Psychopharmacology and Somatic Treatment in MDE and the Medically Ill

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Declaration - conflict of interest

None

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Learning objectives

- Appreciate how medical illnesses can impact and add to the complexity of biological treatments for depression.
- Develop an approach to psychopharmacology when treating depression in patients with (multiple) medical comorbidities.
- Identify considerations for medically ill patients who might receive somatic treatments, ie. neurostimulation.

Depression in medically ill

- Depression rates likely doubled in those with chronic medical illness
- Increasing rates with multiple comorbities
- Rates of MDD in …
  - Cancer 10-20%
  - HIV 25-40%
  - COPD 20-30%
  - Autoimmune disorders 10-30%
  - Neurological disease 20-40%
- Depressive symptoms can interfere with behaviours that improve physical health
- Reduced medication adherence, attendance of medical appointments, reduced physical activity …

Rosenblat, 2019

Case

45 year-old man who was referred for depression.

Past medical history of chronic HIV infection, stroke 2018, atrial fibrillation, hyperlipidemia, diabetes, GERD, COPD.

Medications include: elvitegravir/cobicistat/tenofovir/emtricitabine, dabigatran, metoprolol, metformin, rosuvastatin, pantoprazole, and budesonide inhaler.

No substance use.

Presentation and history consistent with Major Depressive Disorder.

Would like to start on antidepressants – what do you have to consider?

Starting with guidelines

The Canadian Journal of Psychiatry /
La Revue Canadienne de Psychiatrie
1-21

DOI: 10.1177/0706743716659417
TheCJP.ca | LaRCP.ca
SAGE

Canadian Network for Mood and Anxiety Treatments (CANMAT) 2016 Clinical Guidelines for the Management of Adults with Major Depressive Disorder: Section 3. Pharmacological Treatments

Sidney H. Kennedy, MD[1*], Raymond W. Lam, MD[2*], Roger S. McIntyre, MD[1], S. Valérie Tourjman, MD[3], Venkat Bhat, MD[4], Pierre Blier, MD, PhD[5], Mehrul Hasnain, MD[6], Fabrice Jollant, MD, PhD[4], Anthony J. Levitt, MD[1], Glenda M. MacQueen, MD, PhD[7], Shane J. McInerney, MB, MSc[1], Diane McIntosh, MD[2], Roumen V. Milev, MD, PhD[8], Daniel J. Müller, MD, PhD[1], Sagar V. Parikh, MD[1,9], Norma L. Pearson, BSc (Pharm)[10], Arun V. Ravindran, MB, PhD[1], Rudolf Uher, MB, PhD[11], and the CANMAT Depression Work Group[12]

"limited evidence to guide antidepressant choice in the management of MDD with comorbid conditions".

Kennedy, 2018

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Using a systematic approach

Questions to ponder on…

1. Psychiatric symptoms caused or exacerbated by medical illness?
   - HIV related neuropsychiatric symptoms
   - Post stroke depression

2. Neuropsychiatric side effects of medical treatment?
   - Metoprolol adding to fatigue and CNS depressant effect

3. Does psychotropic in consideration affect the medical illness?
   - Which neuroleptic should one use to augment treatment in patients with metabolic disorders already?

4. Does medical illness affect the way the medication goes through the body?
   - Are there any absorption, distribution, metabolism, or excretion issues altered by the medical disease?

