Supplemental Online Content

Schwartz KL, Ivers N, Langford BJ, et al. Effect of antibiotic-prescribing feedback to high-volume primary care physicians on number of antibiotic prescriptions: a randomized clinical trial. *JAMA Intern Med*. Published online July 6, 2021. doi:10.1001/jamainternmed.2021.2790

eFigure 9. Forest plot showing subgroup analysis of duration letter compared to control for the outcome of total antibiotic use

eFigure 10. Forest plot showing subgroup analysis of the initiation or duration letters compared to control for the outcome of total antibiotic use

eFigure 11. Forest plot showing subgroup analysis of the initiation or duration letters compared to control for the outcome of prolonged antibiotic duration

This supplemental material has been provided by the authors to give readers additional information about their work.

eAppendix. Initiation and Duration Letters

***Initiation* Letter**

Public Health Ontario | Santé publique Ontario SGFP GENERAL & FAMILY PRACTICE Tools and resources from: Choosing Wisely Ontario

November 23, 2018

Dr. Jane Smith
123 Family Doctor Ave.
Toronto, ON
M1N 2O3

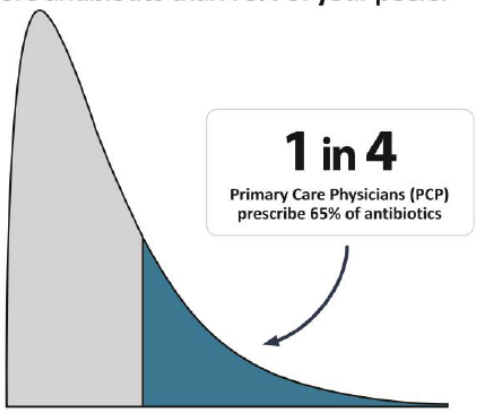
Dear Dr. Smith

Every day, family doctors like you are doing everything you can to help your patients become and stay healthy. Choosing when and how you prescribe antibiotics is a crucial decision-making step, especially during flu season. That's why we're writing to you personally, to support you in prescribing antibiotics appropriately for your patients.

Across care settings, research has shown that practice habits and expectations around antibiotic prescribing are leading causes of over-prescription. Knowing where each of us are on the spectrum of prescribing habits provides a chance to reflect and consider changes.

How you prescribe antibiotics compared to your peers

You are receiving this letter because you prescribe more antibiotics than 75% of your peers.



As context, it might be useful for you to be aware that **you're one of the 25% of primary care physicians who prescribe 65% of antibiotics.** Reviewing the reasons why that may be happening, and considering how unnecessary prescriptions can be avoided are important ways to improve the health of your patients. Enclosed, you'll find tools and information to help reduce antibiotics safely.

Aside from the immediate risks of adverse reactions, research shows us that antibiotics are overprescribed for many respiratory infections, and this is contributing to growing antibiotic resistance in many of our communities. We're putting patients and families at risk when we over-prescribe antibiotics. Each time you're faced with the choice, you'll now have options that make our communities' future safer, so we have antibiotics that still work when we really need them.

Public Health Ontario | Santé publique Ontario SGFP General & Family Practice Tools and resources from: Choosing Wisely Ontario

With your own eyes, you've seen how medical treatments have come a long way in recent decades. New and growing bodies of evidence give us more reassurance that we're doing the right thing when we choose to avoid or delay initiating antibiotics. **Enclosed you'll find a quick reference guide from Choosing Wisely Canada with tools and information to help you decide if you need to initiate antibiotics in clinical settings.** This gives you options to help safely reduce the medication and side effect burden for your patients.

By taking on the challenges to improve their care for patients, family physicians have shown incredible adaptive skills and abilities. We see the evidence in the greater depth and breadth of care you provide every day. Your commitment to assess and improve the quality of care your patients receive can be seen in your daily efforts, and there are resources to support you to achieve that goal.

How can you receive a confidential practice report from Health Quality Ontario to support you in caring for your patients?

As of right now, 3000+ of your peers have signed up to receive MyPractice Primary Care reports. If you're a non-salaried family physician, visit this website to sign up and see what indicators are currently available for your practice.
Use this link or scan the barcode with your smart phone www.hqontario.ca/pc-sign-up.

Thanks for all you do to keep improving the care you provide for your patients! Each step you take in our shared fight against antimicrobial resistance helps to improve outcomes for our patients and communities.

Sincerely,

Dr. Gary Garber MD FRCPC
Chief, Infection Prevention and Control
Public Health Ontario

Dr. Asad Razzaque, MD CCFP
Family Physician
Chair, OMA Section on General and Family Practice

The data for this letter is derived from IQVIA Xponent™. If you have questions about this letter or wish to opt-out of future letters please email the Public Health Ontario antimicrobial stewardship team: asp@oahpp.ca

Public Health Ontario | Santé publique Ontario

SGFP General & Family Practice

Tools and resources from: Choosing Wisely Ontario

How can you optimize antibiotic prescribing for acute uncomplicated respiratory infections?

