Therapeutics Initiative

Better prescribing. Better health.

PharmacoEpidemiology Group (PEG)

Impact Evaluation of the Therapeutic Initiative's Uncomplicated Acute Cystitis Personalized Portrait and Therapeutics Letter

Analytic Protocol

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Contents

Document Control

Version	Date	Author(s)	Type of change
0.1	April 08, 2022	GC	First Draft
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Study Name: Impact Evaluation of the Therapeutic Initiative's Uncomplicated Acute Cystitis Personalized Portrait and Therapeutics Letter

Nickname: UTI Evaluation

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Data Access: Health*ideas* including: ClaimsHist, MSP fee-for-service, hospital discharge abstracts, client roster, physician roster.

1. Introduction

Indicators show that infections caused by antimicrobial resistant organisms continue to increase in Canada,[i] and despite decades of antimicrobial stewardship programs the quality of antibiotic prescribing remains suboptimal.[ii-iv] Continued efforts to preserve the effectiveness of antimicrobials to treat infectious diseases are essential, since misuse of antimicrobials is the primary mechanism driving resistance. [v-viii] The treatment of cystitis is one indication where a change in antibiotic use was necessary. Uncomplicated acute cystitis (UAC) is the most prevalent form of urinary tract infection in women, and is most commonly caused by *escherichia coli* (E. coli). [ix,x] UAC is a common indication for antimicrobial treatment in healthy, non-pregnant women.[xi,xii] E. coli resistance to TMP-SMX and fluoroquinolones, historically the antibiotics most often used for UAC, has exceeded 20% in all areas of British Columbia, thus limiting the empirical effectiveness of these treatments. Due to increased resistance, Nitrofurantoin is now the best evidence supported treatment of infections caused by E. Coli or Staphylococcus Saprophyticus.[xiii]

2. Purpose

Study Purpose

To conduct a randomized trial testing the effectiveness of personalized prescribing portraits and therapeutic letters on appropriate treatment for uncomplicated acute cystitis.

Research Question(s) / Hypothesis

Research Question: Determine the change in nitrofurantoin prescribing associated with the personal prescribing portrait and the therapeutics letter for UAC.

Hypothesis: The personal prescribing feedback portrait and the letter will each be associated with an increase in nitrofurantoin prescribing.

3. Objectives

To conduct a randomized trial testing the effectiveness of personalized prescribing portraits and therapeutic letters on appropriate treatment for uncomplicated acute cystitis.

4. Methods

We conducted a randomized trial to analyze the effectiveness of a personalized prescribing portrait in the primary care setting in the province of British Columbia between September 2021 and March 2022.

Physicians are randomized to three groups:

	Arm A ~33%	Arm B ~33%	Arm C ~33%
Initial mailing Sept 23, 2021	Early Portrait + Letter	Nothing	Early Letter Only
Delayed mailing Mar 28, 2022		Delayed Portrait + Letter	Delayed Portrait + Letter

*Approximately 1,691 physicians were randomized to each group. However, not all will receive materials due to opt-outs and incorrect addresses.

Study Dates:

-Early mailing (groups A and C): 23-Sept-2021
-Delayed mailing (groups B and C): 28-Mar-2022
-Letter & Portrait topic released publicly on website: 28-Mar-2022

Study Period: September 24th, 2021 to March 28, 2022.
Delay Period: March 29, 2022 to Sept 28, 2022

Study Comparisons:

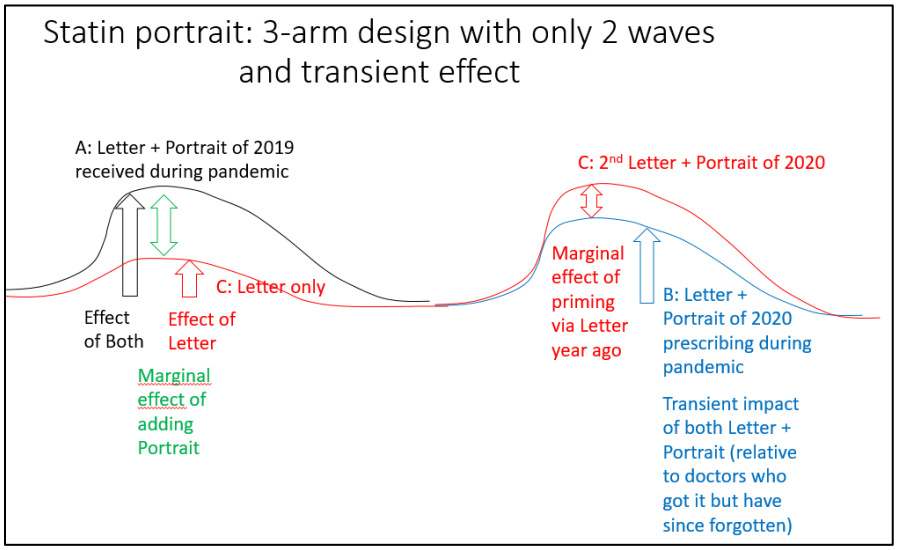
There will be four comparisons:

During the study period (Sept 23, 2021 to Mar 28, 2022):

i. Arm A vs Arm B (impact of L+P combined)
ii. Arm A vs Arm C (The added impact of P in physicians who received L)
iii. Arm C vs Arm B (Impact of L)

During the study period (Sept 23, 2021 to Sept 28, 2022):

iv. Arm B vs Arm C (repeated messaging)



Data sources

B.C. Ministry of Health Health*ideas* data warehouse, including: ClaimsHist, MSP fee-for-service, hospital discharge abstracts, client roster, physician roster.

Estimated number of records/charts to be examined: 1691 physicians randomized to each group = 5,073. Estimate 6 UTI treated visits per physician = **30,438 patient records** to be included in the analysis.

Population (cohorts)

Physicians:

Physician eligibility criteria for randomization:

i. Registered with the College of Physicians and Surgeons of B.C. (CPSBC)
ii. Defined as a *General Practitioner* or *FP – Emergency Medicine* according to the B.C. Ministry of Health's Medical Services Plan (MSP) with a license status of *private practice, temporary license, salaried, or post graduate*.
iii. Valid mailing address in B.C according to the College of Physicians and Surgeons of British Columbia's public physician information.
iv. Had >=100 prescriptions filled at a community pharmacy in 2020 according to PharmaNet claims.

*Approximately 1,691 physicians were randomized to each of the 3 study groups.

Physician eligibility criteria to receive a prescribing portrait:

i. Met the criteria for randomization above
ii. Diagnosed >= 1 eligible patient with UAC in 2019 or 2020 (for delay group: 2020 to 2021

Patients:

Patient visits for UAC were identified from MSP billing records in which the first 3 digits of the ICD-9 diagnosis code in the record indicated 595 - Cystitis.

Include UTI codes:

1. 595, 595.0, 595.3-595.9 (cystitis) (but do not include 595.1, 595.2 chronic cystitis)
2. 599 or 599.0, 599.8, 599.9 UTI, site not specified (do not include if 599.1-599.7)
3. 788 or 788.9 or 788.1 symptoms involving urinary system or dysuria (do not include if 788.0, 788.2-788.8)
4. 596, 599.7, or 791

These UAC patients were then categorized according to whether they received antibiotic treatment on or within 5 days of the physician office visit recorded in the MSP billing record. Only count events where the diagnosing and prescribing physician are the same.

Patient exclusions:

- less than 77 days (2.5 months) MSP enrolment in the 91 days prior to visit
- Age <15 at time of UTI diagnosis
- Male or missing sex
- Recurrent UTI:
    - A visit with a diagnosis of UTI in the prior 90 days, and/or
    - More than 4 visits in the 1095 days (3 years) before visit with a diagnosis of UTI
- Complicating factors:
    - Discharge from hospital in prior 30 days
    - Severe disease/infection of the kidney (pyelonephritis), ICD9: 590, 590.1, 590.2, 590.8, 590.9; ICD10: N10, N12, N15.1, N16 (within previous or following 10 days). Hospital admission or ED.
    - Indwelling catheter, based on ICD-9: V53.6, 996.64, 996.76, 996.31. ICD10: T83.0x, Z46.6, Z96.0, in 91 days prior to UTI diagnosis
    - Impaired renal function, fee item: 33758, 33723, 33759, 33761 or if they have a visit with a nephrologist (prior 365 days)
    - Structural and functional abnormality of urinary tract (prior 365 days) [ICD9: 16.9, 137.2, 997.5, 939.3, 939.9, 947.4, V130 ICD10: A181, B901, N998, N999, T198, T199, T283, T288, Z874.]
    - Pregnant women, fee item: 14090, 14091, 36360, 36361, 04717 codes or ICD 646.6, V22.x, V23.x in the 270 days before the UTI visits + no record of pregnancy outcome after pregnancy code and before UTI event (ICD9 630.x, 631.x, 632.x, 633.x, 634.x, 635.x, 636.x, 637.x, V24.x, V27.x, 656.4 or ICD10 O00.x, O01.x, O02.x, O03.x, O04.x, O05.x, Z37.x, O36.4x)

- Diagnosis of STI within 14 days before or after UTI visit (ICD9: 090-099, ICD10: A50-A64)
- Chronic Kidney Disease (ICD9: 585.x, ICD10: N18) MSP complex care code: N585, R585, I585, H585, D585, C585, K573) in previous 365 days
- Physician visit where patient had any oral, intravenous, or injection antibiotics (ATC: J01) in previous 91 days dispensed by any physician
- Patients with a dispensation under Plan P or B (on abx fill date or within 3 months after)

Exposures

Female patient visits for UAC identified from physician MSP billing records in which the first 3 digits of the ICD-9 diagnosis code in the record indicated *595 – Cystitis.*

Medications

All oral formulation prescription antibiotics available in BC were included in the portrait.

Nitrofurantoin identified using ATC: J01XE01

Outcomes

The primary outcome is the incidence of women treated with nitrofurantoin in the 5-day period following a diagnosis of Uncomplicated Acute Cystitis, including the day of diagnosis.

5. Statistical Analysis Plan

1. **Baseline Characteristics:** Physicians and Patients by Study Group. Age (mean, sd), age groups, sex, urban vs rural.

2. **Trends:** Weekly prescribing line chart by randomized physician group of Nitrofurantoin, Ciprofloxacin, and TMP-SMX, from 6 months prior to first mailing to the end of the delay period - 6 months after the delayed mailing (September 2022). This will illustrate background trends in prescribing patterns.

3. **Relative Risk:** Prescribing in the early and delayed intervention groups will be compared 6 months pre/post intervention. A 4-way comparison of numerators during the pre/post periods between the early and delay groups will provide an odds ratio that approximates the relative risk.[xiv,xv] Do this for each of the four study comparisons listed in Section 4.

Acute cystitis episodes = n

Outcome Measures	Expected Change	Intervention Physicians: Time Period Pre YES	Intervention Physicians: Time Period Pre NO	Intervention Physicians: Time Period Post YES	Intervention Physicians: Time Period Post NO	Delayed Contol Physicians: Time Period Pre YES	Delayed Contol Physicians: Time Period Pre NO	Delayed Contol Physicians: Time Period Post YES	Delayed Contol Physicians: Time Period Post NO	Crude OR	Adjusted OR	95% CL
Nitrofurantoin	+	a	b	c	d	e	f	g	h			
Ciprofloxacin	-											
TMP_SMX	-											
Other	-											
No Treatment	n/c											

$$\text{Crude OR} = \left[\frac{(c * h)}{(g * d)}\right]$$

Evaluation is a 4-way comparison: the ratio of change in the early group between pre and post intervention is compared to the same ratio of change in the delayed group.

$$\text{Adjusted OR} = \frac{\text{Crude OR}}{\left[\frac{(a * f)}{(e * b)}\right]}$$

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2. Dormuth 2012. A randomized trial assessing the impact of a personalized feedback portrait on statin prescribing in primary care. *J Contin Educ Health Prof.*

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