

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Misericordia

Identifying the research question…

- It is important to have a clear question before starting to design your study
- This will allow you to make the most appropriate decisions surrounding:
  - The study population
  - The choice of study design
  - The method of collecting data
  - The primary outcome of interest
  - The main exposure/predictors of interest (if applicable)
  - The number of patients to be recruited

Identifying the question…example

QUESTION: Are we treating our HIV-infected patients adequately?

Is this a clearly defined question?

Identifying the question…example

QUESTION: Are we treating our HIV-infected patients adequately?

Think about three main factors:

- the **intervention / exposure**
- the **population**
- the **outcome**

Identifying the question…example

QUESTION: Are we treating our HIV-infected patients adequately?

The Intervention / exposure

How do we define ‘treatment’?

- HAART?
- PCP prophylaxis?
- General medical care?

Identifying the question…example

QUESTION: Are we treating our HIV-infected patients adequately?

The Population

How do we define 'HIV-infected'?

- Antibody positive?
- Symptomatic / AIDS?
- on ART / not on ART?

Identifying the question…example

QUESTION: Are we treating our HIV-infected patients adequately?

The outcome:

How do we define 'adequate'?

- Increase in CD4 count?
- Viral load suppression?
- Improvement in clinical outcome?
- Improvement in survival?
- Some other measure?

Identifying the question…example

QUESTION: Are we treating our HIV-infected patients adequately?

REVISED QUESTION: What proportion of patients starting antiretroviral therapy (ART) achieve viral load suppression at 12 months after starting first-line ART?

The research question should be…

- Clear
- Unambiguous
- Measurable
- Of clinical / biological relevance
- Realistic within the resource setting

DON'T BE TOO FOCUSED.

The more focused the less the answer will mean to the wider patient population

Keeping it real!!

- Study subjects should be representative of the population to which the results will be generalized - '*real world*'
- Inclusion criteria should be clearly stated in the study protocol
- Be careful of selection so the chosen sample represents the population of interest – don't put too many exclusions in place
- Consider excluding *important* confounders or groups at risk of harm
- Try to avoid excluding minority populations

What to do with your research question?

- Make sure it hasn't already been answered!!
  - Colleagues
  - PubMED / Google
- Design your research question
  - Hypothesis, hypothesis, hypothesis……
- Determine if you are able to answer the question
  - Do you have the resources?
  - Do you have the correct population?
  - Do you have the time?

What to do with your research question?

DESIGN THE RIGHT STUDY TO ANSWER YOUR QUESTION

Developing a research question…practice

Identifying the question…

QUESTION:

Do HIV-infected injecting drug users (IDU) have worse outcomes than non-IDU, HIV+ patients?

Is this a clearly defined question?

Identifying the question…

QUESTION:
Do HIV-infected injecting drug users (IDU) have worse outcomes than non-IDU, HIV+ patients?

Intervention

How do we define IDU?

Previous history of IDU - transmission risk?
Ever vs. ex-regular vs. ongoing IDU - ongoing risk?
Type of IDU – heroin / cocaine / met-amphetamine / methadone maintenance treatment (MMT)

Identifying the question…

QUESTION:

Do HIV-infected patients with ongoing injecting heroin or cocaine use have worse outcomes than HIV+ patients who are not injecting drug users?

Population

Can we further define the population?

- ART exposure – on ART / not on ART / ART naïve
- On MMT
- Viral hepatitis co-infection (RNA status)
- Adherence

Identifying the question…

QUESTION:

Do HIV-infected patients with ongoing injecting heroin or cocaine use (with or without viral hepatitis co-infection) who are on stable antiretroviral therapy with undetectable HIV RNA have worse outcomes than treated and suppressed HIV+ patients who are not injecting drug users?

Outcome

Can we better define the outcome?

- Morbidity
- Mortality
- Efficacy

Identifying the question…

QUESTION:

Do HIV-infected patients with ongoing injecting heroin or cocaine use (with or without viral hepatitis co-infection) who are on stable antiretroviral therapy with undetectable HIV RNA have worse outcomes than treated and suppressed HIV+ patients who are not injecting drug users?

Outcome

Can we better define the outcome?