Here's some helpful tips endorsed by Choosing Wisely Canada. For more information and resources, visit: **choosingwiselycanada.org/antibiotics**

Syndrome	Criteria for antibiotics in Canadian primary care settings
Otitis media in vaccinated children >6 months	Perforated tympanic membrane with purulent discharge or a bulging tympanic membrane with either: • fever ≥39°C OR • moderately or severely ill OR • symptoms lasting > 48 hours
Pharyngitis	Centor score is ≥ 2 AND throat swab culture (or rapid antigen test if available) confirms presence of Group A Streptococcus. Don't perform throat swabs at all for patients with Centor score ≤ 1, OR if there are symptoms of a viral infection such as rhinorrhea, oral ulcers or hoarseness.
Sinusitis	Patient has at least 2 of the below PODS symptoms, one of those being O or D AND • Symptoms lasting greater than 7-10 days OR • The symptoms are severe OR • There is no response after a 72 hour trial with nasal corticosteroids. **P:** Facial Pain/pressure/fullness; **O:** Nasal Obstruction; **D:** Purulent/ discolored nasal or postnasal Discharge; **S:** Hyposmia/anosmia (Smell)
Pneumonia	Objective evidence on a chest x-ray if available.
Upper respiratory infection (Common cold)	Not indicated unless there is clear evidence of secondary bacterial infection (see the recommendations for otitis media, pharyngitis, sinusitis, pneumonia).
Bronchitis/asthma	Not indicated
Acute exacerbation of Chronic Obstructive Pulmonary Disease	Increase in sputum purulence with either increase in sputum volume and/or increased dyspnea.

***Duration* letter**

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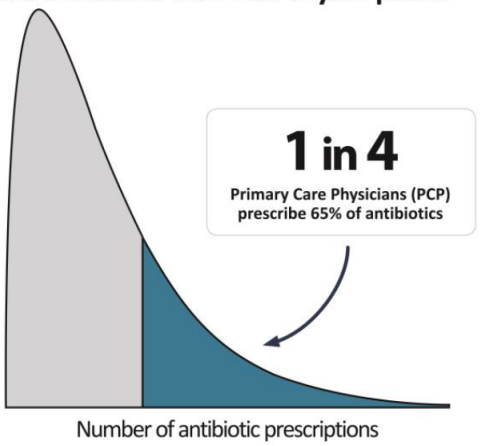

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Research shows us that antibiotics are frequently prescribed for too long, and this is contributing to adverse reactions and growing antibiotic resistance in many of our communities. We're putting patients and families at risk when we over-prescribe antibiotics. Each time you're faced with the choice, you'll now have options that make our communities' future safer, so we have antibiotics that still work when we really need them.

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With your own eyes, you've seen how medical treatments have come a long way in recent decades. New and growing bodies of evidence give us more reassurance that we're doing the right thing when we optimize antibiotic prescribing. **Enclosed you'll find a quick reference guide on appropriate antibiotic durations supported by Choosing Wisely Canada.**

By taking on the challenges to improve their care for patients, family physicians have shown incredible adaptive skills and abilities. We see the evidence in the greater depth and breadth of care you provide every day. Your commitment to assess and improve the quality of care your patients receive can be seen in your daily efforts, and there are resources to support you to achieve that goal.

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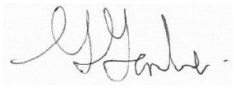

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How can you optimize antibiotic prescribing durations?

Antibiotics are often prescribed for too long. As you may know, unnecessarily prolonged courses of antibiotics lead to antibiotic related side effects (e.g., diarrhea, allergic reactions) and resistance. The majority of bacterial infections can be treated with 7 days of antibiotics or less, however more than one third of antibiotic prescriptions by primary care physicians in Ontario are for more than 7 days.

These are the recommended antibiotic durations for treating uncomplicated bacterial infections based on most current evidence for the majority of patients:

Syndrome	Recommended duration
Acute sinusitis	5 days
Pneumonia	5 days
Cellulitis	5-7 days
Otitis Media	5 days (10 days in children <2 years)
Cystitis	3-5 days
Pyelonephritis	7 days
Acute exacerbation of Chronic Obstructive Pulmonary Disease	5 days

eTable 1: Oral Outpatient Antibiotic Drugs Included in the Various Antibiotic Classes

Antibiotic Class	Antibiotic Drug Name	Most Common Indication for Use
Penicillin without Beta-lactamase Inhibitors	Amoxicillin Ampicillin Cloxacillin Penicillin V potassium Pivmecillinam	Respiratory infections
Penicillin with Beta-lactamase Inhibitors	Amoxicillin-clavulanate	Respiratory infections
First Generation Cephalosporins	Cefadroxil Cephalexin	Skin infections
Second/Third Generation Cephalosporins	Cefaclor Cefdinir Cefixime Cefpodoxime Cefprozil Ceftibuten Cefuroxime	Respiratory infections
Second Generation Fluoroquinolones	Gemifloxacin Ciprofloxacin Norfloxacin Ofloxacin	Urinary infections
Third Generation Fluoroquinolones	Levofloxacin Moxifloxacin	Respiratory infections
Macrolides	Azithromycin Clarithromycin Erythromycin Spiramycin Telithromycin	Respiratory infections

Trimethoprim and/or Sulphonamides	Sulfamethoxazole Sulfamethoxazole-trimethoprim Sulfisoxazole Trimethoprim	Urinary infections
Tetracyclines	Doxycycline Minocycline Tetracycline	Other
Lincosomides	Clindamycin	Skin infections
Nitrofurantoin	Nitrofurantoin	Urinary infections
Metronidazole	Metronidazole	Other
Others	Rifabutin Rifampin Fidaxomicin Fosfomycin Linezolid Methenamine Tedizolid Vancomycin	Other

eTable 2: Comparison of primary care physicians in Ontario, Canada included and not included in this intervention

