Common PCP questions along the LTBI care cascade

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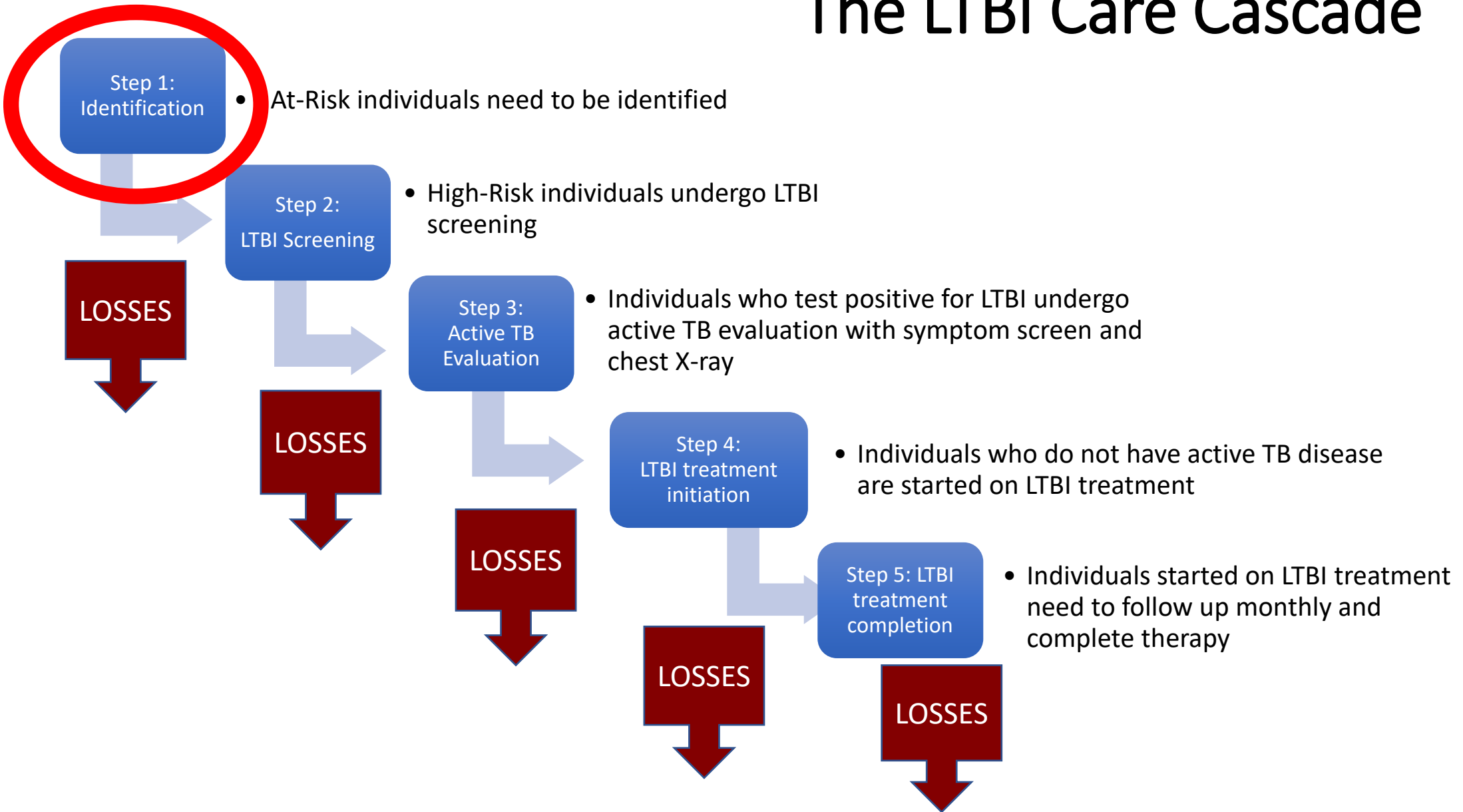
Learning Objectives

- Describe the components of the LTBI care cascade
- Consider the most common LTBI questions in primary care that come up throughout the cascade and how to address them
- Identify an individual who can help answer other LTBI questions quickly so that care can continue in primary care

The LTBI Care Cascade



Check appropriate risk factor boxes below.

Latent TB infection testing is recommended if any of the 3 boxes below is checked.

