



UNIVERSITY OF
ALBERTA

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

June 11, 2017





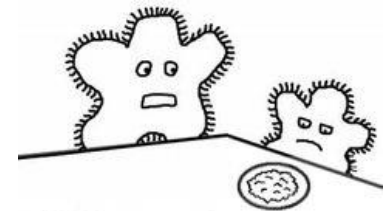
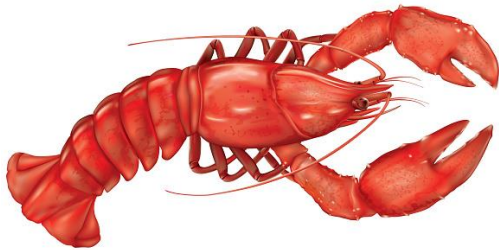
Overview

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.**



"But Timmy, you have to eat your antibiotics or you'll never become a big strong bacteria."

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



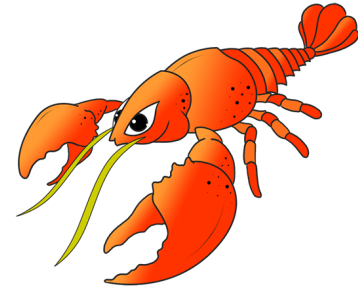
Urinary Tract Infection (UTI)

- 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.

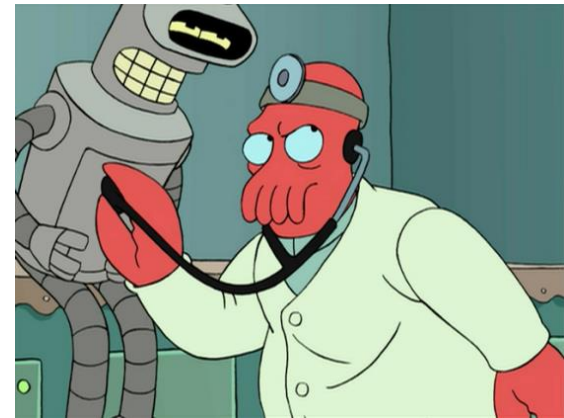


UTI Microbiology

- ***Escherichia coli*** (up to 95% of uncomplicated UTIs)
- Others:
 - *Klebsiella pneumonia*
 - *Proteus mirabilis*
 - *Staphylococcus saprophyticus*
 - *Pseudomonas aeruginosa*
 - *Enterococcus spp*



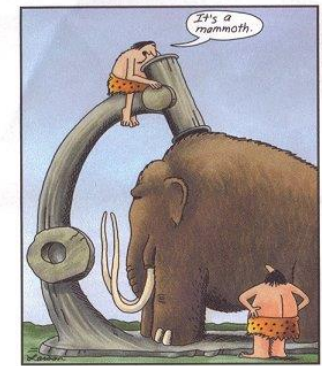
UTI Investigations



- 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 \neq UTI symptoms

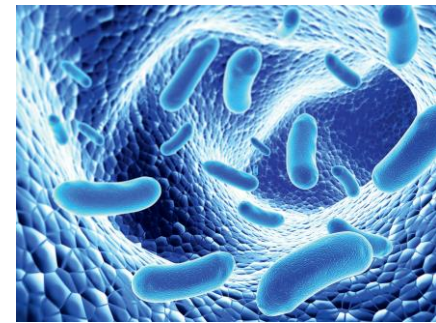
UTI Investigations

- Pyuria identified by urine dipstick or urinalysis \neq infection
- Urine culture usually not necessary in uncomplicated UTI setting
 - Instances when more strongly indicated:
 - Early (< 1 month) recurrence of infection
 - Atypical presentation
 - Pyelonephritis
- Vaginal discharge/irritation, especially in absence of urinary frequency/urgency, would be indications for pelvic exam and STI work-up



Early microscope

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 Antibigram

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
 - Fosfomicin 3g po once
 - Trimethoprim 200mg po once daily x 3 days
 - Cefuroxime axetil 500mg po BID x 7 days