Ferrando, S, Levenson J, 2011

Questions to ponder…

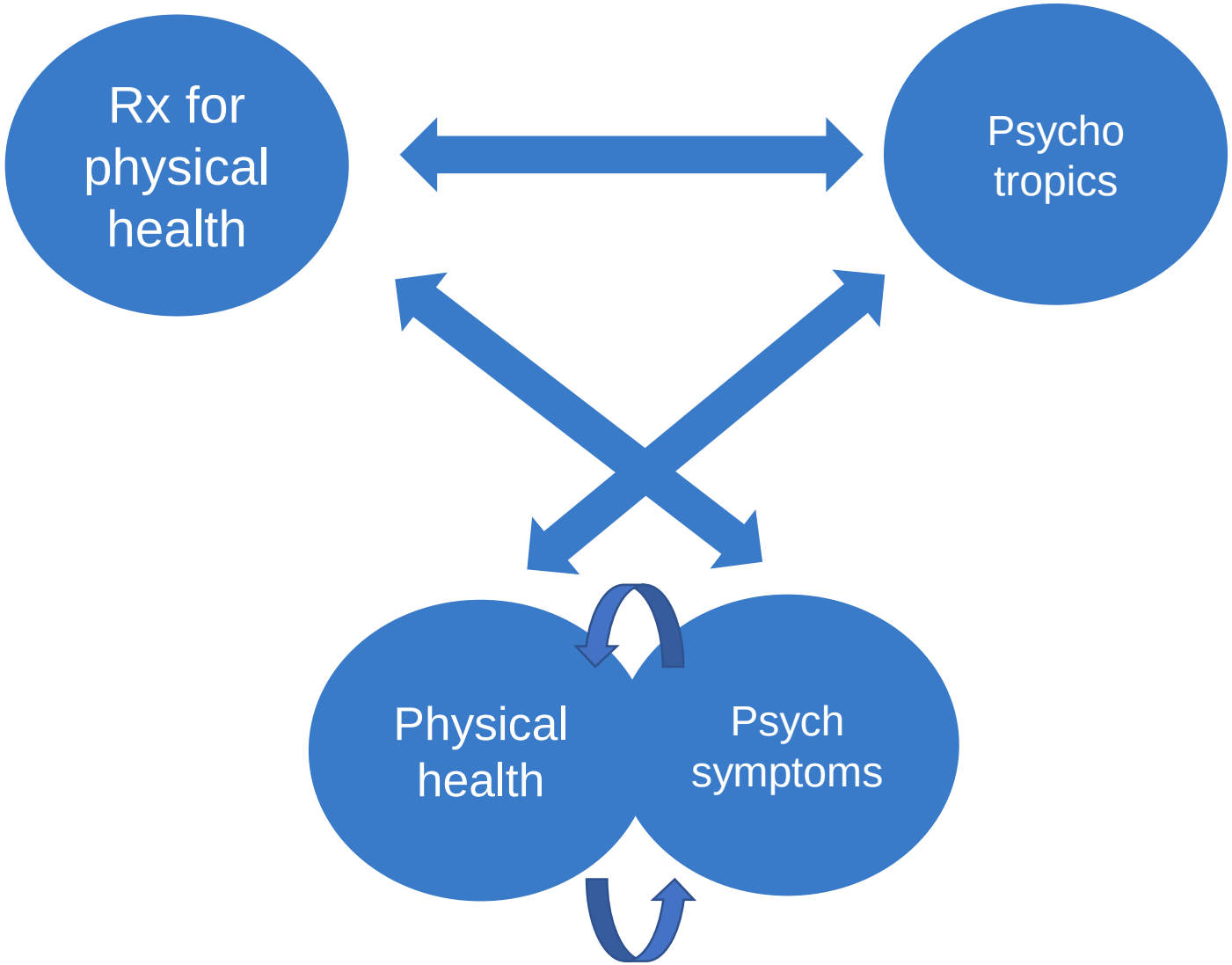
5. Does medical illness increase likelihood of psychotropic adverse effects?
   - If I add antipsychotics as adjunct- can HIV infection increase risk of movement disorder side effects?

6. Drug drug interactions?
   - How does cobicistat inhibit metabolism of antidepressants?

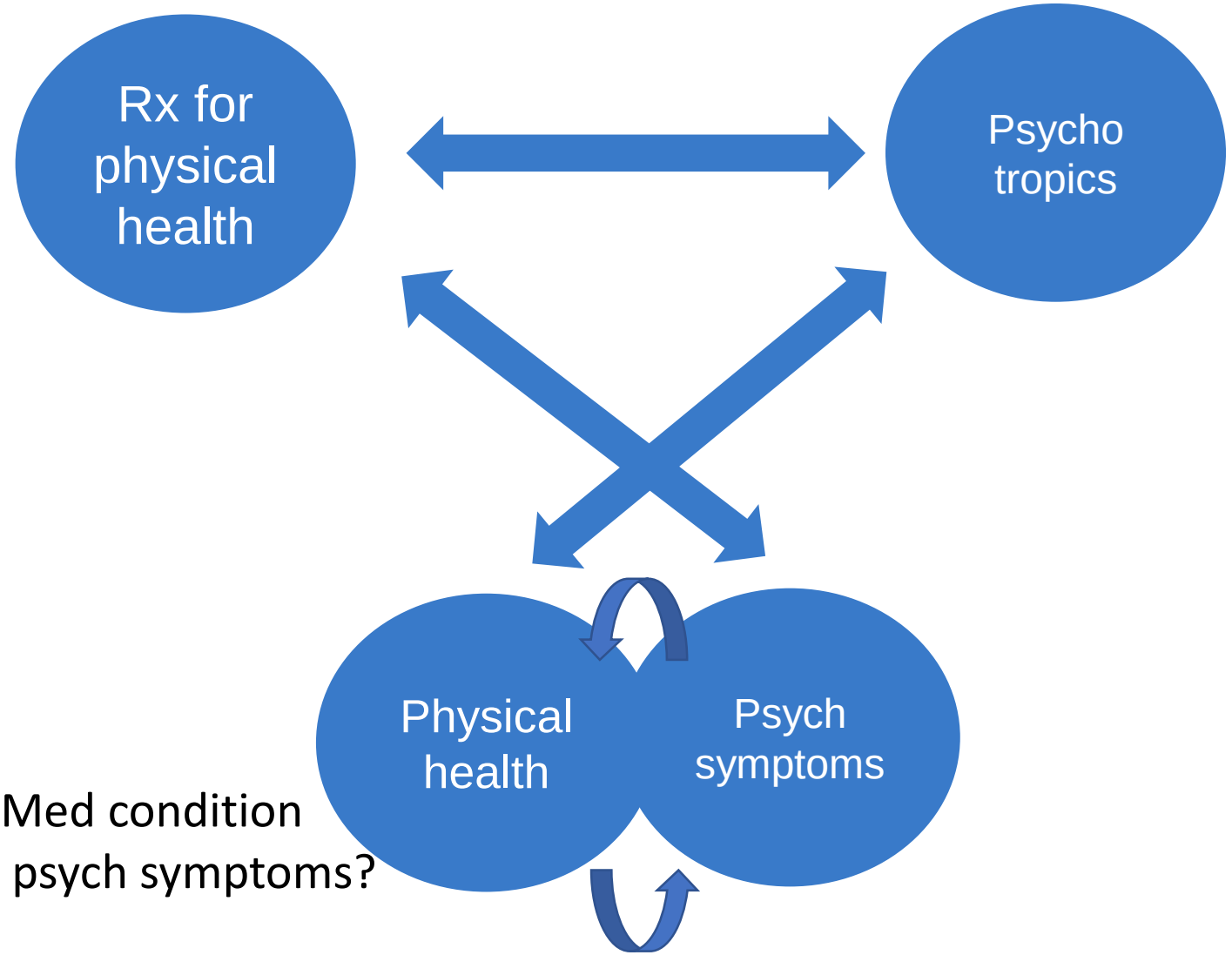
7. Evidence for psychotropics in medical-psychiatric presentation?
   - What is evidence for post stroke depression treatment, HIV depression treatment?