If latent TB infection test result is positive and active TB disease is ruled out, treatment of latent TB infection is recommended.

REPORT Latent TB Infection and Active or Suspected Active TB Disease

Go to www.mass.gov/tuberculosis for reporting forms

☐ **Born or lived in** a country with an elevated TB rate

- Includes any country other than the United States, Canada, Australia, New Zealand, or a country in western or northern Europe.
- If resources require prioritization within this group, prioritize patients with at least one medical risk for progression (see User Guide for list).
- Interferon Gamma Release Assay (IGRA) is preferred over Tuberculin Skin Test (TST) for foreign-born persons ≥2 years old. The TST is an acceptable test for all ages when administered and read correctly.

☐ **Immunosuppression**, current or planned

HIV infection, organ transplant recipient; treated with TNF-alpha antagonist (e.g., infliximab, etanercept, others), steroids (equivalent of prednisone ≥15 mg/day for ≥1 month) or other immunosuppressive medication

☐ **Close contact** to someone sick with infectious TB disease *since last TB Risk Assessment*

Just remember…Screen if patient is from a country other than…

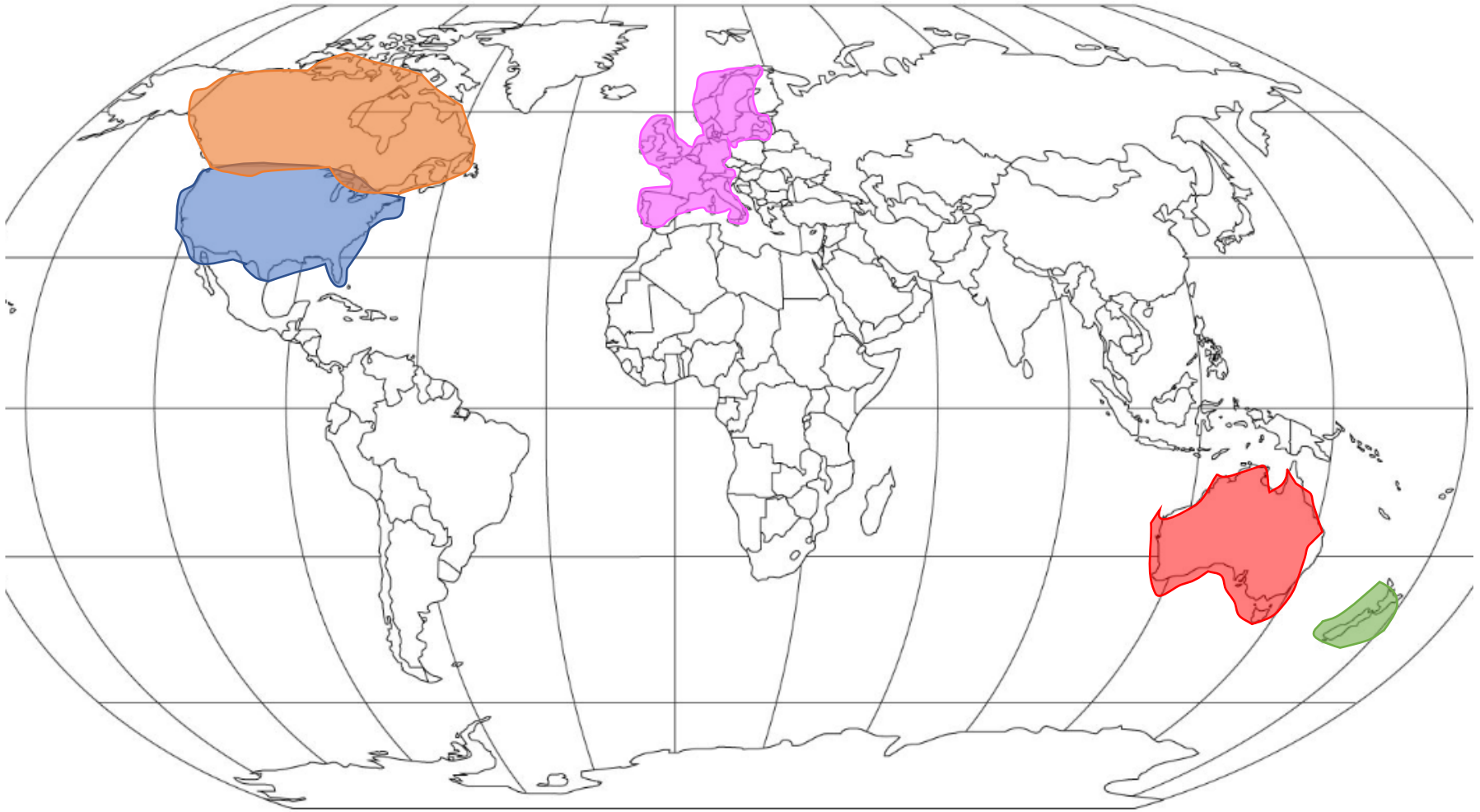
US

Canada

Australia

New Zealand

Western and Northern Europe



But what about….

- A patient who immigrated from Puerto Rico 20 years ago?
- A six month old refugee who moved to the US from Afghanistan with family 2 months ago
- A medical student who worked in a rural hospital in Kenya for a year
- A 50 year old who visits family each year in Liberia for two months

A Decision to Test, is a Decision to Think….

- What is the risk of exposure to TB infection?
  - Consider risks such as family members who have had TB, where was the patient living while in a TB endemic region etc.
- What is the risk of TB disease progression?
  - Consider factors that increase risk of progression to TB disease such as immunocompromised state, age. Don’t forget the risk to others if patient progresses to TB disease (i.e medical student)
- What is the post-test probability – in other words, if the test is positive in your patient, how likely is it that they have TB infection?
  - Consider factors that may impact the specificity or sensitivity of your tests (BCG vaccination, immunosuppression)

Context matters for all scenarios below….

- A patient who immigrated from Puerto Rico 20 years ago?
- A six month old refugee who moved to the US from Afghanistan with family 2 months ago
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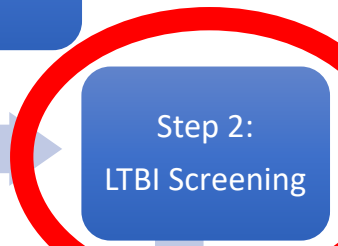
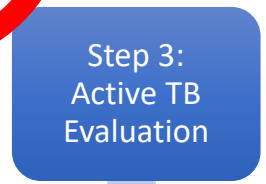
The LTBI Care Cascade

- At-Risk individuals need to be identified



- High-Risk individuals undergo LTBI screening



- Individuals who test positive for LTBI undergo active TB evaluation with symptom screen and chest X-ray

- Individuals who do not have active TB disease are started on LTBI treatment

- Individuals started on LTBI treatment need to follow up monthly and complete therapy

TB Infection Testing Interpretation

- Neither PPD or IGRAs differentiates b/w latent TB infection or active TB disease
- Neither is used to follow response to treatment
- After TB infection both may remain + for life

But what about…

- A low risk patient who was screened for work and has a positive TST?
- An 8 month old from Afghanistan with a 15mm TST?
- A patient who will start a biologic medication and has had two indeterminate IGRAs?

Consider an alternate test?

