Outcomes of Urinary Tract Infection Management by Pharmacists (R_xOUTMAP) Investigators Meeting

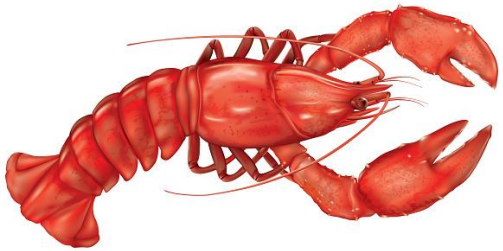
June 11, 2017

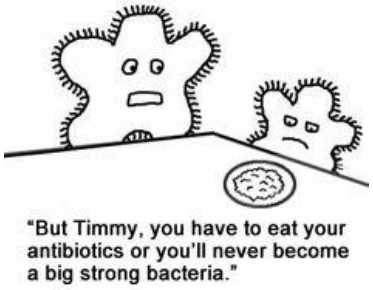
Overview

1. Introductions and Opening Remarks
2. Epidemiology and Definitions
3. UTI Assessment and Management
4. R_xOUTMAP Study Protocol and Processes
5. Database (REDCap) Overview and Walkthrough
6. Reimbursement
7. Contacts
8. Questions

Objectives

- **Understand the principles of assessment of urinary tract infection (UTI).**
- **Review the appropriate management of UTI.**
- **Familiarize with the processes of the R_xOUTMAP study.**





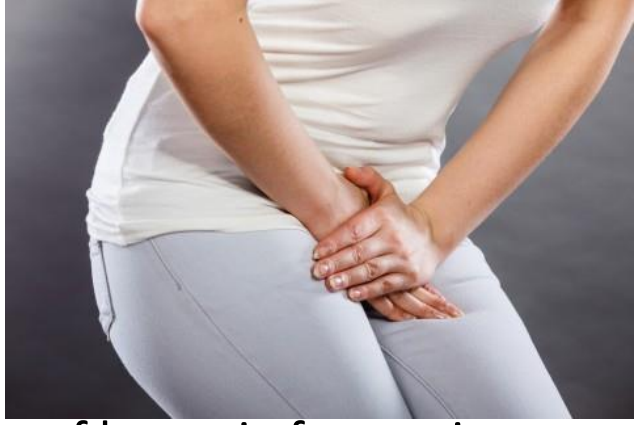
Epidemiology

- Urinary tract infection (UTI) is 8th most common for ambulatory clinic visits and 5th most common reason for emergency department visits in Canada

- Incidence in ♀ ≈ 12% annually
  50% of ♀ report to have had UTI by age 32
  Significantly less common in ♂
  Incidence increases with age (as does asymptomatic bacteriuria)

- Recurrence occurs in 25% of ♀ within 6 months of 1st UTI
  - Increases when > 1 prior UTI experienced

Urinary Tract Infection (UTI)



- Bacterial infection of urinary tract

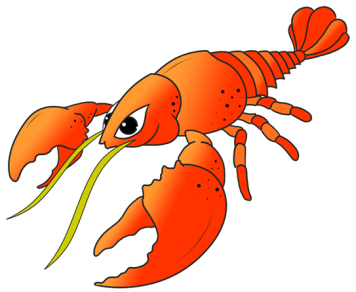
- **Asymptomatic bacteriuria (ASB)** – isolation of bacteria from urine specimen in quantitative counts that are consistent with growth in bladder/kidneys in absence of acute clinical signs or symptoms referable to the urinary tract.
  - With exceptions of pregnant or undergoing invasive genitourinary surgery, treatment of ASB not shown to be beneficial and associated with worse outcomes.

- **Cystitis (lower UTI)** – symptoms of dysuria with or without urgency, frequency, suprapubic pain/discomfort, or hematuria.

- **Pyelonephritis (upper UTI)** – symptoms of fever, flank pain/tenderness, nausea/vomiting with or without typical symptoms of cystitis

Urinary Tract Infection (UTI)

- **Complicated UTI** – symptomatic UTI in presence of complicating factors (structural, functional, or metabolic conditions that promote UTI and put the patient at risk of resistant pathogens and treatment failure.
  - Examples of complicating factors:
    - Male gender
    - Chronic obstruction
    - Diabetes (*poorly controlled*)
    - Indwelling urinary catheter
    - Nephrolithiasis
    - Immunosuppression
    - Pregnancy

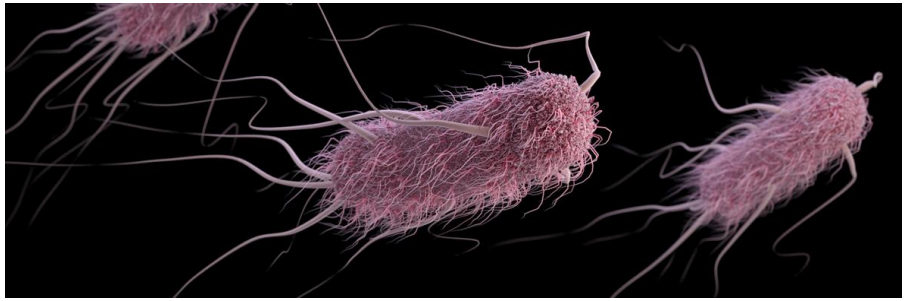


- **Clinical cure** – full resolution of acute symptoms.

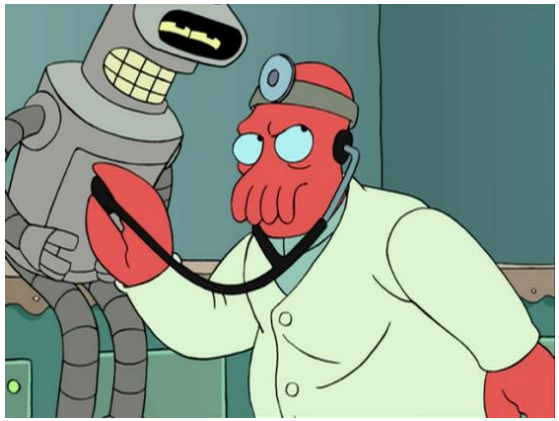
UTI Microbiology

- ***Escherichia coli*** (up to 95% of uncomplicated UTIs)

- Others:
  - *Klebsiella pneumonia*
  - *Proteus mirabilis*
  - *Staphylococcus saprophyticus*
  - *Pseudomonas aeruginosa*
  - *Enterococcus spp*



UTI Investigations



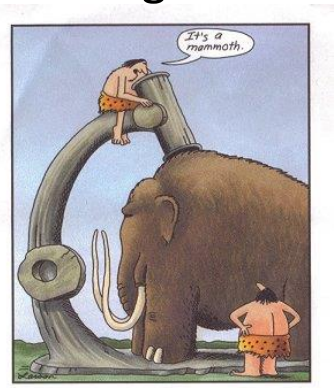
- Symptoms to ask about
  - Dysuria, frequency, urgency, suprapubic pain, hematuria
  - Vaginal discharge, odour, pruritis; painful intercourse (vaginitis becomes more likely when these are present, especially if no urinary frequency or urgency)
  - Flank pain/tenderness, fever/chills, nausea/vomiting

- Cloudy, foul-smelling urine ≠ UTI symptoms

UTI Investigations

- Pyuria identified by urine dipstick or urinalysis ≠ infection

- Urine culture usually not necessary in uncomplicated UTI setting
  - Instances when more strongly indicated:
    - Early (< 1 month) recurrence of infection
    - Atypical presentation
    - Pyelonephritis



Early microscope

- Vaginal discharge/irritation, especially in absence of urinary frequency/urgency, would be indications for pelvic exam and STI work-up

Treatment Considerations

- Recent microbiology culture results (when applicable)

- Collateral damage
  - Ecological adverse effects (i.e. selection of resistant organisms)
  - Should keep this to a minimum
  - Nitrofurantoin and fosfomycin thought to cause only minor collateral damage
  - Consider spectra of activity

- Patient-specific factors
  - Allergies, recent antibiotic exposure, historical urine culture results, drug interactions, renal function, cost, etc.