Ferrando, S, Levenson J, 2011

Mapping medical and psychiatric interactions



Mapping medical and psychiatric interactions



1. Med condition
→ psych symptoms?

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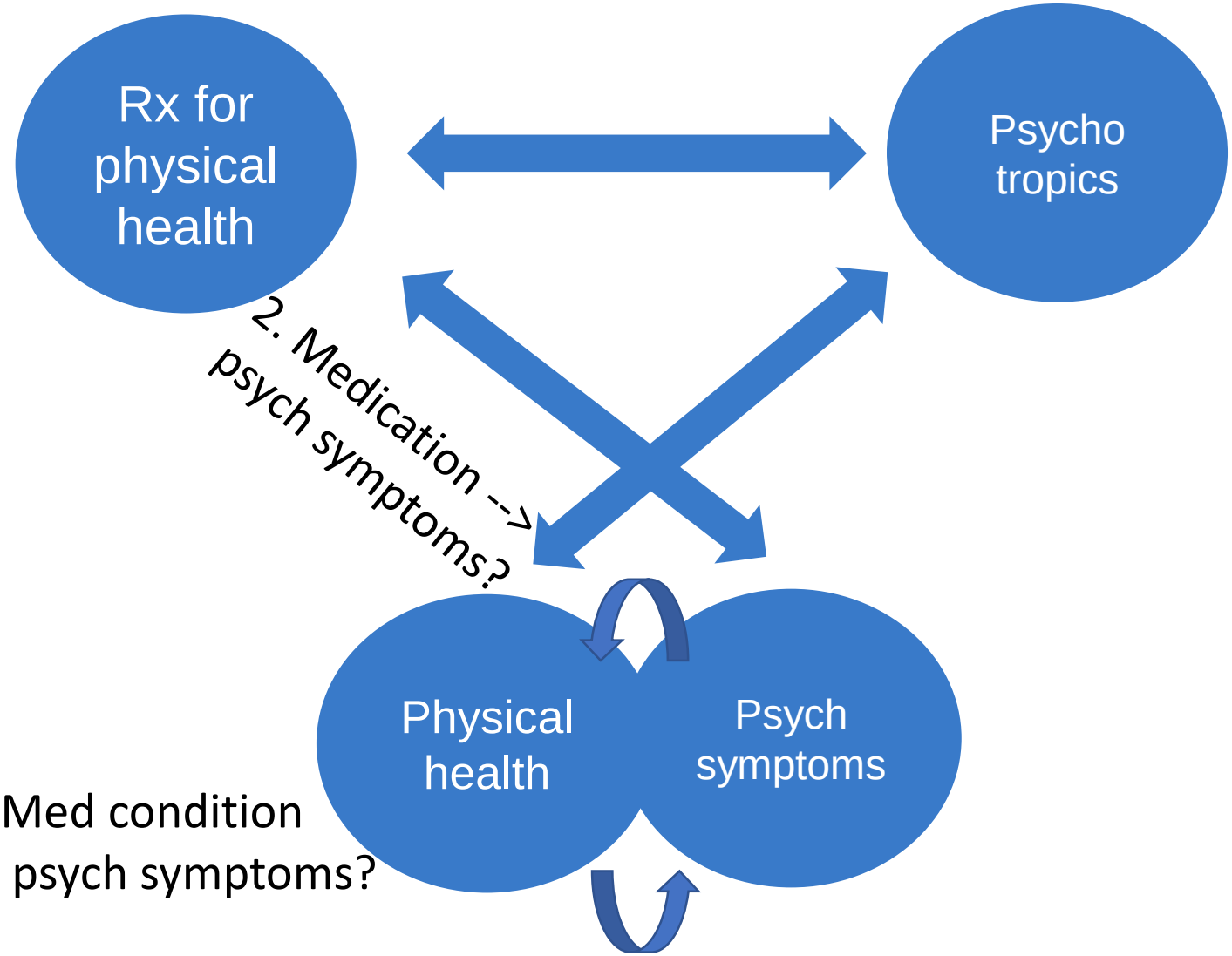
Mapping medical and psychiatric interactions