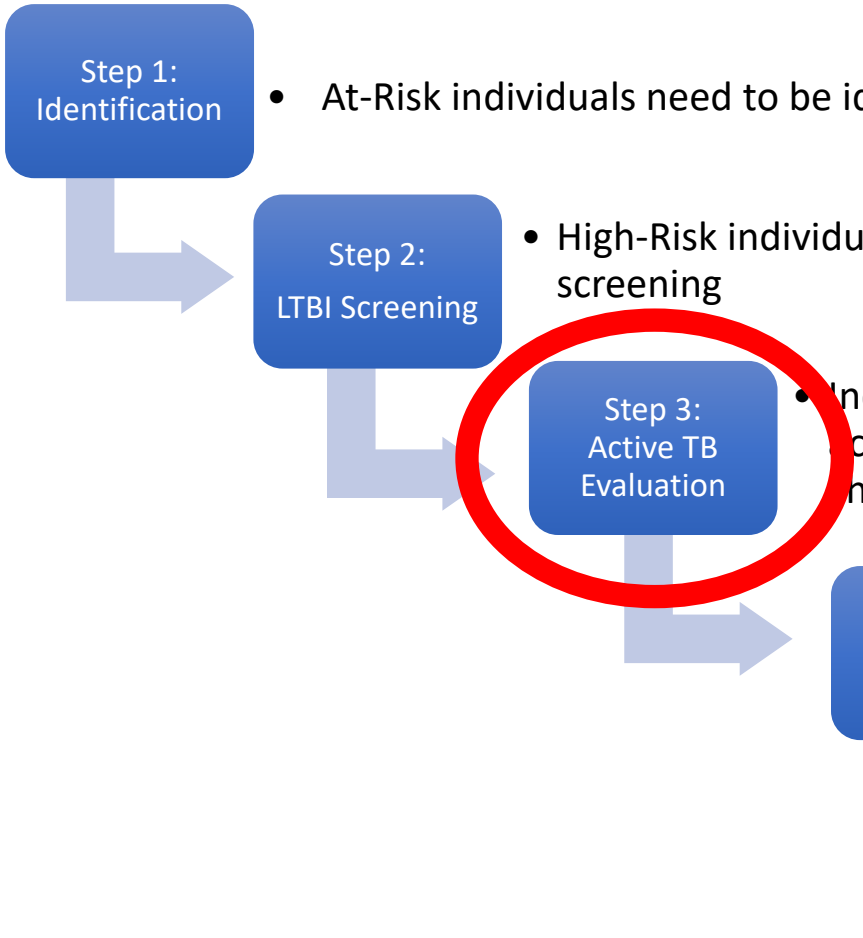
- A decision to test is a decision to think!
  - Will it change your management? (e.g. perhaps the low risk patient works in a NICU, if the IGRA is positive in an 8 month old you may go ahead and treat, if the TST is negative in the person starting a biologic you may not treat)

- Context matters – again risk of exposure, risk of progression, risk of disease transmission to others

TB infection testing interpretation, Context matters!

- + PPD, - IGRA test
  - 8 yr old healthy girl from Brazil, PPD 10mm, IGRA neg
  - 60 yr old female from Brazil, uncontrolled DM and CKD, PPD 10mm, IGRA neg