Treatment Considerations

- Moncton Hospital Antibiogram

	Antibiotics - % Susceptible (based on 2016 data)												
Gram Negative Bacilli	# of Isolates	ampicillin	cefuroxime (oral)	cefTRIAXone[1]	cefTAZidime	PIP-TAZO	gentamicin	tobramycin	TMP-SMX	ciprofloxacin	nitrofurantoin[2]	meropenem	imipenem
Citrobacter freundii*	**58**						95	95	86	98	98	100	100
E. coli	**1919**	59	86	93	94	90	95	95	84	84	95	100	100
Enterobacter cloacae complex*	**124**						98	98	94	96	44	100	98
Klebsiella oxytoca	**111**		86	88	99	84	100	100	96	99	94	100	100
Klebsiella pneumonia	**473**		91	94	93	94	96	95	91	96	41	100	100
Morganella morganii*	**39**						80	87	74	74	0	100	48
Proteus mirabilis	**192**	86	98	99	99	99	97	97	74	96	0	100	
Pseudomonas aeruginosa	**346**				94	95	97	100		90		95	94
Serratia marcescens*	**47**						100	85	99	96	0	98	92

Treatment Recommendations

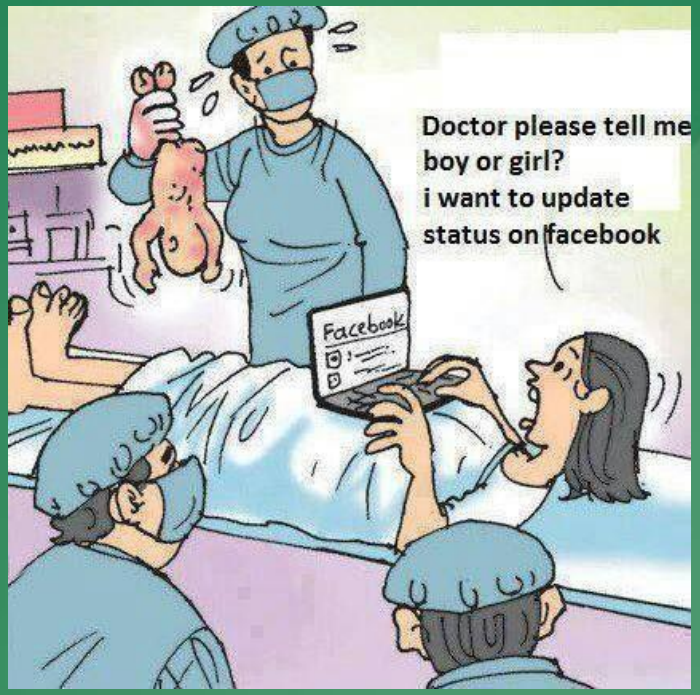
- Preferred regimen:
  - Nitrofurantoin monohydrate/macrocrystals 100mg po BID x 5 days
- Alternative first-line options:
  - Sulfamethoxazole-trimethoprim 800-160mg (DS) po BID x 3 days
  - Fosfomycin 3g po once
  - Trimethoprim 200mg po once daily x 3 days
  - Cefuroxime axetil 500mg po BID x 7 days

Treatment Recommendations

- <u>Avoidance of fluoroquinolones</u>
  - Broader spectrum than necessary → increased rates of antimicrobial resistance and *C. difficile* infection
  - Need to preserve this class for more severe types of infections
  - FDA warning (2016): risk of serious side effects outweighs benefits in uncomplicated UTI; should be avoided for this indication

Study Design

- **Prospective registry**
  - https://redcap.ualberta.ca



Patients

- **Adult (19 years or older)**
- **Written, informed consent provided**
- **Presenting with symptoms suggestive of UTI <u>without</u> prescription from another health care provider (Arm 1)**
  OR
  Presenting <u>with</u> prescription for antibacterial for UTI from another health care provider (Arm 2)
- **Included patients:**
  - Arm 1: uncomplicated UTI
  - Arm 2: uncomplicated UTI or asymptomatic bacteriuria

Patients

- **Exclusions:**
  - Complicated UTI (Arm 1 or 2)
  - Asymptomatic bacteriuria in patients that are pregnant or are undergoing invasive genitourinary surgery (Arm 2)
  - UTI prophylaxis

- **These patients will be referred to physician (Arm 1) or simply documented, but not intervened on (within reason) (Arm 2)**

Initial Presentation

1. Obtain consent for study participation

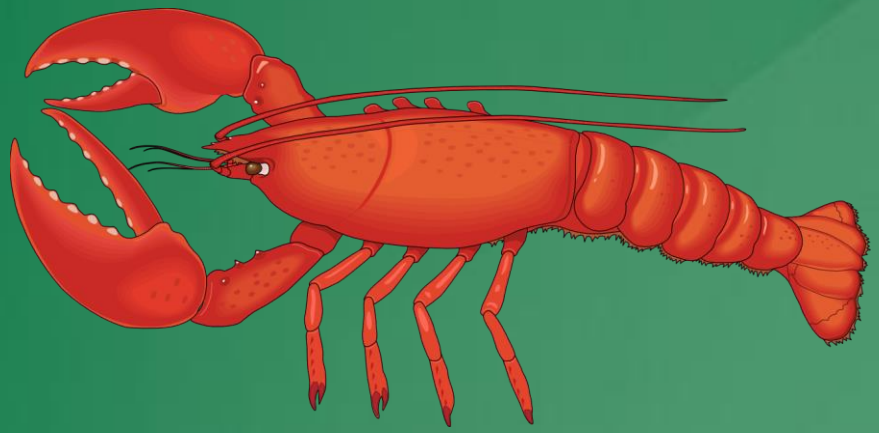
- Need consent before screening
- Patient info sheet goes with patient. Signed consent form stays locked in the pharmacy until the end of the study, at which time they will all be sent to the office of Dr. Dan Smyth

2. Assess for symptoms of UTI

- Do this in registry
- Even for patients that end up being excluded, we need to capture data on screening and referrals
- Also look at laboratory results (i.e. SCr, recent microbiology, etc.) and recent antibacterial exposure

Initial Presentation

3. **Once determined symptomatic, assess for presence of complicating factors and red flags**
    - If asymptomatic, complicating factors are irrelevant
4. **If complicating factors or red flags present, refer to physician (Arm 1) or document, but do not intervene (within reason) (Arm 2)**



Initial Presentation

5. **If no complicating factors or red flags:**
   - Arm 1: initiate empiric treatment
   - Arm 2: assess appropriateness of prescribed treatment, taking into consideration patient-specific factors.
     - If suboptimal: optimize therapy.