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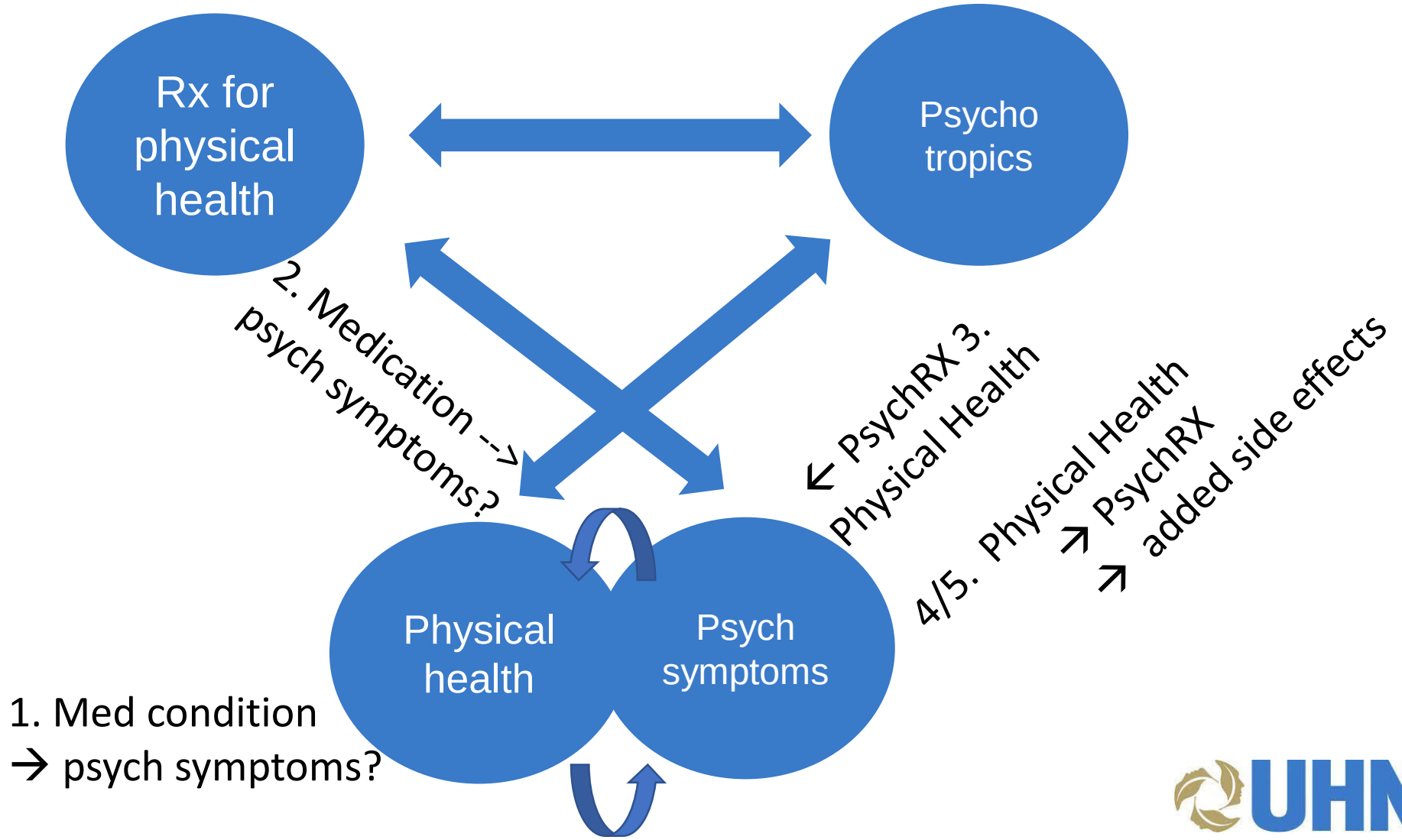