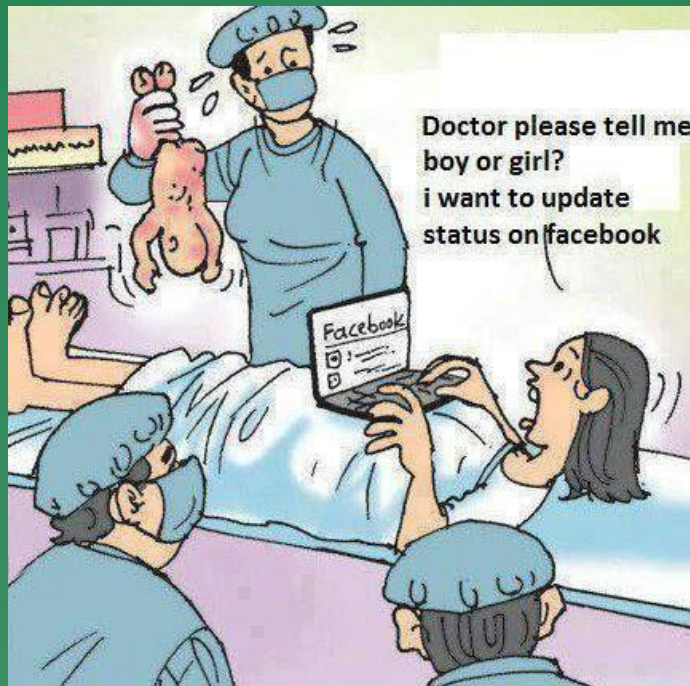


Treatment Recommendations

- Avoidance of fluoroquinolones
 - 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



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



- **Adult (19 years or older)**
- **Written, informed consent provided**
- **Presenting with symptoms suggestive of UTI without prescription from another health care provider (Arm 1)
OR
Presenting with 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



- **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)**



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

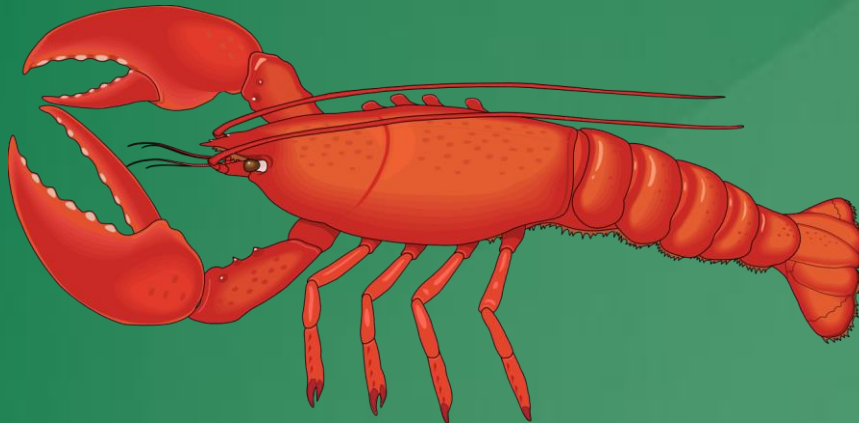
- Do this in registry
- Even for patients that end up being excluded, we need to capture data on screening and referrals
- Also look at laboratory results (i.e. SCr, recent microbiology, etc.) and recent antibacterial exposure



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)



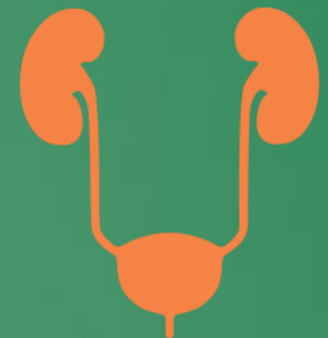
5. If no complicating factors or red flags:

- 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



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

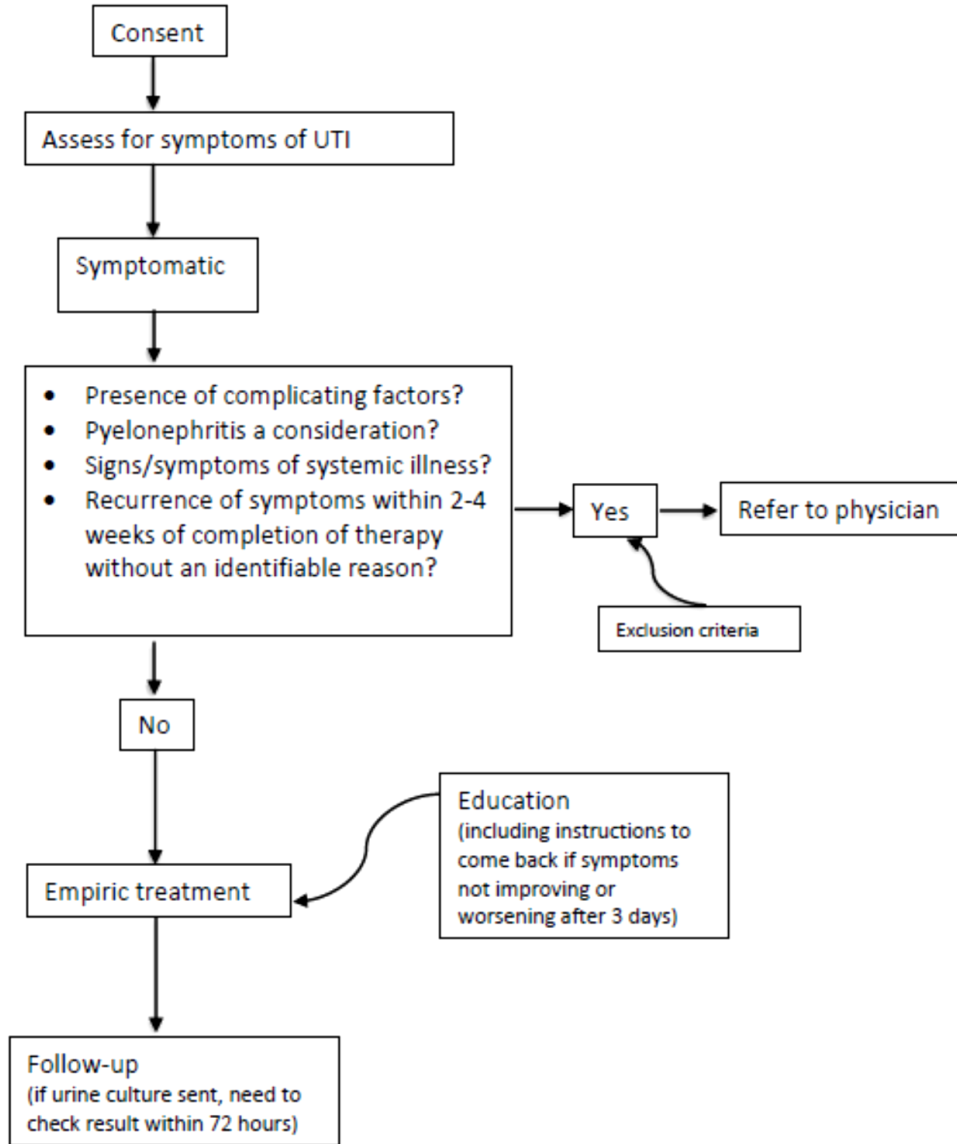
10. Patient satisfaction survey



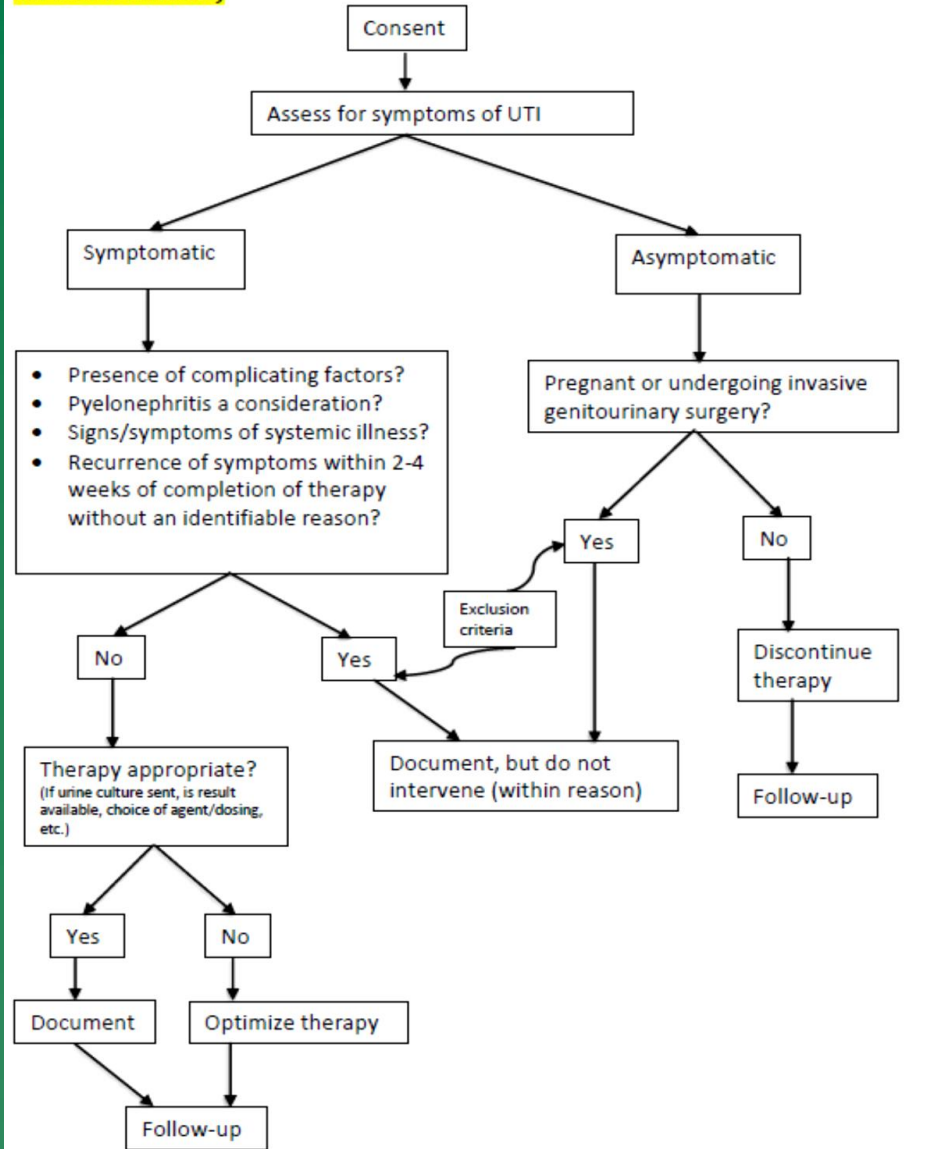
- **Assess for sustained symptom resolution**
 - If not achieved, need to look for identifiable reasons for this
- **Assess adherence**
- **Assess for adverse events**
- **Assessment and Plan**
- **Communication to physician**



Appendix 1: Algorithm for new patient presentation (Not presenting with prescription)



Appendix 2: Algorithm for new patient presentation (Presenting with prescription for UTI treatment)



- 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





Log In



Through the support of the Women & Children's Health Research Institute (WCHRI) and in collaboration with the EPICORE Centre and the Northern Alberta Clinical Trials and Research Centre (NACTRC), we are pleased to provide you with access to REDCap.

WCHRI was the first Canadian organization to implement REDCap and we continue to promote and support its adoption in research centres across Canada. WCHRI is a partnership between the University of Alberta and Alberta Health Services, with core funding from the Stollery Children's Hospital Foundation (SCHF) and the supporters of the Lois Hole Hospital for Women (LHHW)

For additional information please refer to our support pages.

Please log in with your user name and password. If you are having trouble logging in, please contact [the REDCap System Administrator](#).

Username:

Password:

Log In

[Forgot your password?](#)



Log In



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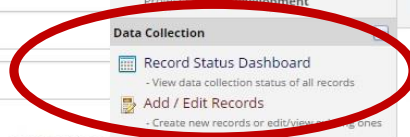
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Username:

Password:

Log In



Logged in as nbeahm | Log out

- My Projects
- Project Home
- Project Setup
- Project Status Development
- Data Collection**
 - Record Status Dashboard
 - View data collection status of all records
 - Add / Edit Records**
 - Create new records or edit/view existing ones
- Applications
 - Request a New Project
 - REDCap Training Registration
 - Support Materials
 - Data Privacy Policy
- Help & Information
 - Help & FAQ
 - Video Tutorials
 - Suggest a New Feature
- Contact REDCap administrator



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RxOUTMAP

Add / Edit Records

You may view an existing record/response by selecting it from the drop-down lists below. To create a new record/response, click the button below.

Total records: 18

Choose an existing Study ID

-- select record --

Add new record

Data Search

Choose a field to search

(excludes multiple choice fields)

All fields

Search query

Begin typing to search the project data, then click an item in the list to navigate to that record.

NOTICE:

This project is currently in Development status. **Real data should NOT be entered** until the project has been moved to Production status.