6. **If asymptomatic (Arm 2) and:**
   - Not pregnant
   - Not undergoing invasive genitourinary surgery

work with patient to discontinue therapy

Initial Presentation

7. Provide education

- Including what to expect, instructions to come back if symptoms not improving or worsening after 3 days, etc

8. Schedule follow-up

- Follow-up at 2 weeks
  - Each site will have to decide how to organize themselves/keep track of these
- If urine culture was done and results pending, need to check this result within 72 hours

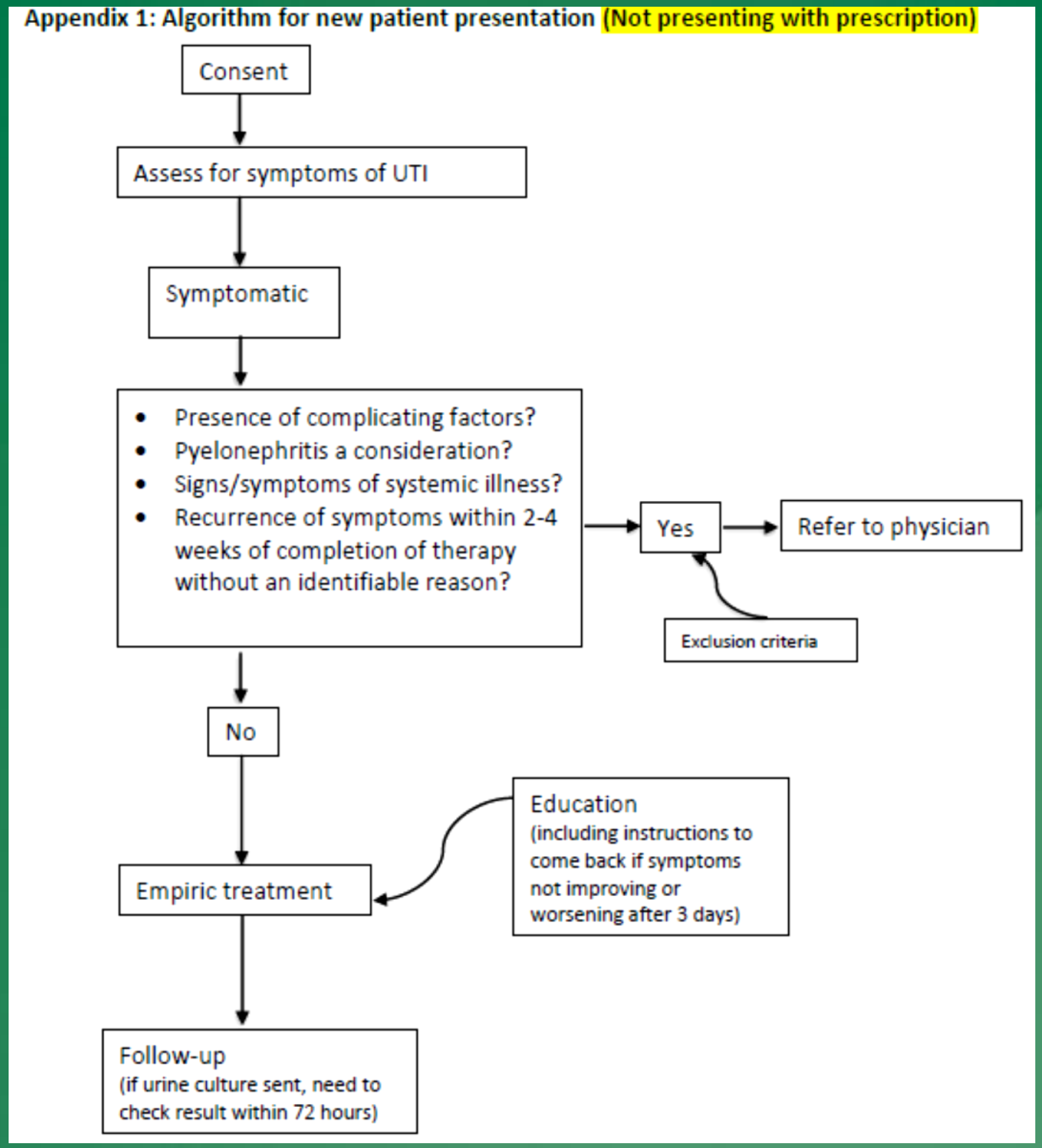
9. Communication to primary physician

10. Patient satisfaction survey

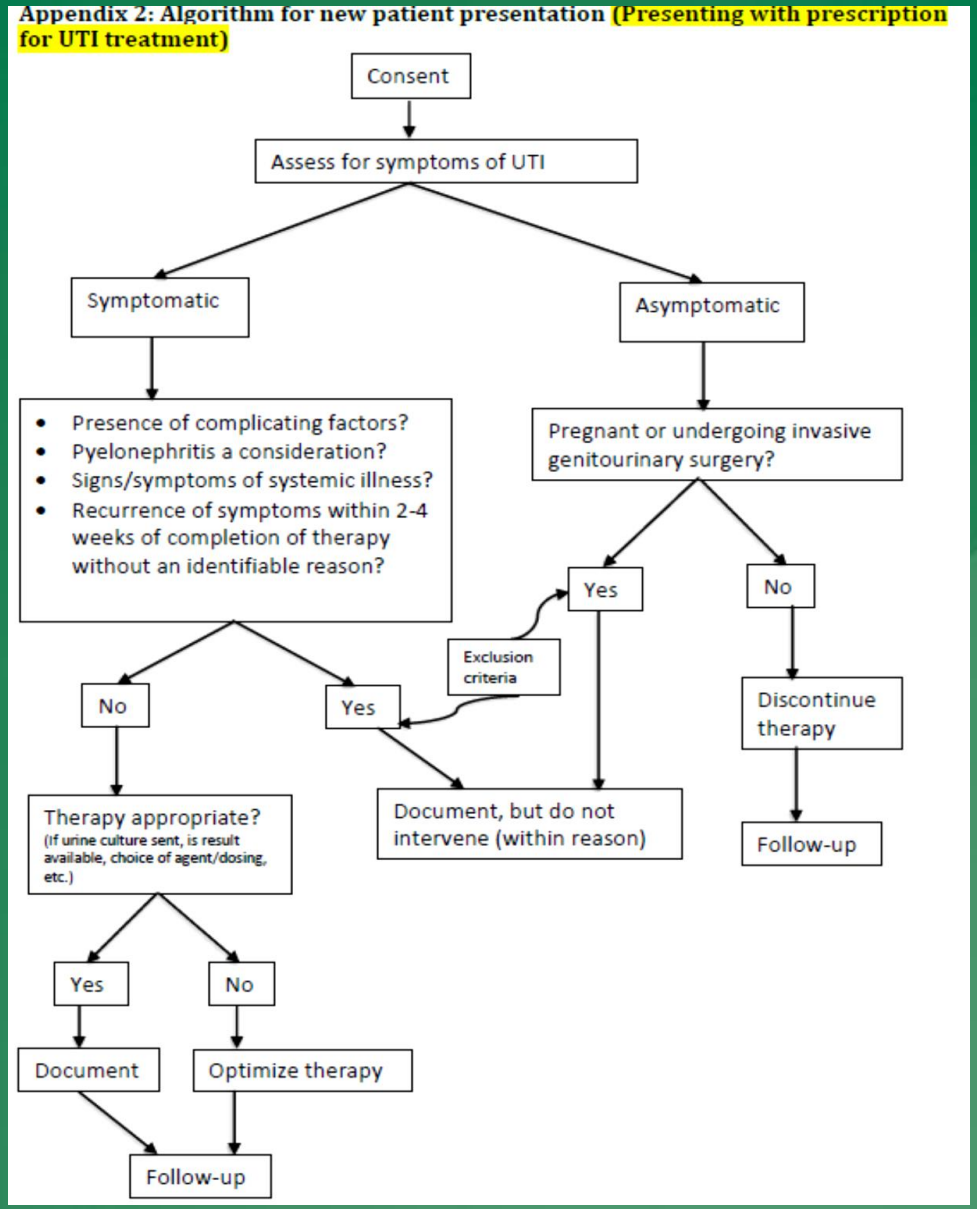
Follow-up

- **Assess for sustained symptom resolution**
  - If not achieved, need to look for identifiable reasons for this
- **Assess adherence**
- **Assess for adverse events**
- **Assessment and Plan**
- **Communication to physician**