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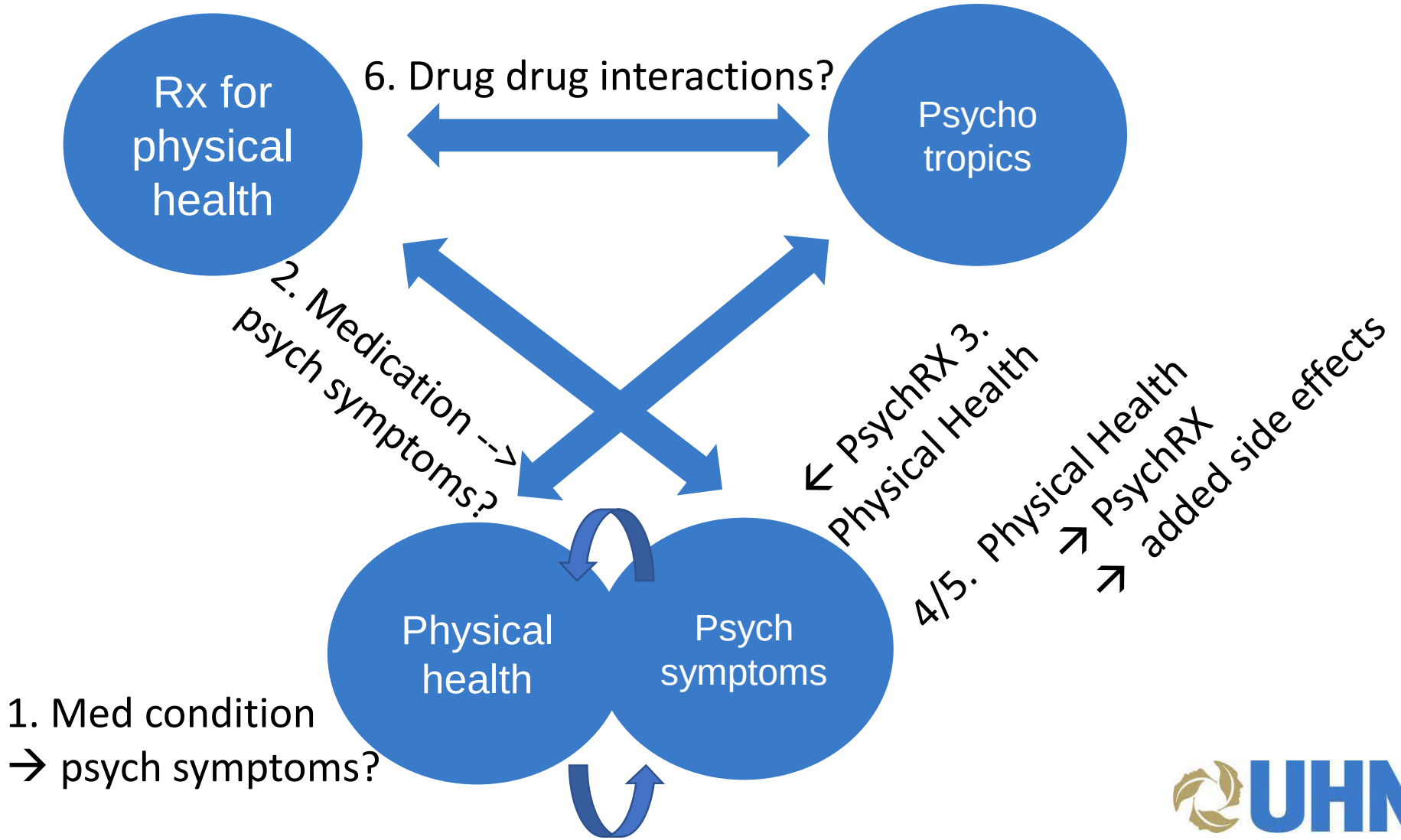

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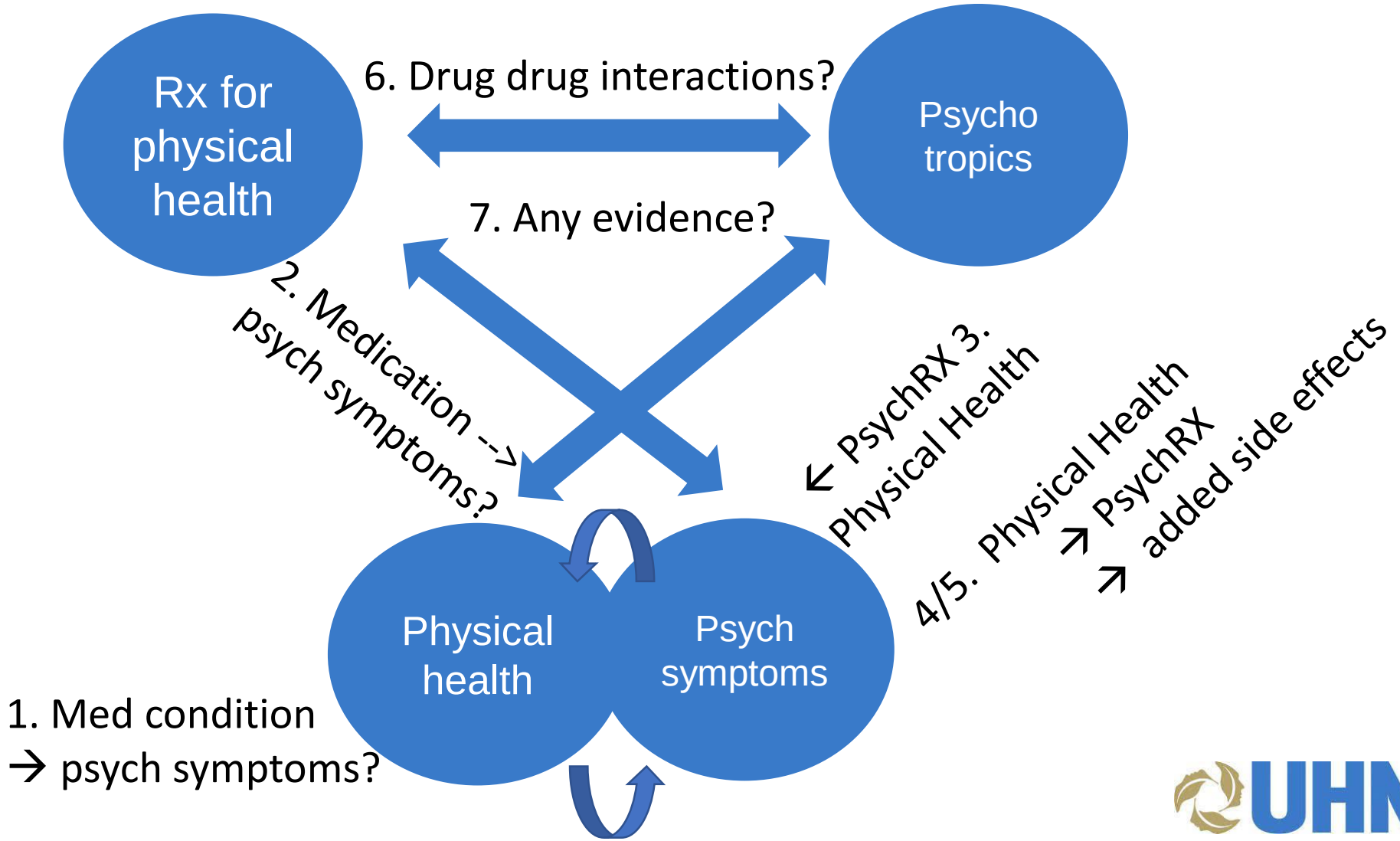