Mortality
- All cause mortality
- AIDS-related mortality
- Liver failure

Identifying the question…

QUESTION:

Do HIV-infected patients with ongoing injecting heroin or cocaine use (with or without viral hepatitis co-infection) who are on stable antiretroviral therapy with undetectable HIV RNA have worse outcomes than treated and suppressed HIV+ patients who are not injecting drug users?

Outcome

Can we better define the outcome?

Morbidity
- Disease progression
- Liver failure
- Hospital admissions

Identifying the question…

QUESTION:

Do HIV-infected patients with ongoing injecting heroin or cocaine use (with or without viral hepatitis co-infection) who are on stable antiretroviral therapy with undetectable HIV RNA have worse outcomes than treated and suppressed HIV+ patients who are not injecting drug users?

Outcome

Can we better define the outcome?

Efficacy - CD4 responses
- HIV RNA levels

Which study fits the question?

QUESTION:

Do HIV-infected patients with ongoing injecting heroin or cocaine use (with or without viral hepatitis co-infection) who are on stable antiretroviral therapy with undetectable HIV RNA have higher all-cause mortality than treated and suppressed HIV+ patients who are not injecting drug users?

Prospective cohort

Retrospective cohort

Which study fits the question?

QUESTION:

Do HIV-infected patients with ongoing injecting heroin or cocaine use (with or without viral hepatitis co-infection) who are on stable antiretroviral therapy with undetectable HIV RNA have higher all-cause mortality than treated and suppressed HIV+ patients who are not injecting drug users?

Prospective cohort

- endpoints relatively few
- large study
- long-term follow up
- expensive – who will fund?

Retrospective cohort

Which study fits the question?

QUESTION:

Do HIV-infected patients with ongoing injecting heroin or cocaine use (with or without viral hepatitis co-infection) who are on stable antiretroviral therapy with undetectable HIV RNA have higher all-cause mortality than treated and suppressed HIV+ patients who are not injecting drug users?

Prospective cohort

Retrospective cohort - cheapest design
- easiest to do
- prone to multiple bias
- missing data

Research questions and hypotheses:

QUESTION:

Do HIV-infected patients with ongoing injecting heroin or cocaine use (with or without viral hepatitis co-infection) who are on stable antiretroviral therapy with undetectable HIV RNA have higher all-cause mortality than treated and suppressed HIV+ patients who are not injecting drug users?

The research question then defines the hypothesis:

'HIV-infected patients with ongoing injecting heroin or cocaine use (with or without viral hepatitis co-infection) who are on stable antiretroviral therapy with undetectable HIV RNA will have higher all-cause mortality than treated and suppressed HIV+ patients who are not injecting drug users.'

Research questions and hypotheses:

START study

'..among asymptomatic participants with a CD4+ count greater than 500 cells/mm3, immediate use of ART that results in suppression of HIV RNA levels and increases in CD4+ cell counts and potentially other beneficial effects will delay the development of AIDS, non-AIDS, and death from any cause.'*

Research questions and hypotheses:

ALTAIR study

'In treatment-naïve HIV-infected subjects, combination antiretroviral therapy including efavirenz combined with tenofovir and emtricitabine will offer non-inferior antiretroviral efficacy over 48 weeks, compared to either atazanavir boosted with ritonavir combined with tenofovir and emtricitabine or tenofovir and emtricitabine combined with zidovudine and abacavir, as assessed by change from baseline plasma HIV-1 RNA viral load.'

Topics for this year

- Co-infections / Co-morbidities
- Long term management
- Cascade of care
- Diagnosis and initiation of treatment

Organisation of working groups : Monday

- Select one topic within the main orientation of the group for further development (60 minutes*)
- Develop topic into a formal research question (30 minutes*)
- Discuss pros and cons of different study designs (30 minutes*)

* For guidance only

Organisation of working groups : Tuesday

- Prepare protocol (120 minutes*)
  - Identify the appropriate study population
  - Identify and define the key outcomes
  - Define the intervention (or key exposure variables)
  - Identify potential confounders (if applicable)
  - Determine approach for enrolling and following study subjects

* For guidance only

Organisation of working groups : Thursday

- Sample size and other statistical issues
- Prepare presentation
  - 1 presenter for each subgroup

* For guidance only