REDCap
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RxOUTMAP

Record Status Dashboard (all records)

Displayed below is a table listing all existing records/responses and their status for every data collection instrument (and if longitudinal, for every event). You may click any of the colored buttons in the table to open a new tab/window in your browser to view that record on that particular data collection instrument. Please note that if your form-level user privileges are restricted for certain data collection instruments, you will only be able to view those instruments, and if you belong to a Data Access Group, you will only be able to view records that belong to your group.

Legend for status icons:
 Incomplete (no data saved)
 Unverified
 Many statuses (all same)
 Complete
 Many statuses (mixed)

Dashboard displayed: [Default dashboard]
 Displaying record: Page 1 of 1: "1" through "18" of 18 records
 ALL (18) records per page

Displaying: Instrument status only | Lock status only | All status types

Study ID	Baseline	2 Week Follow-Up	As needed				
	Baseline	2 Week Follow-Up	Urine Culture	Other Follow-Up	Adverse Event Log	Early Withdrawal	
1	●	●	●	●	●	●	
2	●	●	●	●	●	●	
3	●	●	●	●	●	●	
4	●	●	●	●	●	●	
5	●	●	●	●	●	●	
6	●	●	●	●	●	●	
7	●	●	●	●	●	●	
8	●	●	●	●	●	●	
9	●	●	●	●	●	●	
10	●	●	●	●	●	●	

- 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



REDCap
 Logged in as nbeahm | Log out
 My Projects
 Project Home
 Project Setup
 Project status: Development

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RxOUTMAP

Add / Edit Records
 You may view an existing record/response by selecting it from the drop-down lists below. To create a new record/response, click the button below.

Total records: 18

Choose an existing Study ID: -- select record --
 Add new record

Data Search

Choose a field to search (excludes multiple choice fields): All fields

Search query: []

NOTICE:
 This project is currently in Development status. Real data should NOT be entered until the project has been moved to Production status.

REDCap – Key points

- 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)

- To generate a documentation note, the form status needs to be “complete”

Date of follow-up on urine culture Today D-M-Y
* must provide value (dd/mm/yyyy)

Form Status

Complete? Complete

Lock this record for this form?
If locked, no user will be able to edit this record on this form until someone with Lock/Unlock privileges unlocks it.

Lock

Save & Exit Form Save & Stay -- Cancel --

Delete data for THIS FORM only

NOTE: To delete the entire record action drop-down at top. Also, to delete all the data from bottom row of the status table.

REDCap™

Logged in as nbeahm | Log out

- My Projects
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- Project status: Development

Data Collection

Applications

- Request a New Project
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Help & Information

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- Suggest a New Feature

Contact REDCap administrator



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

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RxOUTMAP

Record Home Page

The grid below displays the form-by-form progress of data entered for the currently selected record. You may click on the colored status icons to access that form/event.

Choose action for record

Legend for status icons:

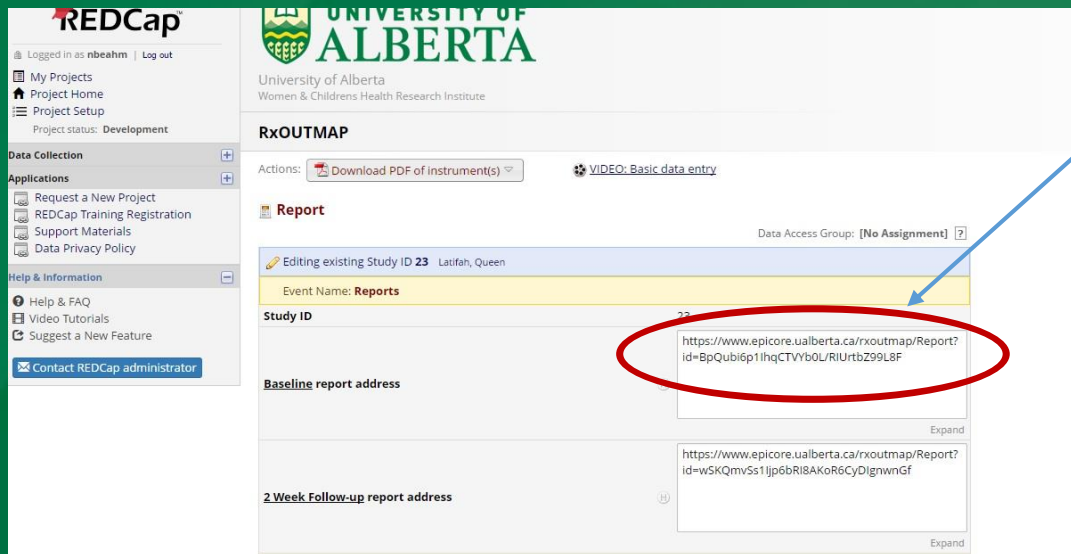
- Incomplete
- Unverified
- Complete
- Many statuses (mixed)
- Incomplete (no data saved)
- Partial Survey Response
- Completed Survey Response
- Many statuses (all same)