Arm 1 – Flow Chart



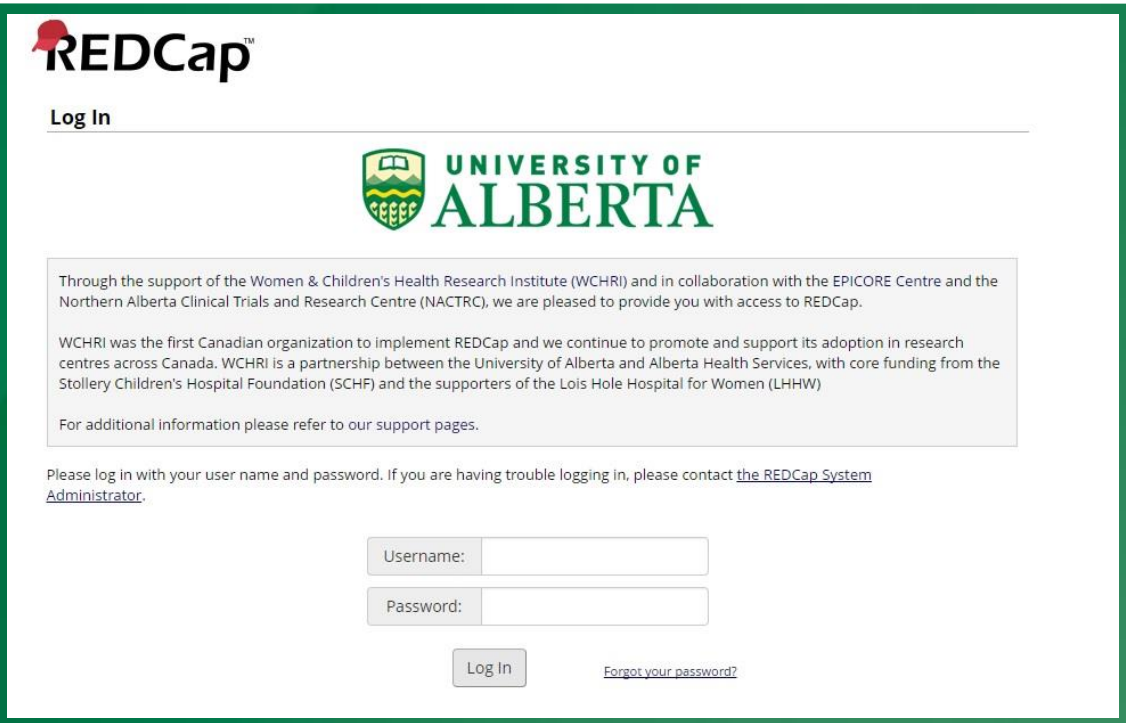
Arm 2 – Flow Chart



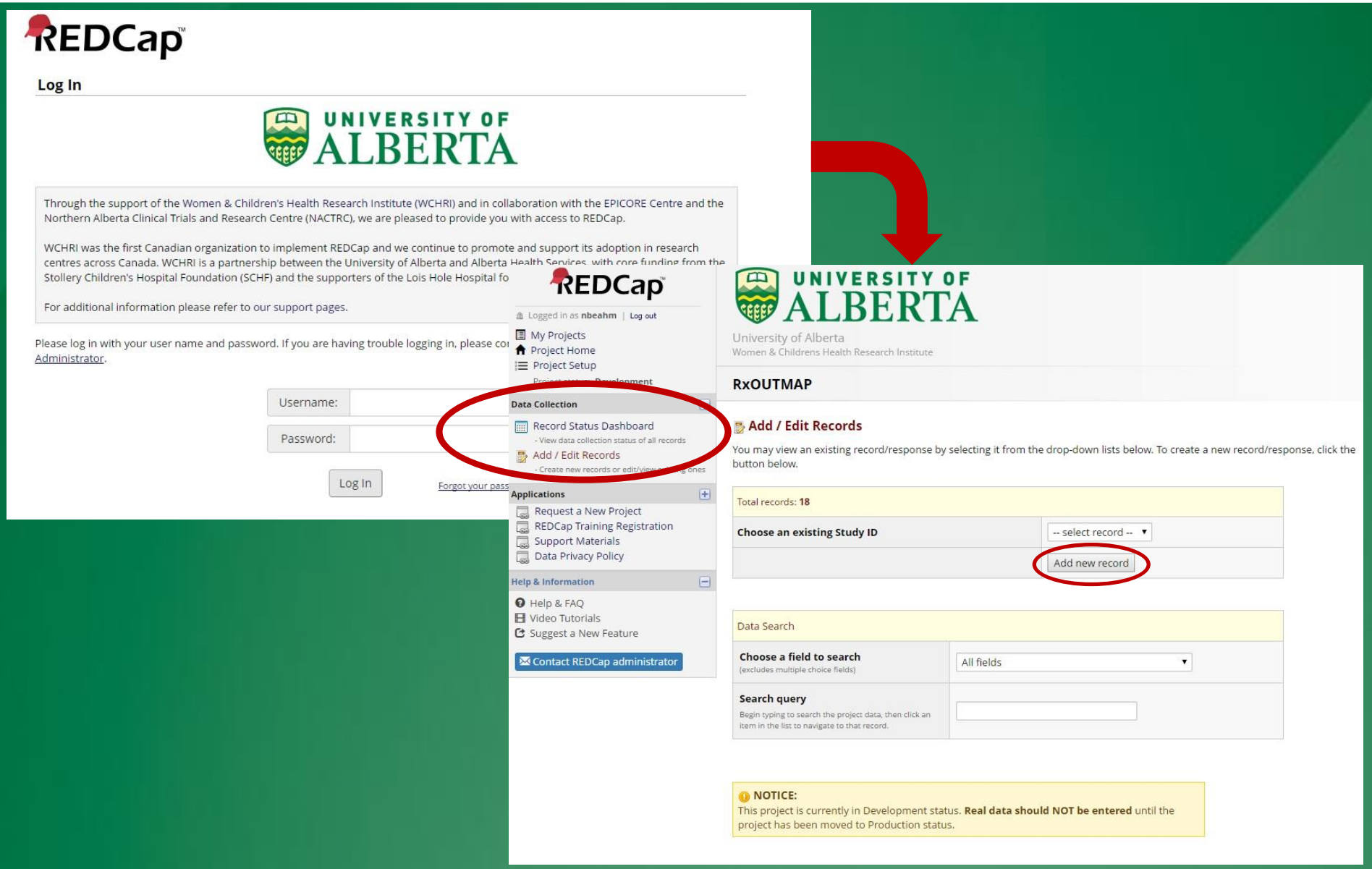
Outcomes

- **The primary outcome will be clinical cure at 2 weeks**
- **Secondary outcomes will include:**
  - Medications used
  - Number and nature of pharmacist interventions
  - Patient adherence
  - Adverse events