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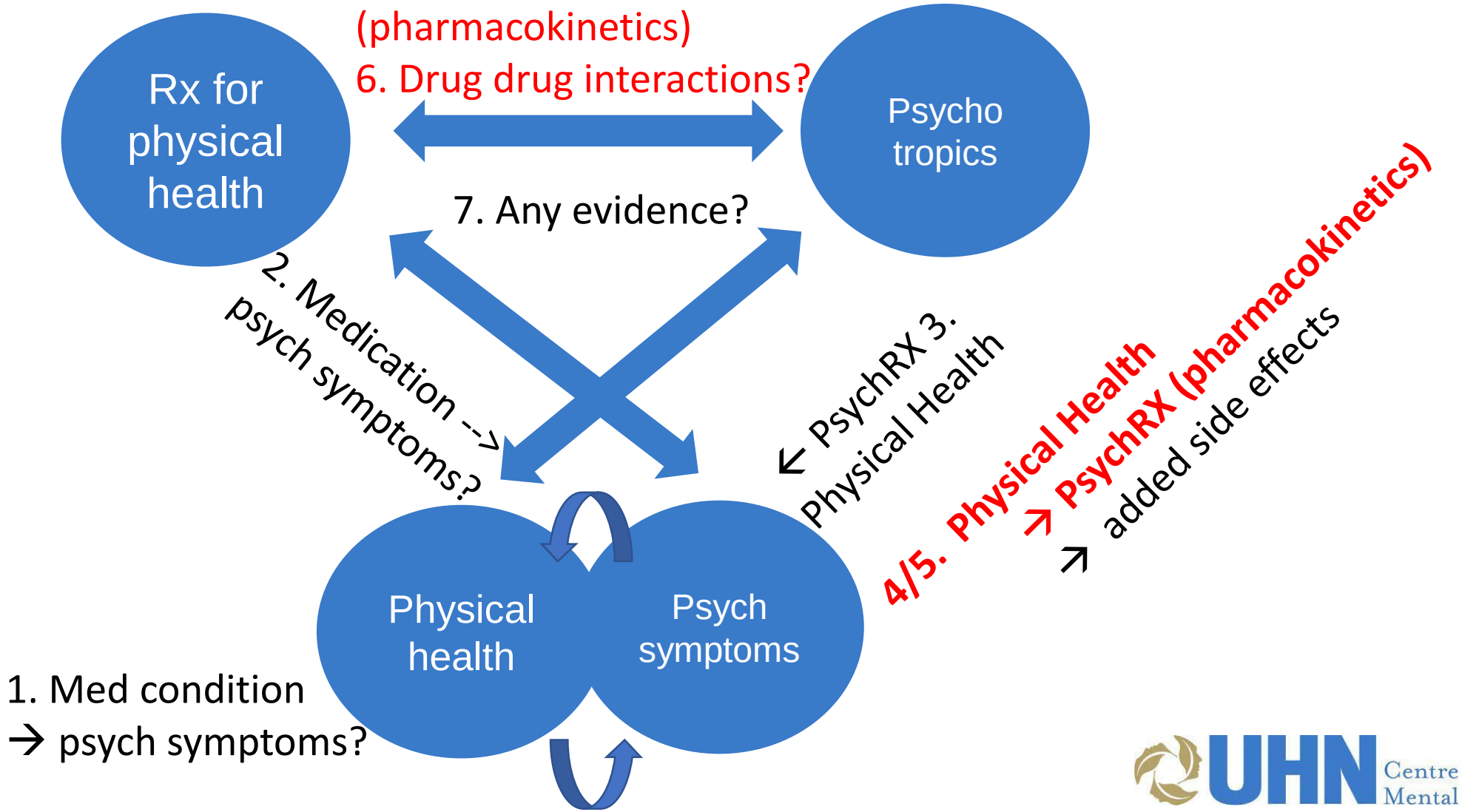