Physician variables	Primary care physicians not included in study (n=9,388)	Physicians randomized to receive a letter (n=3000)	p-value
Gender			<0.0001
Male	4456 (47.5%)	2086 (69.5%)	
Female	4932 (52.5%)	914 (30.5%)	
Years from medical graduation			<0.0001
≤10 years	2022 (21.5%)	366 (12.2%)	
11-24 years	2911 (31%)	791 (26.4%)	
≥25 years	4455 (47.5%)	1843 (61.4%)	
Practice region			<0.0001
Rural	747 (8%)	177 (5.9%)	
Urban	8641 (92%)	2823 (94.1%)	
Antibiotic prescriptions in the previous 12 months, median (IQR)	182 (74 to 304)	740 (562 to 1160)	
Proportion of antibiotics prescribed to patient age and sex groups (%)			<0.0001
<18 year males	7.5%	9.4%	
<18 year females	7.8%	9.5%	
18-64 year males	18.1%	21.9%	
18-64 year females	36.6%	36.9%	
≥65 year males	10.9%	8.6%	
≥65 year females	19.2%	13.6%	

eTable 3: Absolute mean number of total antibiotic prescriptions and marginal differences compared to controls

Group	Number of Antibiotic Prescriptions, mean (SD)		Marginal difference compared to control	
	Baseline	12 months	Marginal RR (97.5%CI)	p-value
Control	988 (723)	881 (695)	-	-
All letters	994 (737)	850 (721)	-37.0 (-70.8 to -1.7)*	0.017
Initiation letter	988 (732)	849 (730)	-32.0 (-68.1 to 5.8)	0.423
Duration letter	1,000 (743)	851 (711)	-41.9 (-78.5 to -3.6)*	<0.001

*Statistically significant at p<0.025; SD=standard deviation; RR=relative risk; CI=confidence interval

eTable 4: Absolute mean number of prolonged duration (>7 days) antibiotic prescriptions and marginal differences compared to controls

Group	Number of Prolonged (>7 days) Antibiotic Prescriptions, mean (SD)		Marginal difference compared to control	
	Baseline	12 months	Marginal RR (97.5%CI)	p-value
Control	347 (430)	299 (351)	-	-
All letters	333 (389)	278 (355)	-14.9 (-28.3 to -0.9)*	0.017
Initiation letter	333 (384)	288 (372)	-5.4 (-20.1 to 10.0)	0.423
Duration letter	332 (393)	268 (337)	-24.1 (-38.7 to -8.6)*	<0.001

*Statistically significant at p<0.025; SD=standard deviation; RR=relative risk; CI=confidence interval

eTable 5: Absolute mean antibiotic costs (CAN$) and marginal differences compared to controls

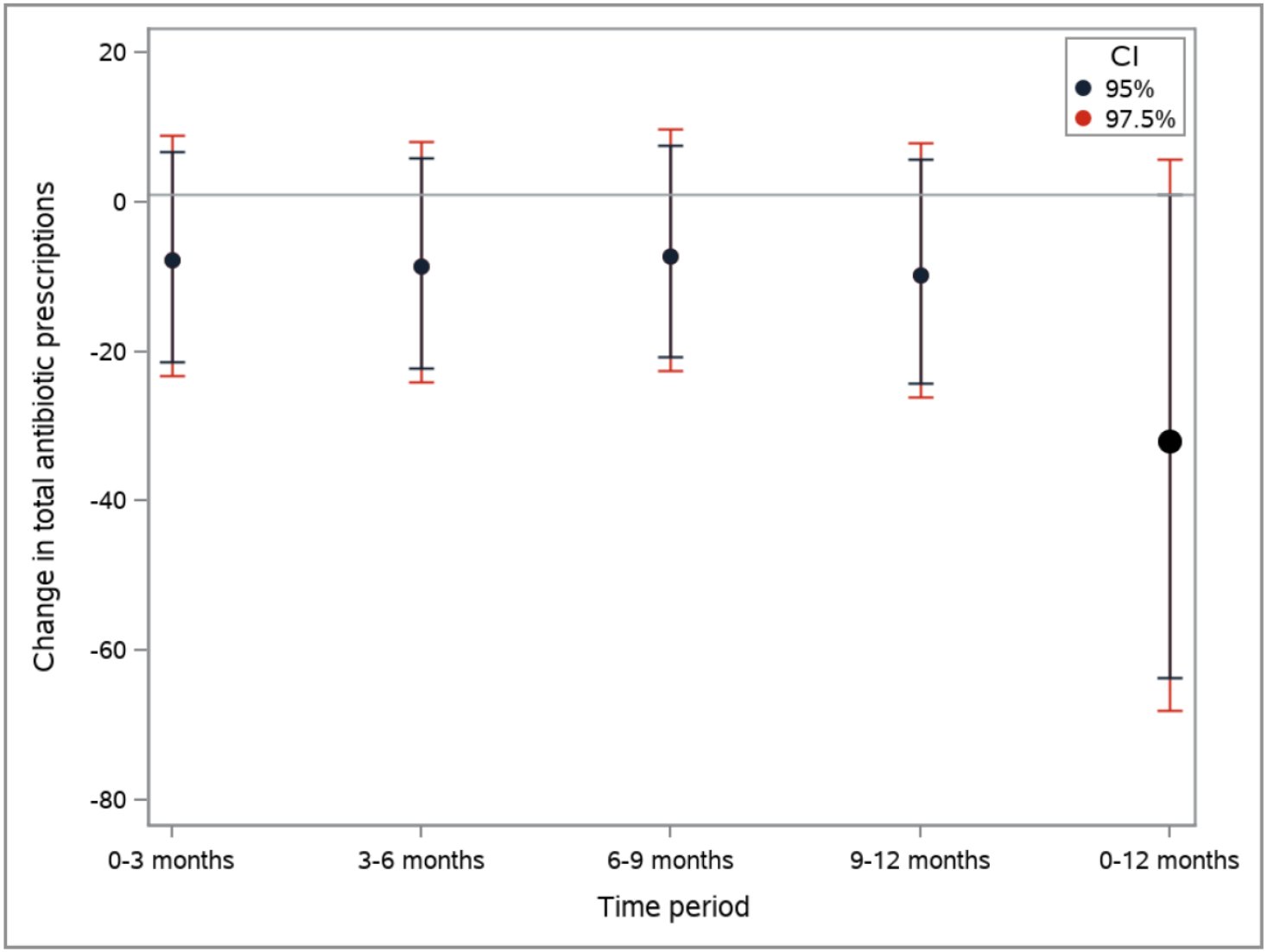
Group	Drug costs, mean (SD)		Marginal difference compared to control	
	Baseline	12 months	Marginal RR (97.5%CI)	p-value
Control	$14,166 ($11,421)	$12,615 ($10,025)	-	-
All letters	$14,338 ($11,162)	$12,181 ($10,703)	-$571 (-$1138 to $21)	0.031
Initiation letter	$14,206 ($10,859)	$12,269 ($10,740)	-$370 (-$973 to $265)	0.187
Duration letter	$14,470 ($11,459)	$12,093 ($10,669)	-$771 (-$1369 to -$140)*	0.006