  - 60 yr female from Brazil, PPD 0mm 2 yrs ago, now a contact of an active smear + case, current PPD 10mm, IGRA neg
  - 8 yr old healthy girl from Kenya, PPD 30mm, IGRA neg
  - 40 yr healthy male from Russia, PPD 10mm, IGRA neg, works in a neonatal ICU

The LTBI Care Cascade



- At-Risk individuals need to be identified
- High-Risk individuals undergo LTBI screening
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Evaluation Recap

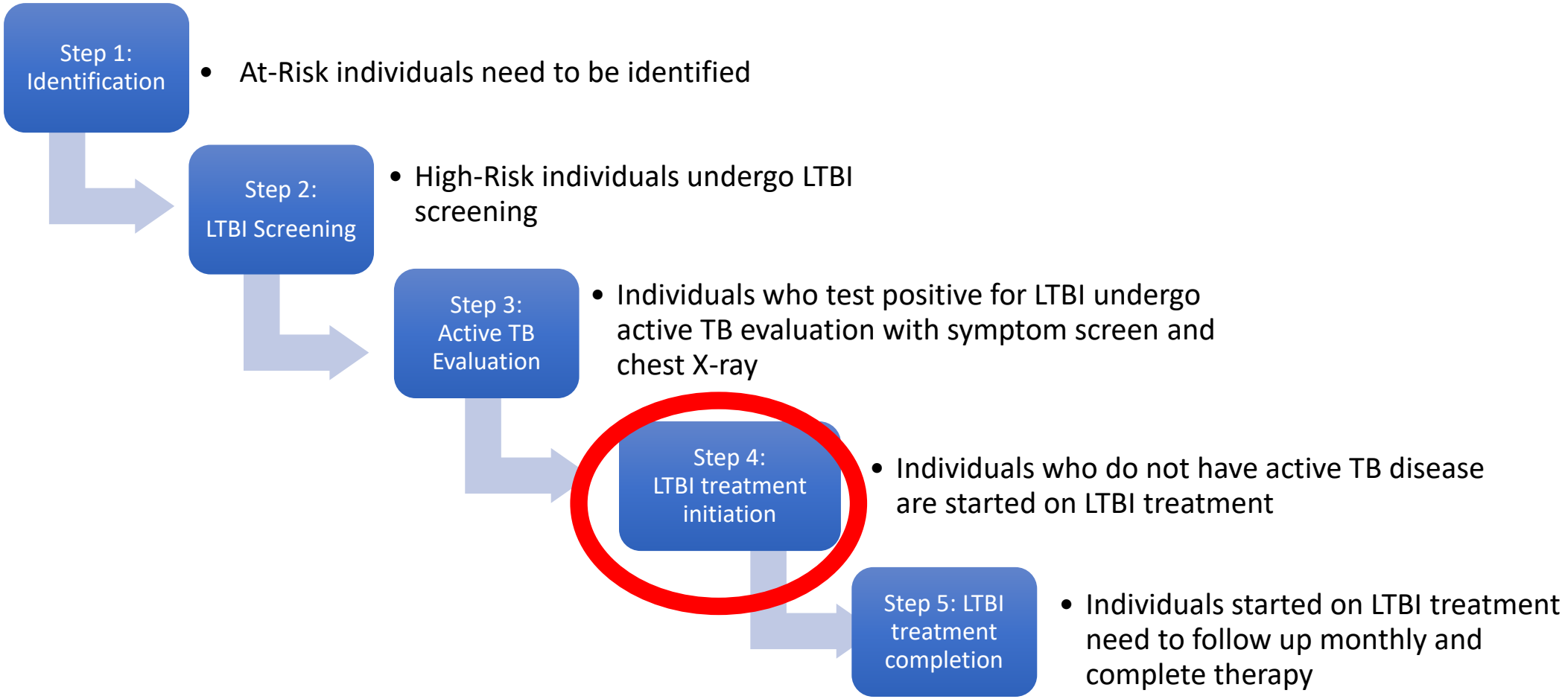
- History and physical examination are key
  - Don’t forget to ask questions and perform physical exam to look for extrapulmonary disease!