  - Treatment failures (including reasons for)
  - Time from symptom onset to access of care
  - Patient satisfaction

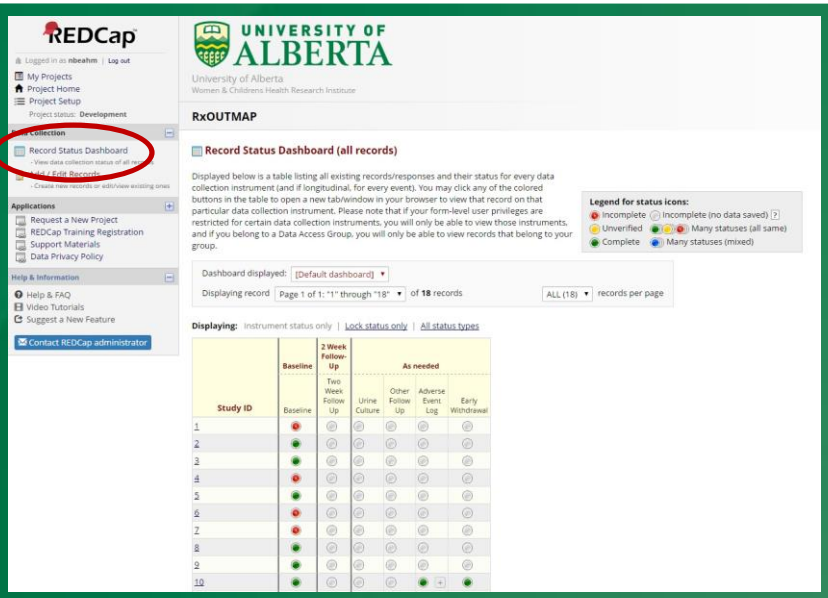
REDCap – Login



REDCap – Login

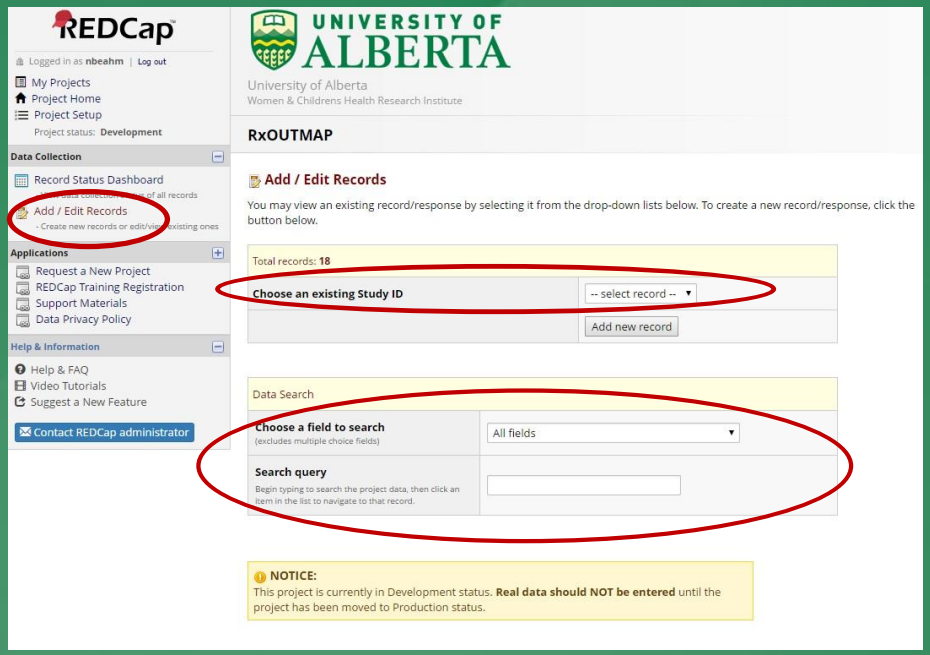


REDCap – Key points



- To view already entered patients for your site (i.e. for follow-up)