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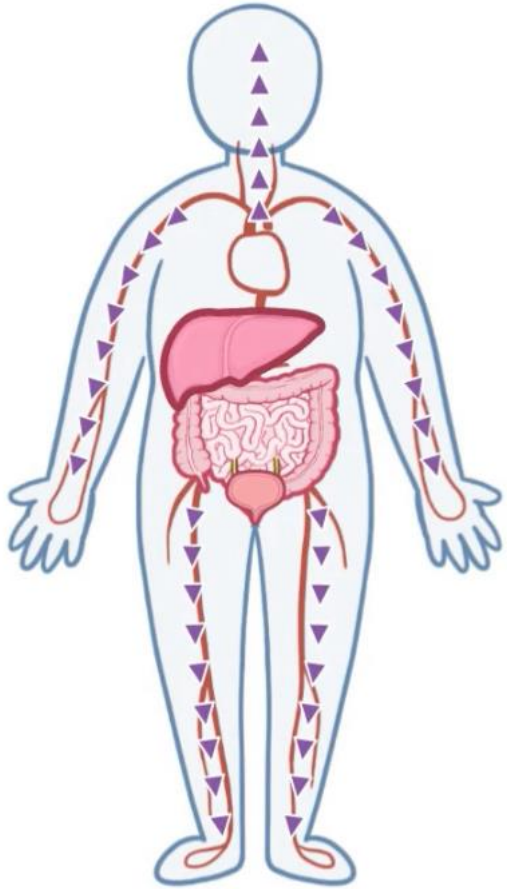
Pharmacokinetics

- Absorption
- Distribution
- Metabolism
    - Drug interactions
- Excretion



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Absorption

- Difficulties swallowing can affect what patients can take for medications –
  - eg. consideration of liquid forms of ssri's (fluoxetine, venlafaxine)
  - or oral disintegrating tablets(mirtazapine)
- NG Tubes – some medications can become clogged – eg. venlafaxine
- Patients with shorter guts (bariatric surgery) might not be able to absorb extended-release formulations
- Delayed emptying (due to eg cannabis + opiates) or increased emptying (metoclopramide) can change absorption

Stern, 2017.

Distribution

- Lithium is likely most affected by volume changes – water soluble
  - Watch for pregnancy states, heart failure, ascities, renal dysfunction
- Some medications are protein-bound with the free-fraction (unbound) being the active component
  - There is generally some homeostasis between bound ←→ unbound

Stern, 2017.

Metabolism

- Most drugs go through some metabolism
- Patients with end stage liver failure may require dose adjustments
- Most drug-drug interactions occur this way through CYP enzymes
- Watching for inducers and inhibitors
- Use a drug-drug interaction app

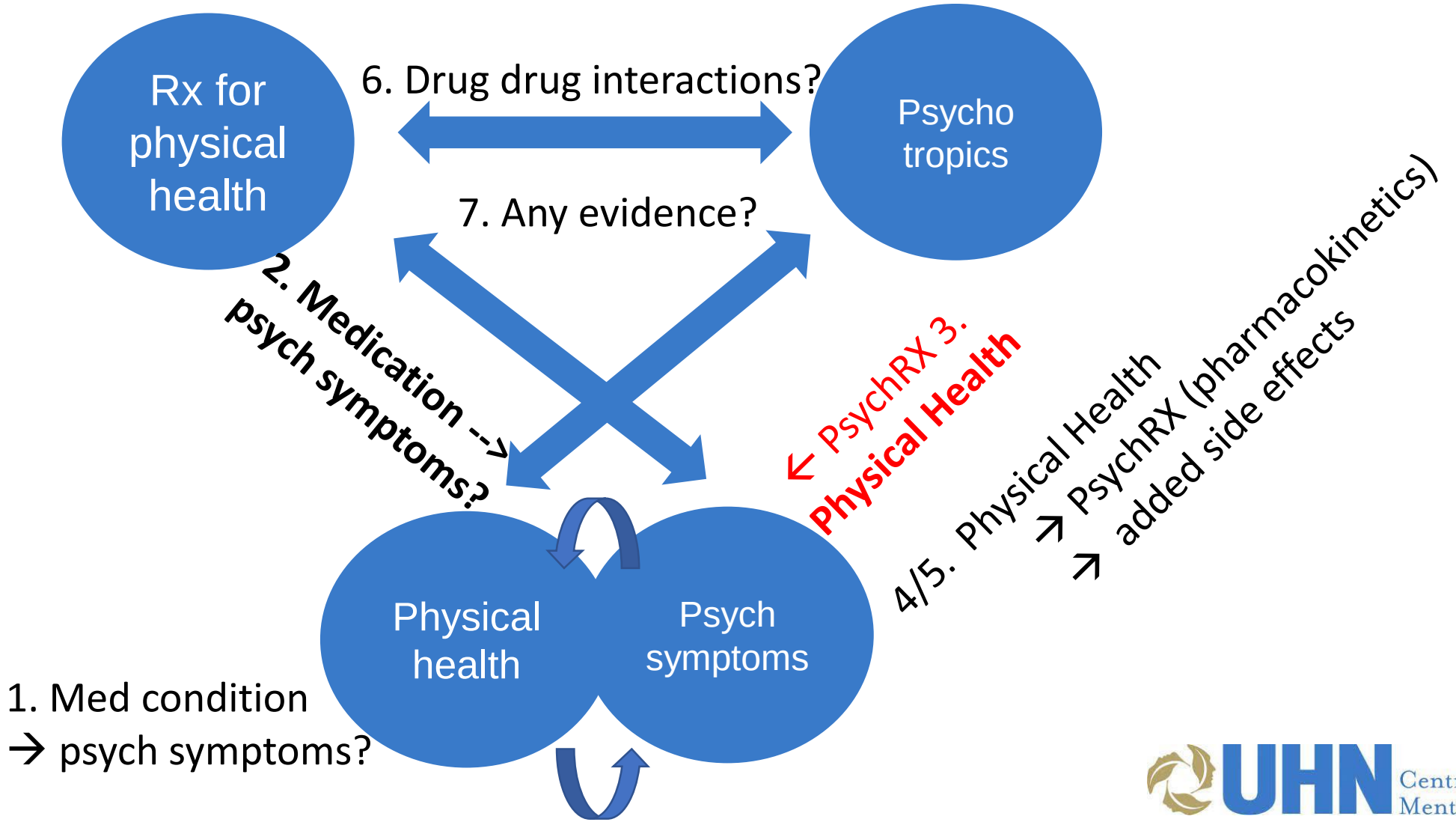
Stern, 2017.