- X-ray recap
  - In adults, one single PA view is sufficient
  - In children, two views needed!
  - Need chest x-ray within 2 months of starting treatment

But what about….

- An abnormal X-ray with evidence of ? Old TB disease or hilar lymphadenopathy
  - Remember, our specialists are always there for us. An abnormal X-ray usually always warrants a discussion with a specialist!
- A 6 month old X-ray
  - Repeat it!
- History and PE suggestive of an abnormality that may or may not be TB (e.g. persistent unilateral adenopathy, fatigue, chronic cough without other symptoms)
  - TB infection treatment is not an emergency! As PCPs we are experts in working up non-specific complaints. Take the time to feel good about finding another diagnosis prior to initiating LTBI treatment

The LTBI Care Cascade



Treatment Regimens for LTBI

Drugs, dose	Dosing frequency	Duration
Rifampin 600 mg (4R)	**Daily**	**4 months**
Isoniazid 300 mg (6-9H)	**Daily**	**6-9 months **9 months preferred**
Isoniazid 900 mg + Rifapentine 900 mg (3HP)	**Once weekly**	**3 months**

But what about…

- Those nitrosamines!
- prescribing 3HP as self- administered?
- those kids who just won’t swallow the medication??

N-nitrosamines, Cancer Risk and TB Medications

- Everyone is exposed to N-nitrosamines in every day life
  - Drinking water, foods (grilled or cured meats, dairy products, and veggies), tobacco exposure and some latex and rubber products
  - There are multiple N-n with varying mutagenic potential
  - In 2018, health authorities starting looking at medications for N-n contamination
    - API, drug synthesis products, cross contamination, recovery processes for solvents or drug degradation
- Acceptable Intake (AI) = daily exposure approximates a cancer risk of 1:100,000 after 70 years of exposure; regulatory bodies have set minimum daily intake limits to remain under this break point
- Present levels of N-n in 4R would be between 1 and 12 months of exposure
- Pharmaceutical companies are working to continue to reduce N-n in all Rifampin compounds and must monitor all batches for specific contamination levels

Suggested Scripts for Nitrosamine Counseling

“Nitrosamines are chemicals that with cumulative exposure can increase risk of cancer. They are found in foods such as smoked meats, liquids such as beer or some water supplies, tobacco and some latex products. The FDA has found the level of nitrosamines in rifampin may be above the accepted limit; the company is working on reducing this level. With this careful oversight, CDC and FDA recommend that rifampin remain available for use due to the importance of treating TB. Taking rifampin for 4 months to treat LTBI is a very small contribution to the total amount of nitrosamine we are exposed to in daily life.