*Statistically significant at p<0.025; SD=standard deviation; RR=relative risk; CI=confidence interval

eTable 6: Regression model coefficients

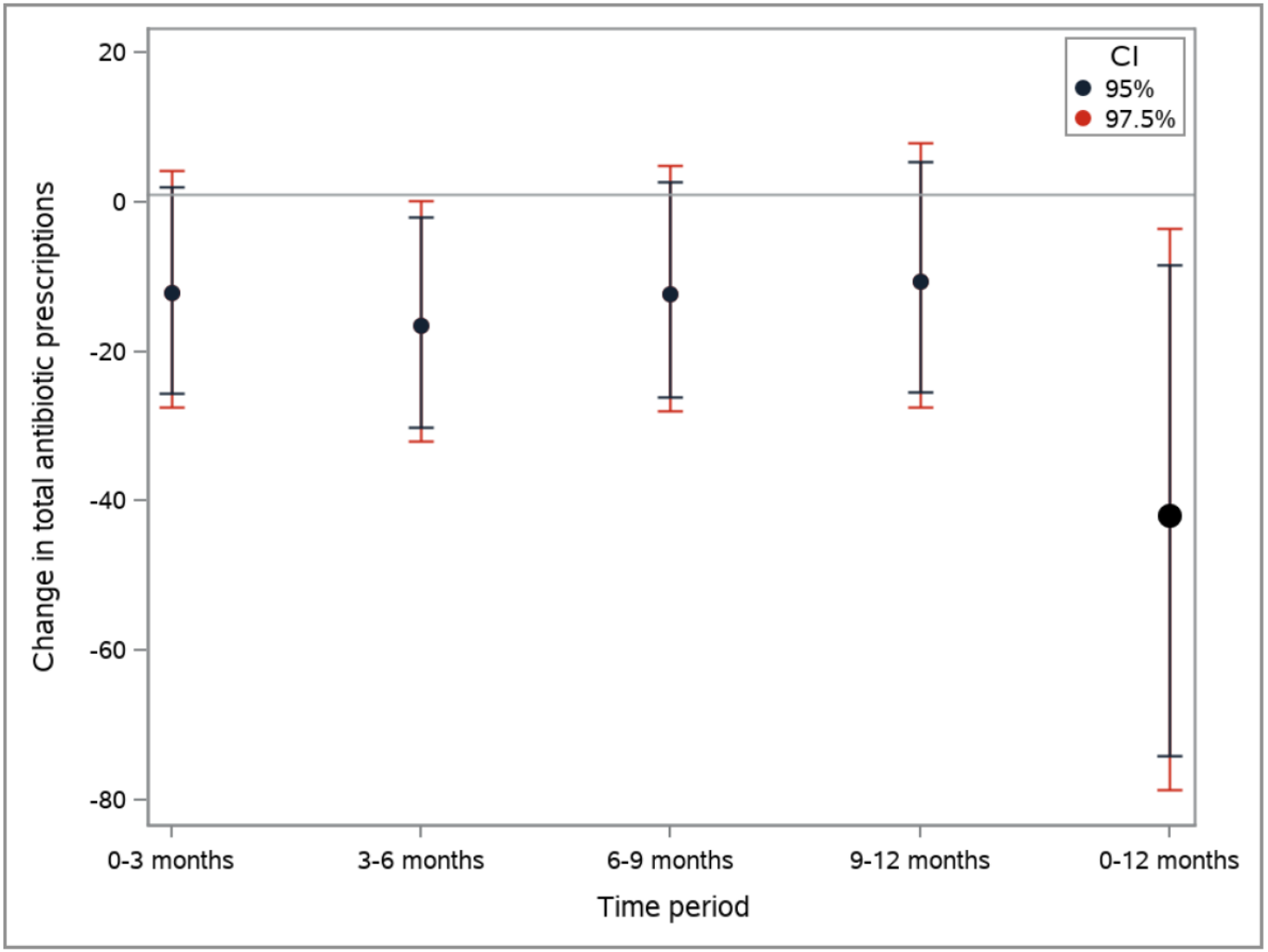
Group	Estimate	Standard deviation	Lower 97.5% confidence interval	Upper 97.5% confidence interval	Z	p-value
Total antibiotic outcome						
Intercept	6.901	0.013	6.873	6.929	548.08	<0.001
Time (12 months)	-0.118	0.017	-0.155	-0.080	-7.04	<0.001
Initiation letter*time	-0.037	0.019	-0.081	0.007	-1.91	0.057
Duration letter*time	-0.049	0.020	-0.093	-0.004	-2.45	0.014
Prolonged duration outcome						
Intercept	5.812	0.020	5.766	5.857	289.13	<0.001
Time (12 months)	-0.137	0.019	-0.179	-0.094	-7.21	<0.001
Initiation letter*time	-0.018	0.023	-0.070	0.033	-0.80	0.423
Duration letter*time	-0.084	0.024	-0.139	-0.029	-3.44	0.001
Cost outcome						
Intercept	9.569	0.013	9.539	9.599	719.25	<0.001
Time (12 months)	-0.120	0.020	-0.165	-0.075	-5.96	<0.001
Initiation letter*time	-0.030	0.023	-0.080	0.021	-1.32	0.187
Duration letter*time	-0.063	0.023	-0.115	-0.011	-2.72	0.007