Excretion

- Most psychotropics go through hepatic metabolism so renal excretion is less impactful aside from lithium
- Patients with end stage renal function may require dose adjustments based on creatinine clearance, a measure of kidney function

Stern, 2017.

Mapping medical and psychiatric interactions



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Pharmacodynamics – drug's actions on body

- Psychotropic medications are "dirty" – actions on multiple receptors

To list a few:

- Additive burden of anticholinergic and hypotensive side effects
- Impacts of psychotropics on cognition and existing cognitive complaints
- Effects on dopamine from psychotropics on dopamine deficient disorders
- Changes to QT interval by affecting ion channels
- Added respiratory depression with benzodiazepines

Guiding principles

- Accurate diagnosis and identification of target symptoms
- Use treatment guidelines to consider steps in pharmacological treatment and use specific evidence based recommendations if available
- Have a systematic approach in considering psychotropics in medically complex patients
- Use the lowest dose that provides effect and simplest regimen accounting for pill burden
- Discussions and liaison with other providers
- Be attentive to side effects of both medical treatment and psychotropic agents
- Check for drug interactions with an up-to-date app – eg. Lexicomp

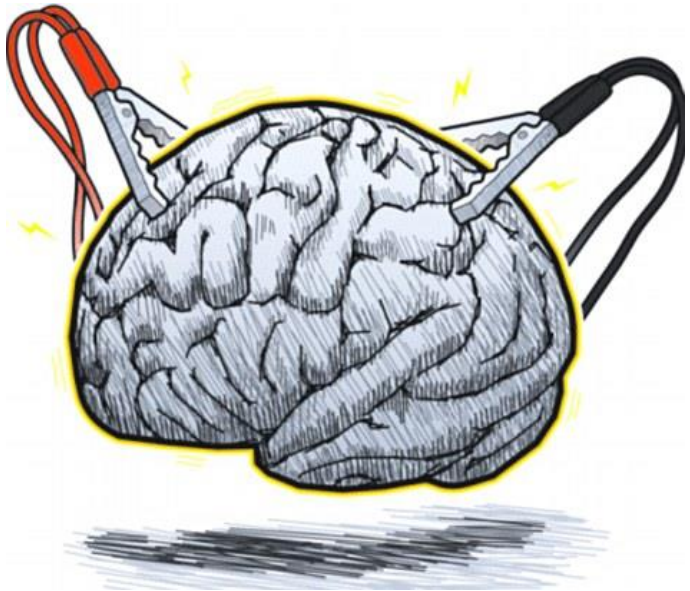
Back to the case…

Ongoing depressive symptoms and despite pharmacological treatment.

What would you consider?

Somatic treatments

- RTMS
- ECT



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ECT for medically ill

- No absolute contraindications
- Exercise caution if – recent ACS or stroke, unstable fracture/dislocation, intracranial lesion with mass effect
- Largest risk associated with general anesthetic and so anesthesia consult when multiple medical issues
- Evidence also in those with movement disorder to help with movement symptoms – eg Parkinson's and Huntington's

Stern, 2017

RTMS for medically ill

- Uses magnetic fields to stimulate specific cortical areas
- Benefit of not using general anesthetic
- Absolute contraindications are for those with metallic implants in area of stimulations (brain stimulators, medication pumps, cochlear implants), and cardiac pace-makers.
- Main safety risk involves potential for seizure induction ~ 1 /30 000
  - Similar in ratio to antidepressant treatment overall
  - Patients need to be screened for epilepsy and and fmhx of such
- Other physical side effects to consider include:
  - Headaches, vasovagal syncope, tinnitus

Stern, 2017

In summary

Medically ill patients are at higher risk of developing major depression.

A systematic approach can increase a clinician's confidence when presin identifying considerations for interplay between physical health states, psychiatric symptoms, psychotropics, and non-psychiatric medications.

Medical comorbidities should not deter one from considering somatic treatments if indicated for treatment of depression.

Discussion/questions

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