If low risk....“It is important for you to choose what feels best for your body. If the risk of rifampin does not feel right to you and you would prefer not to take INH – a longer regimen, we can revisit this discussion in a year or two to see if the company can reduce further the risk”

If high risk.... “You have several risk factors that make you at higher risk for progressing from your TB infection to TB disease, making you both ill and possibly spreading this infection to others. The benefits of treatment for your TB infection likely outweighs the risk of rifampin at this time. I would recommend that you choose a regimen that you are comfortable with and receive treatment as soon as possible”

Isoniazid + Rifapentine

- Isoniazid 900 mg p.o. + rifapentine 900 mg p.o. weekly x 3 months
- DOT (Directly Observed Therapy)
- Not approved in:
  - Children <2 years of age
  - Individuals with presumed infection with INH- or RIF-resistant TB
  - Pregnant people
  - PLHIV

Update of Recommendations for Use of Once-Weekly Isoniazid-Rifapentine Regimen to Treat Latent *Mycobacterium tuberculosis* Infection

Weekly / June 29, 2018 / 67(25);723–726

Andrey S. Borisov, MD[1]; Sapna Bamrah Morris, MD[1]; Gibril J. Njie, MPH[1]; Carla A. Winston, PhD[1]; Deron Burton, MD[1]; Stefan Goldberg, MD[1]; Rachel Yelk Woodruff, MPH[1]; Leeanna Allen, MPH[1]; Philip LoBue, MD[1]; Andrew Vernon, MD[1]
(View author affiliations)

Initiate treatment at the “right” time

- Treatment of LTBI is NOT an emergency (except in very advanced HIV and in the very young, exposed or infected, non BCG-vaccinated children)
- Emphasis must be on shared decision making
- Patient centered care includes a discussion with the patient about life circumstances and willingness to be treated
  - Example:
    - Patient found to have LTBI but she was 6 months away form completing her hormonal therapy for breast cancer
    - Patient found to have LTBI but in the midst of a work up for a colon mass that is going to require surgical resection
    - Patient with LTBI who had a miscarriage at 12 weeks and is in the midst of grieving her pregnancy loss
    - In all of these patients, we together decided to delay treatment. In Patient #1, she returned and completed 4 months of R. In Patient #2, he has recovered from his surgery and started R 4 weeks post op. In patient #3, she returned 2 months later ready to engage in treatment.

Medication administration

- RIF capsules can be broken and powder sprinkled and mixed with foods
- RIF syrup (preferred) or INH syrup for exclusively breastfed infants
- Crushed pills can be mixed with food (don’t let the kid see)
  - Pudding
  - Chocolate syrup
  - Nutella
  - Applesauce
  - Yogurt
  - Double-Stuffed Oreo