eFigure 1: Change in total antibiotic prescriptions over time between the *initiation* letter and control



CI = confidence interval

eFigure 2: Change in total antibiotic prescriptions over time between the *duration* letter and control



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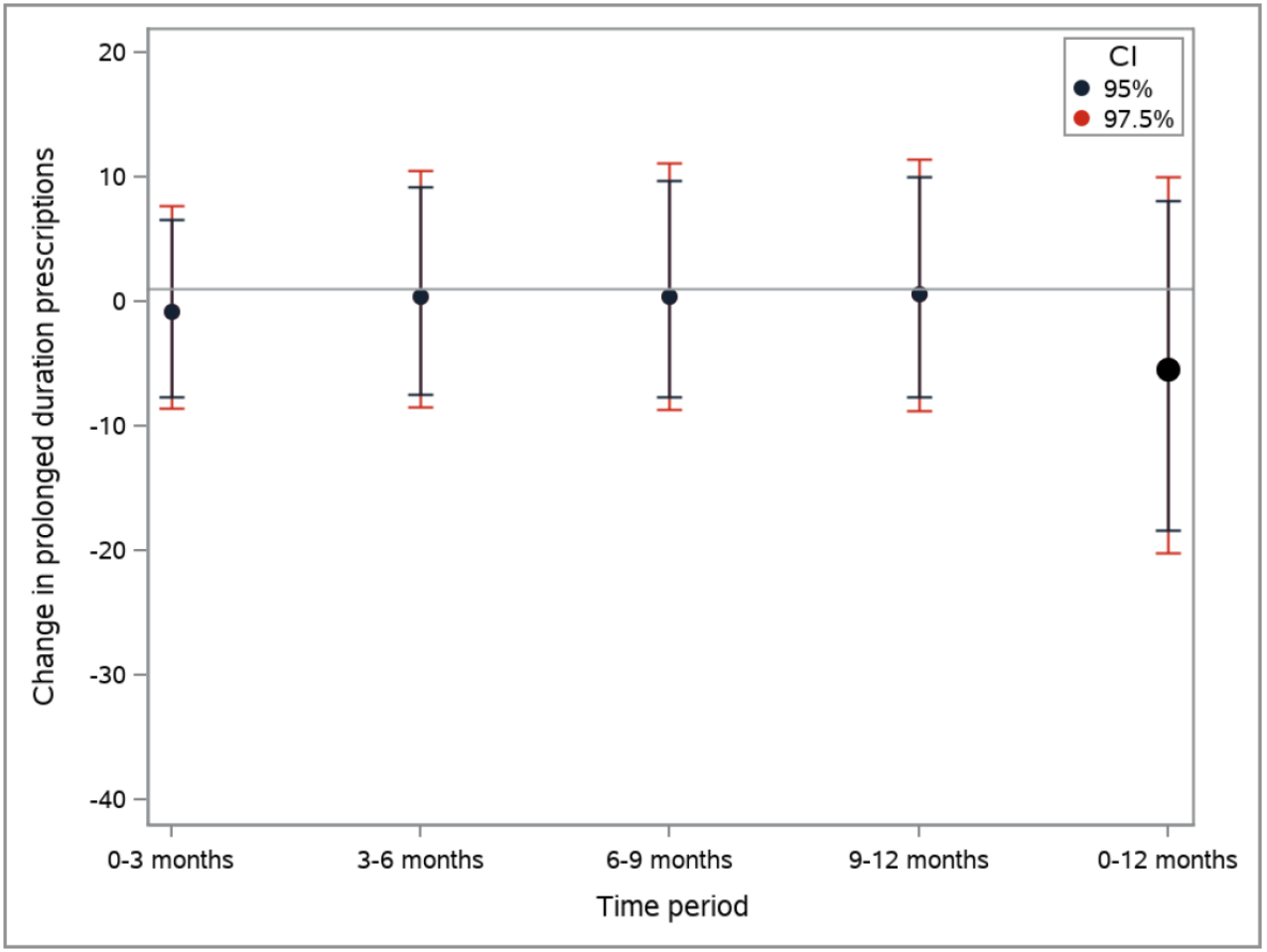
eFigure 3: Change in prolonged duration prescriptions over time between the *initiation* letter and control