- OR…manually search for an individual record from the Add/Edit page



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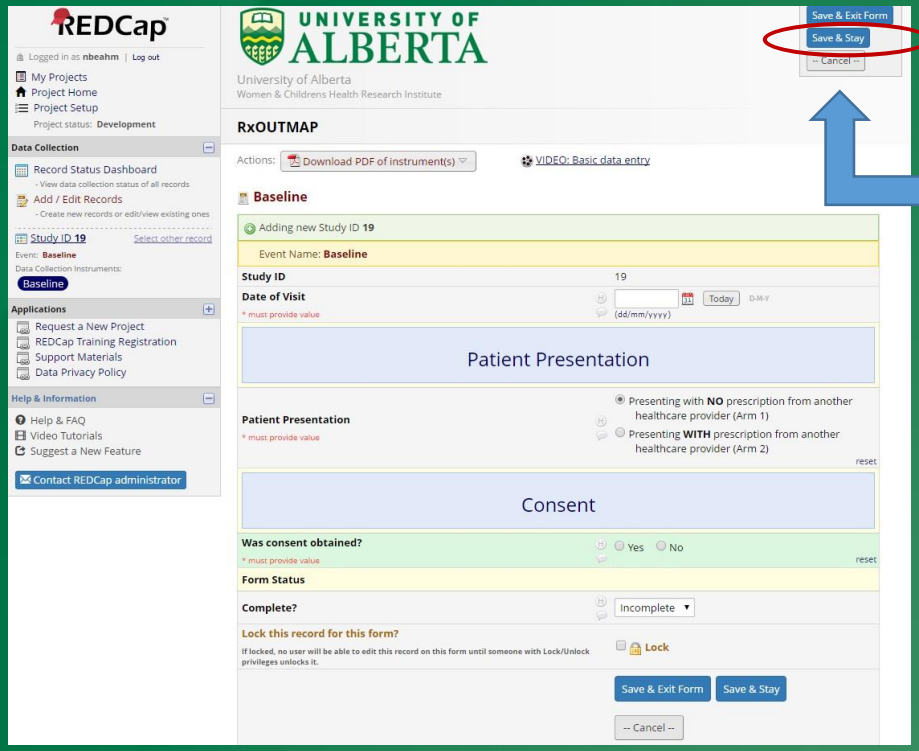
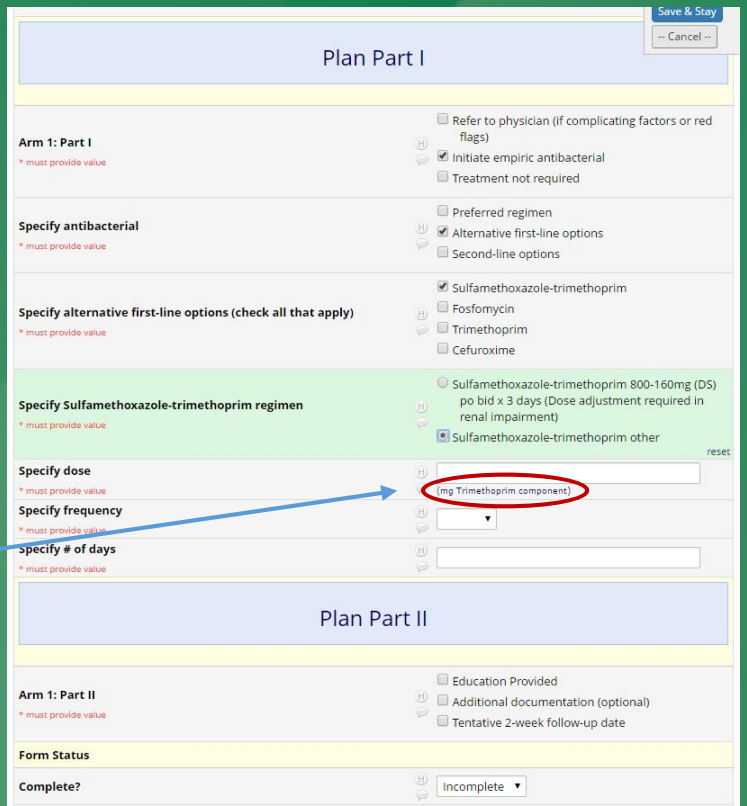


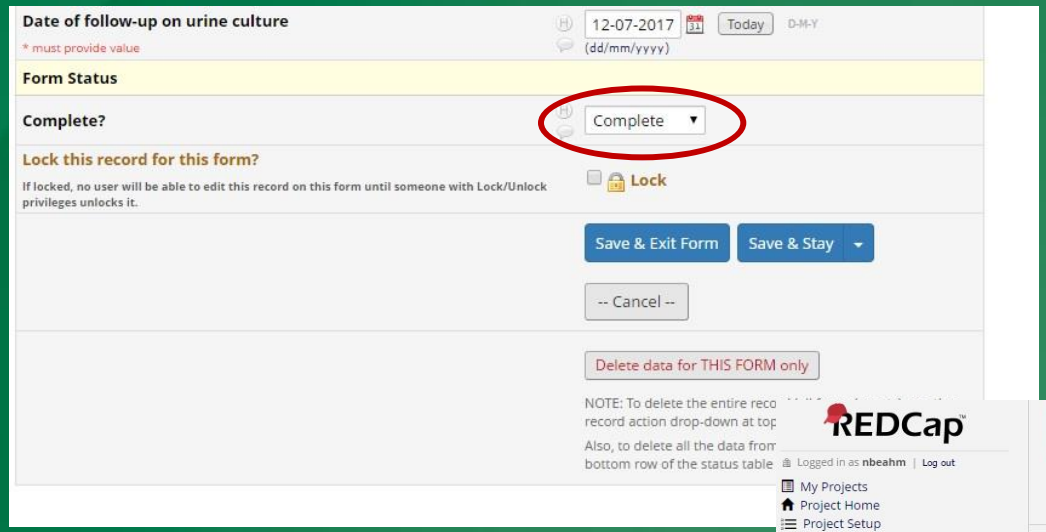
- It might be a good idea to hit “Save & Stay” occasionally

- TMP-SMX free-form dosing based on TMP component (i.e. 160mg if DS tablet)