Study ID 23 Latifah, Queen

Data Collection Instrument	Baseline	2 Week Follow-Up	As needed	Reports
Baseline	●			
Two Week Follow Up		●		
Urine Culture			●	
Other Follow Up			○	
Adverse Event Log			○	
Early Withdrawal			○	
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 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	Laboratory
<input checked="" type="checkbox"/> Dysuria <input type="checkbox"/> Vaginal discharge or odour <input type="checkbox"/> Pruritis <input type="checkbox"/> Painful intercourse <input checked="" type="checkbox"/> None of the above	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)
<input type="checkbox"/> New or increased urinary frequency <input checked="" type="checkbox"/> New or increased urinary urgency <input checked="" type="checkbox"/> Suprapubic pain <input type="checkbox"/> Flank pain/tenderness <input type="checkbox"/> Fever (Temperature ≥38°C or ≥100°F) <input type="checkbox"/> Acute hematuria <input type="checkbox"/> Significant nausea/vomiting <input type="checkbox"/> None of the above	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	Red Flags
<input type="checkbox"/> Pregnant <input checked="" type="checkbox"/> Indwelling urinary catheter <input type="checkbox"/> Diabetes <input type="checkbox"/> Poorly controlled <input type="checkbox"/> Adequately controlled (not considered a complicating factor) <input type="checkbox"/> Chronic obstruction <input type="checkbox"/> Nephrolithiasis <input checked="" type="checkbox"/> Chronic renal insufficiency <input checked="" type="checkbox"/> Immunosuppression <input type="checkbox"/> Chronic high-dose corticosteroid use <input type="checkbox"/> Use of other immunosuppressive agents <input type="checkbox"/> Neutropenia <input checked="" type="checkbox"/> Late-stage HIV <input type="checkbox"/> Other <input type="checkbox"/> None of the above	<input type="checkbox"/> Flank pain/tenderness <input type="checkbox"/> Fever <input type="checkbox"/> Significant nausea/vomiting <input checked="" type="checkbox"/> Rigors <input checked="" type="checkbox"/> Frank hematuria <input type="checkbox"/> 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, 500mg Daily x 5 days • Levofloxacin 600mg 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

Record Status Dashboard (all records)

Legend for status icons:

- Incomplete
- Unverified
- Complete
- Incomplete (no data saved) [?]
- Many statuses (all same)
- Many statuses (mixed)

Study ID	Baseline	2 Week Follow-Up	As needed			Reports
		Two Week Follow Up	Urine Culture	Other Follow Up	Adverse Event Log	Early Withdrawal
1	●	●	●	●	●	●
2	●	●	●	●	●	●
3	●	●	●	●	●	●
4	●	●	●	●	●	●
5	●	●	●	●	●	●
6	●	●	●	●	●	●
7	●	●	●	●	●	●
8	●	●	●	●	●	●

Scheduling

Create Schedule | View or Edit Schedule

Add new Study ID: OR **19 Sauce, Apple**

Start Date:

Generate Schedule

Projected Schedule for "19" (NOTE: The dates below have NOT yet been scheduled.)

The projected schedule below was automatically generated for **Study ID "19"** based on your pre-defined Events. You may change the value of any dates generated below simply by clicking inside the date box and selecting a new date. Any dates generated below that fall on weekends will be listed in red. Click the **Create Schedule** button to finalize this schedule, which will then be added to the Calendar.

Time (optional)	Date / Day of Week	Event Name
<input type="text" value="03-06-2017"/>	Saturday	Baseline
<input type="text" value="04-06-2017"/>	Sunday	2 Week Follow-Up
<input type="text" value="05-06-2017"/>	Monday	As needed
<input type="text" value="06-06-2017"/>	Tuesday	Reports

Create Schedule | Cancel

• 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.

- <https://redcap.ualberta.ca/>



RO'U'TMAP

- **\$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.**

- **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



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