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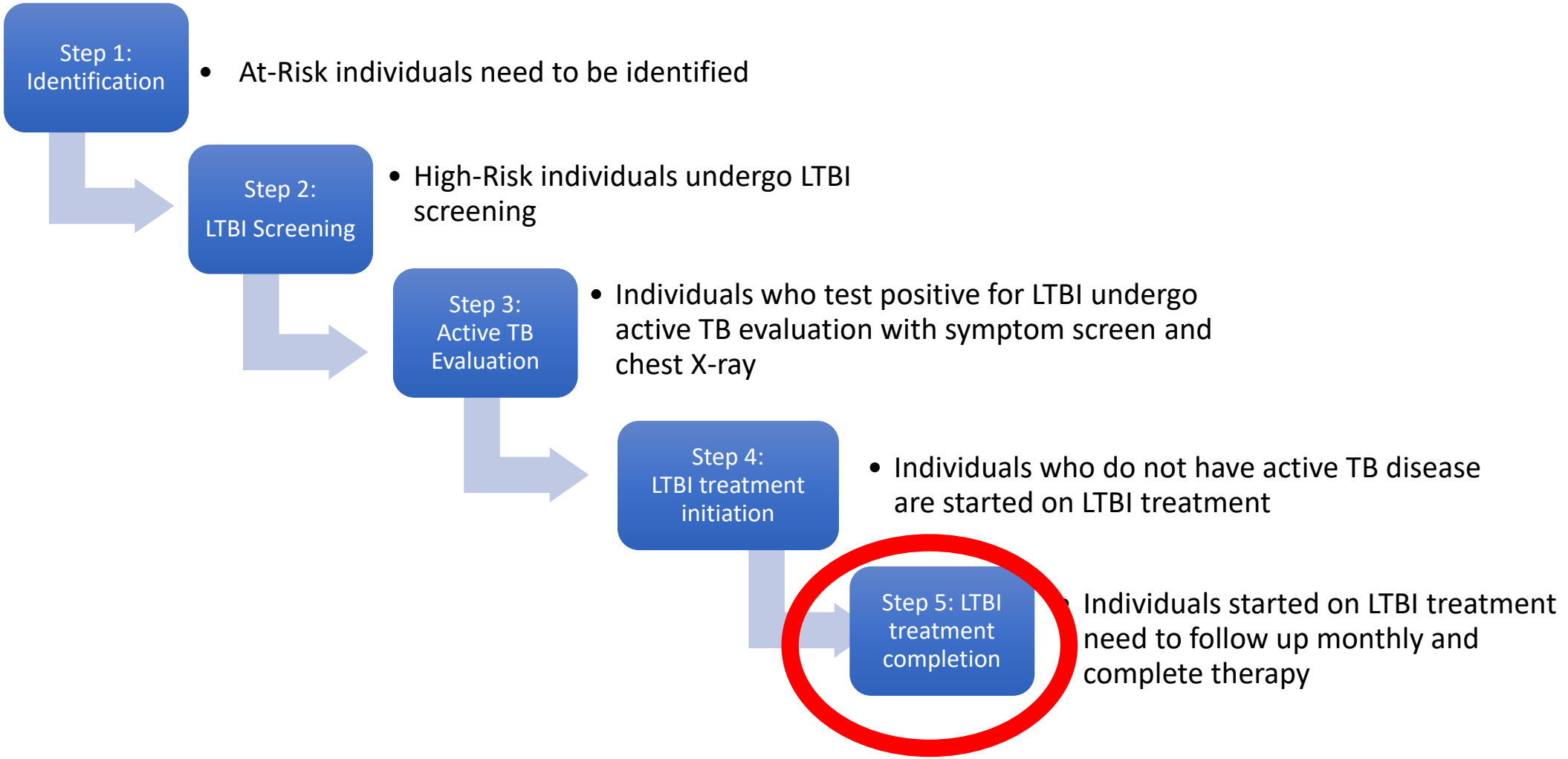

Monitoring of patients on treatment for LTBI

- **Baseline laboratory testing *not needed* except for:**
  - HIV infection
  - Pregnancy
  - History of liver disease/heavy alcohol use
  - Patient on chemotherapy

- **Evaluate monthly for:**
  - Adherence
  - Signs/symptoms of adverse reactions
  - Laboratory studies in persons at-risk (LFT, CBC)
    - If following LFTs: stop treatment if LFTs >3 times upper limit + symptoms OR if LFTs >5 times upper limit + no symptoms

But what about….

- My patient had baseline LFTs done by another provider and I felt obligated to continue checking monthly. Now they are elevated 3 times at month 3! When do I repeat?
  - If asymptomatic, could repeat in 2 weeks to see if stable. Likely would repeat one additional time and then ensure that patient knows to stop medication if any symptoms develop
  - If LFTs are continuing to increase, can call specialist for further guidance

Stop - Start Rules
(How much LFT abnormality can I tolerate?)

- Remember the risk of hepatotoxicity increases with age and with dosing above the recommended weight based guidelines
- The “Stop and Start” rules for monitoring for hepatotoxicity were all developed around both **AST(SGOT) and symptom screens**
- Approximately 1/3 of patients in the first two months of treatment with INH will have mild elevations in their transaminases so intensive blood screening will find this. Not clear how much this happens with Rifampin
- Any elevation in association with symptoms of hepatoxicity should cause the LTBI medications to be stopped (nausea, vomiting, abdominal pain)
- Treatment is halted for > 5x baseline even if asymptomatic
- When transaminases are elevated, a query regarding other hepatotoxins is indicated (Tylenol, ETOH, other viral infections - Hep A?)
- CDC and Massachusetts DPH recommend no blood monitoring but rather symptom screening unless the patient has concomitant risk for hepatotoxicity

Who are these ‘TB specialists’???
How do I find them???