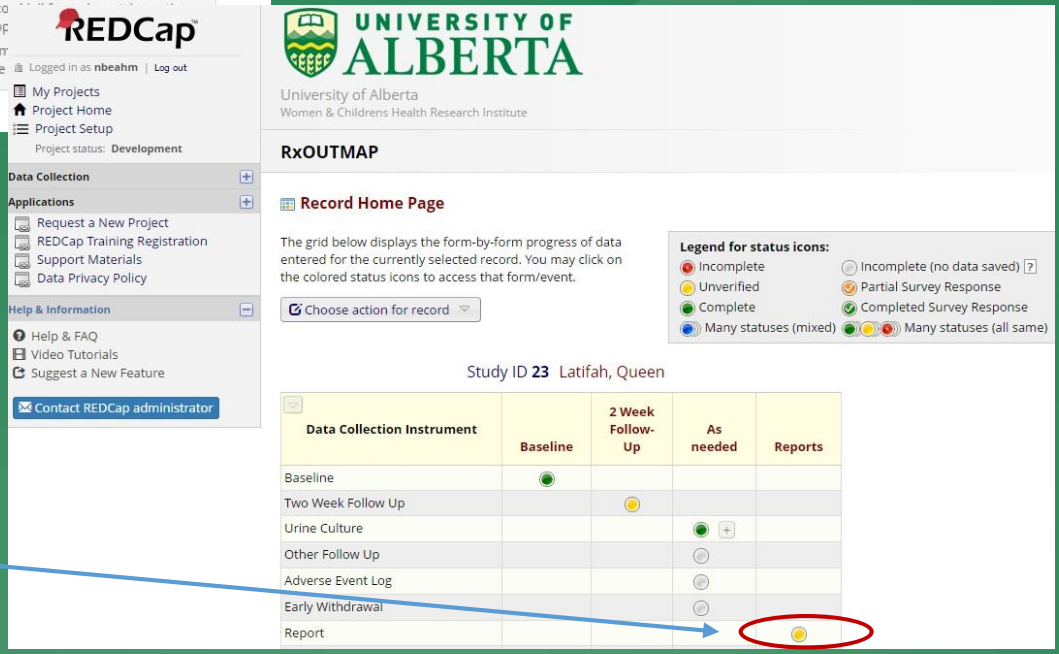


REDCap – Key points

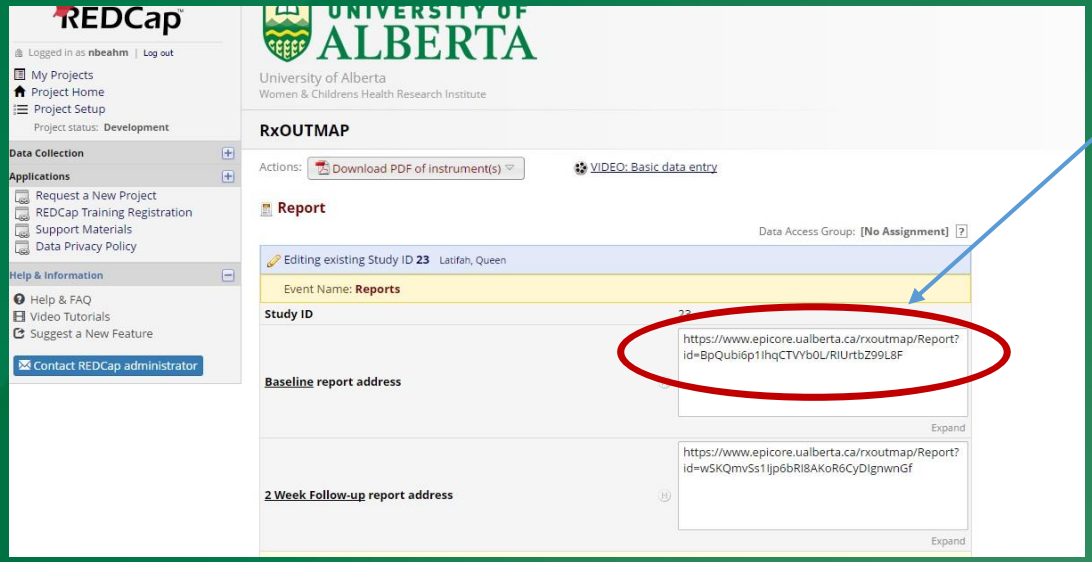
- **To generate a documentation note, the form status needs to be "complete"**



- **Then a yellow dot will appear in the Reports column. Click on this to bring up the link to the report.**



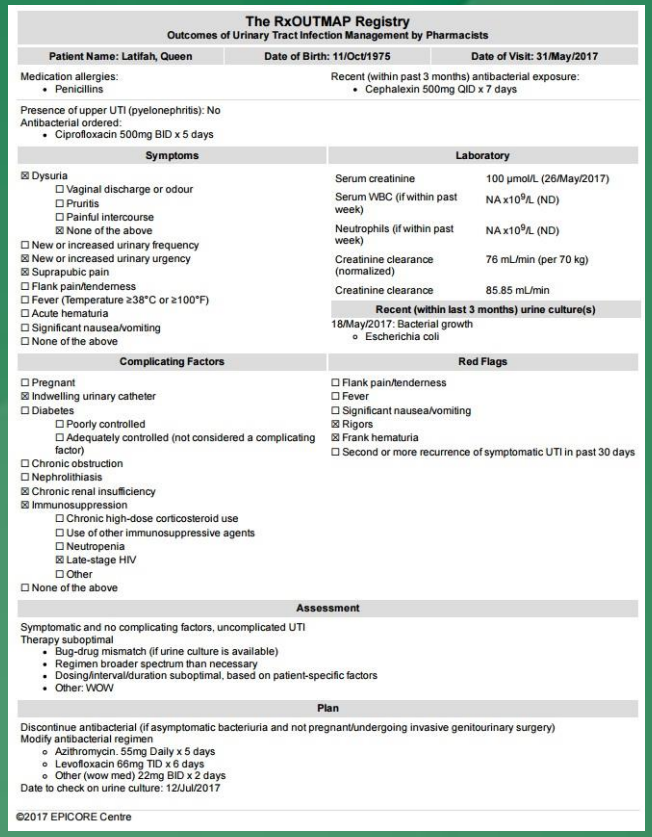
REDCap – Key points



- **Copy the address and paste into web browser to view the documentation note (a crude example note below)**

- **The note can be printed, faxed to physician, kept for your records, etc.**

- **If something needs to be corrected on the documentation note, you need to go back into the relevant form (i.e. Baseline), make the correction and hit "Save and Exit". Then you can refresh the page with the documentation note.**



The RxOUTMAP Registry
Outcomes of Urinary Tract Infection Management by Pharmacists

Patient Name: Latifah, Queen	Date of Birth: 11/Oct/1975	Date of Visit: 31/May/2017

Medication allergies:
- Penicillins

Recent (within past 3 months) antibacterial exposure:
- Cephalexin 500mg QID x 7 days

Presence of upper UTI (pyelonephritis): No
Antibacterial ordered:
- Ciprofloxacin 500mg BID x 5 days

Symptoms

☒ Dysuria
- ☐ Vaginal discharge or odour
- ☐ Pruritis
- ☐ Painful intercourse
- ☒ None of the above

☐ New or increased urinary frequency
☒ New or increased urinary urgency
☒ Suprapubic pain
☐ Flank pain/tenderness
☐ Fever (Temperature ≥38°C or ≥100°F)
☐ Acute hematuria
☐ Significant nausea/vomiting
☐ None of the above

Laboratory

Serum creatinine	100 µmol/L (26/May/2017)
Serum WBC (if within past week)	NA x10^9/L (ND)
Neutrophils (if within past week)	NA x10^9/L (ND)
Creatinine clearance (normalized)	76 mL/min (per 70 kg)
Creatinine clearance	85.85 mL/min

Recent (within last 3 months) urine culture(s)
18/May/2017: Bacterial growth
- Escherichia coli

Complicating Factors

☐ Pregnant
☒ Indwelling urinary catheter
☐ Diabetes
- ☐ Poorly controlled
- ☐ Adequately controlled (not considered a complicating factor)

☐ Chronic obstruction
☐ Nephrolithiasis
☒ Chronic renal insufficiency
☒ Immunosuppression
- ☐ Chronic high-dose corticosteroid use
- ☐ Use of other immunosuppressive agents
- ☐ Neutropenia
- ☒ Late-stage HIV
- ☐ Other

☐ None of the above

Red Flags

☐ Flank pain/tenderness
☐ Fever
☐ Significant nausea/vomiting
☒ Rigors
☒ Frank hematuria
☐ Second or more recurrence of symptomatic UTI in past 30 days

Assessment

Symptomatic and no complicating factors, uncomplicated UTI
Therapy suboptimal
- Bug-drug mismatch (if urine culture is available)
- Regimen broader spectrum than necessary
- Dosing/interval/duration suboptimal, based on patient-specific factors
- Other: WOW