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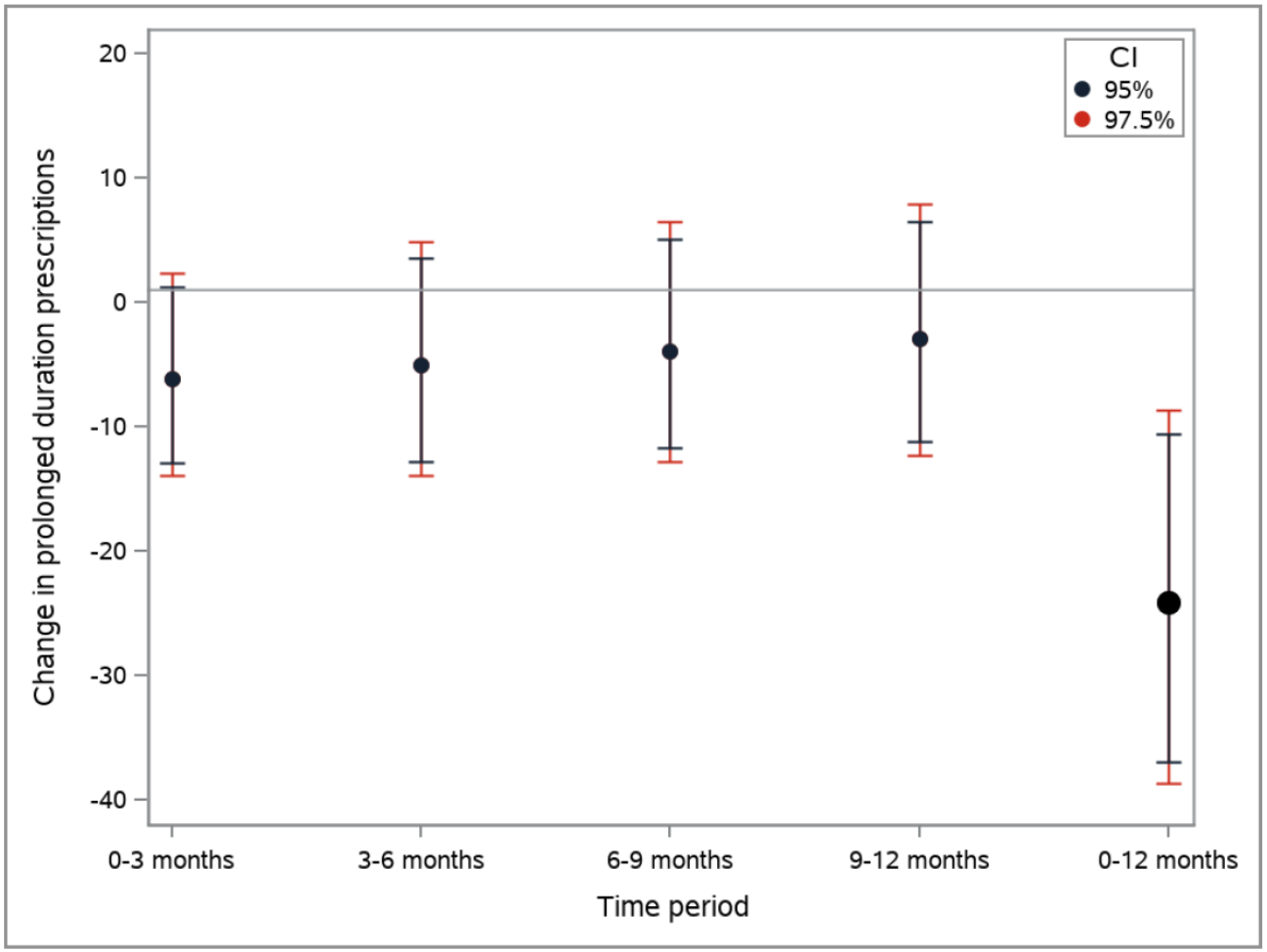
eFigure 4: Change in prolonged duration prescriptions over time between the *duration* letter and control