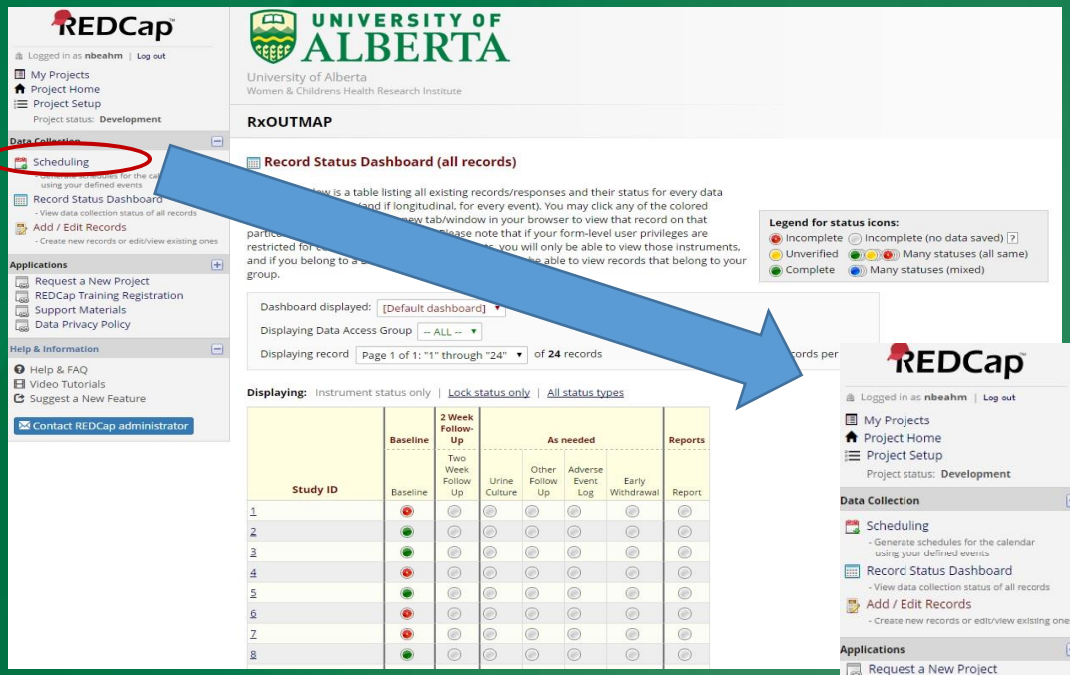
Plan

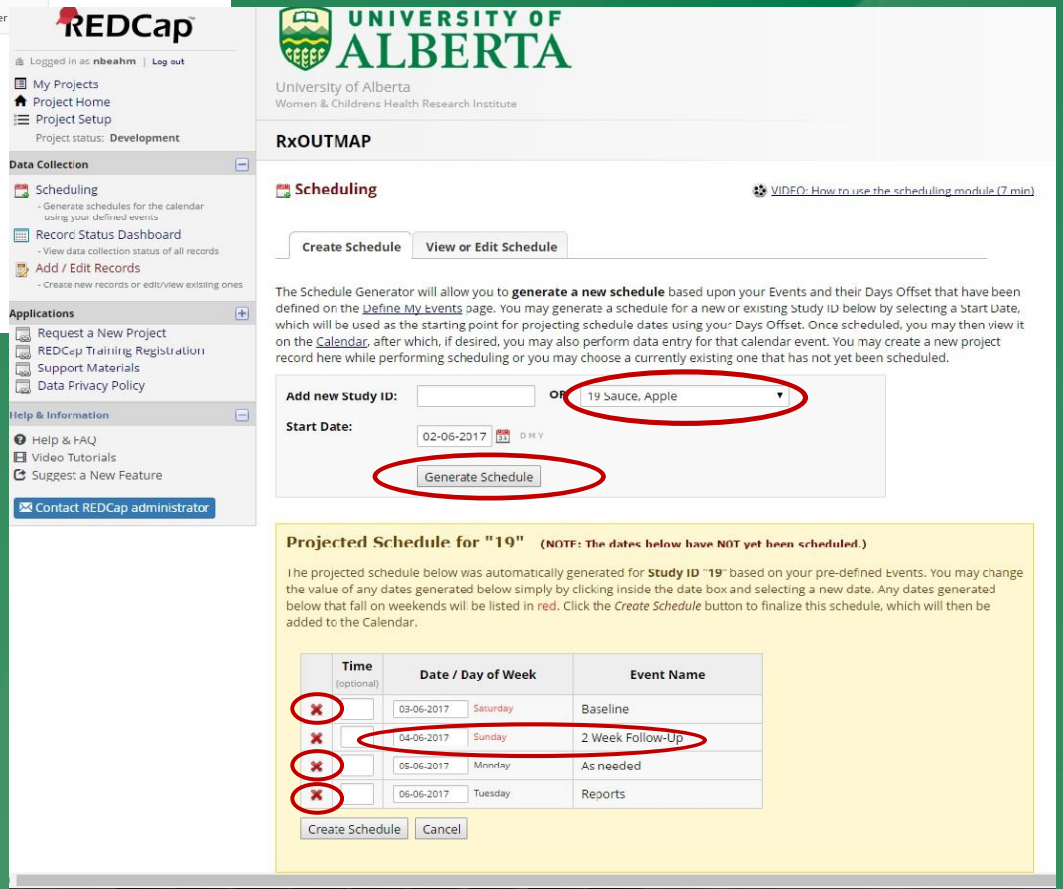
Discontinue antibacterial (if asymptomatic bacteriuria and not pregnant/undergoing invasive genitourinary surgery)
Modify antibacterial regimen
- Azithromycin. 55mg Daily x 5 days
- Levofloxacin 66mg TID x 6 days
- Other (wow med) 22mg BID x 2 days

Date to check on urine culture: 12/Jul/2017

REDCap - Scheduling

- One option to keep track of follow-ups





- For example, to schedule a 2 week follow-up: select the patient from the study ID list on the scheduling page, “x” out the baseline, as needed, and reports options, and then select the date of the 2 week follow-up. Click “create schedule”. It will now be visible in calendar.

REDCap – Walk-thru

- https://redcap.ualberta.ca/

Reimbursement

- **$25 for baseline; $25 for follow-up**
  - $25 for follow-up includes all necessary follow-up, but must do the 2-week follow-up to qualify
- **The assessment fee to the patient should be waived for those consenting to participate in the study**
  - i.e. no double-billing
  - But explain to the patient that the cost of the service is covered by participating in the study
- **Reimbursement will only happen for the patients that get enrolled (i.e. not meeting exclusion criteria); however, you should still be using the database for the screening process (as this is part of the assessment) – need to also be able to show that pharmacists are able to safely screen and refer patients**
- **Reimbursement will occur as a lump sum to each site at the end of the study. No need to bill for it – we will be able to see what was done from the database.**

Contacts

- **For any questions/issues around study procedures or the database – contact Nathan**
  - via email is preferable
  - If urgent, can either try the phone (I am in the office from 1030hrs – 1830hrs Atlantic Time most days) OR email with "URGENT" in the subject line and a brief description of the issue and the phone number I can reach you at in the email body – I will respond quickly

Contacts

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Questions?


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Dist. by King Features
We're out of antibiotics. Take a quarter-pound of ground beef every twelve hours.
6·4·15
W/ Jeff Topper
PHARMACY