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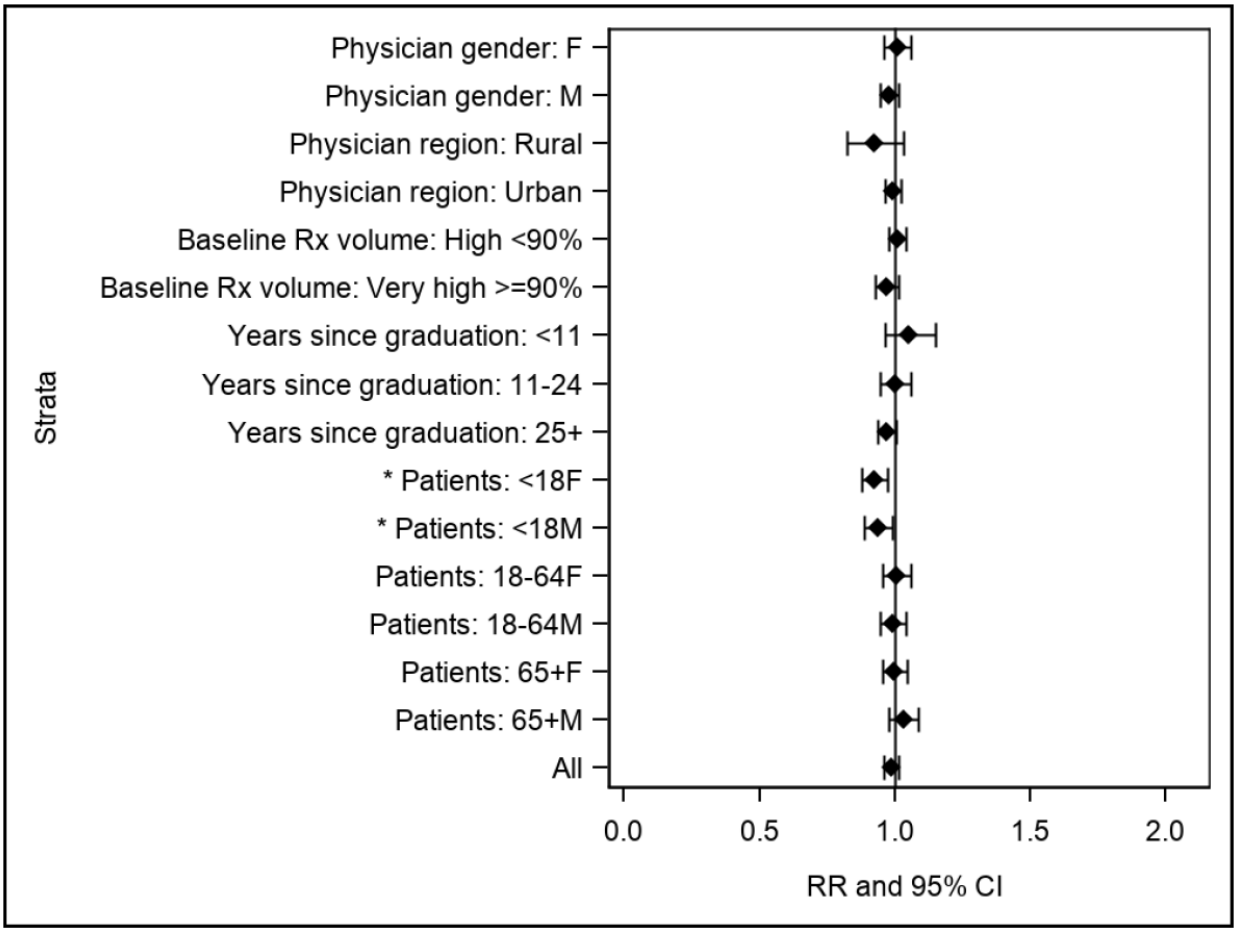
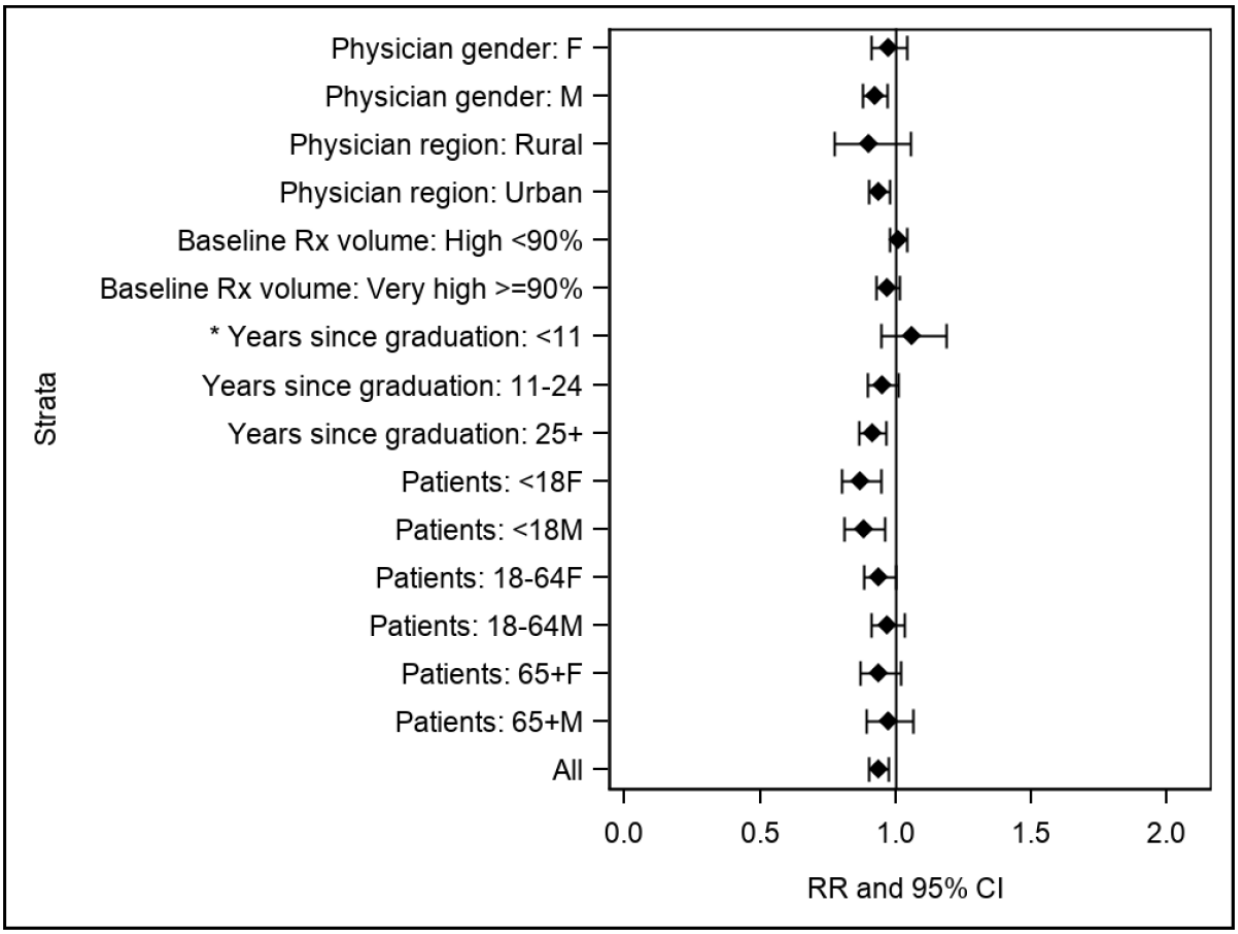
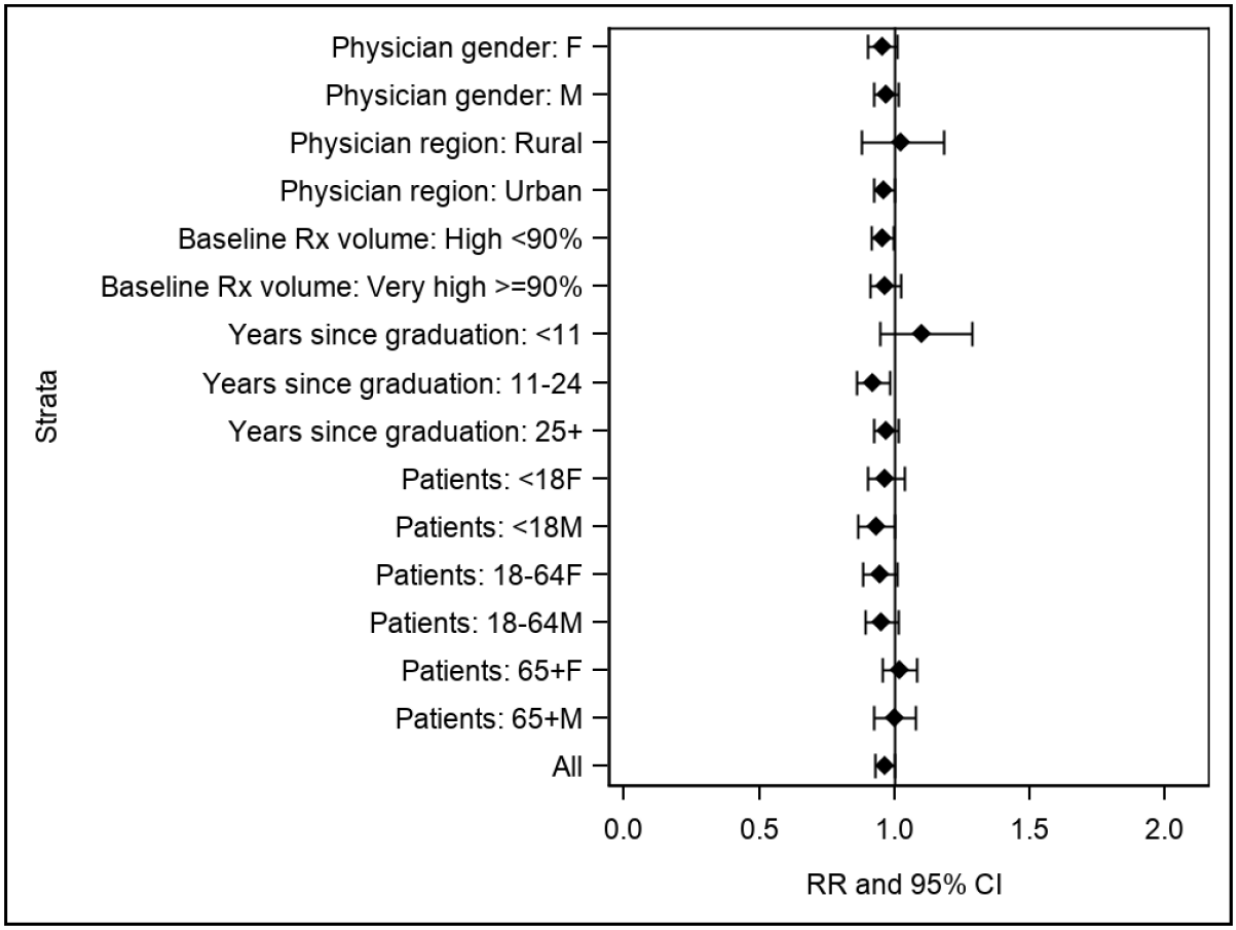


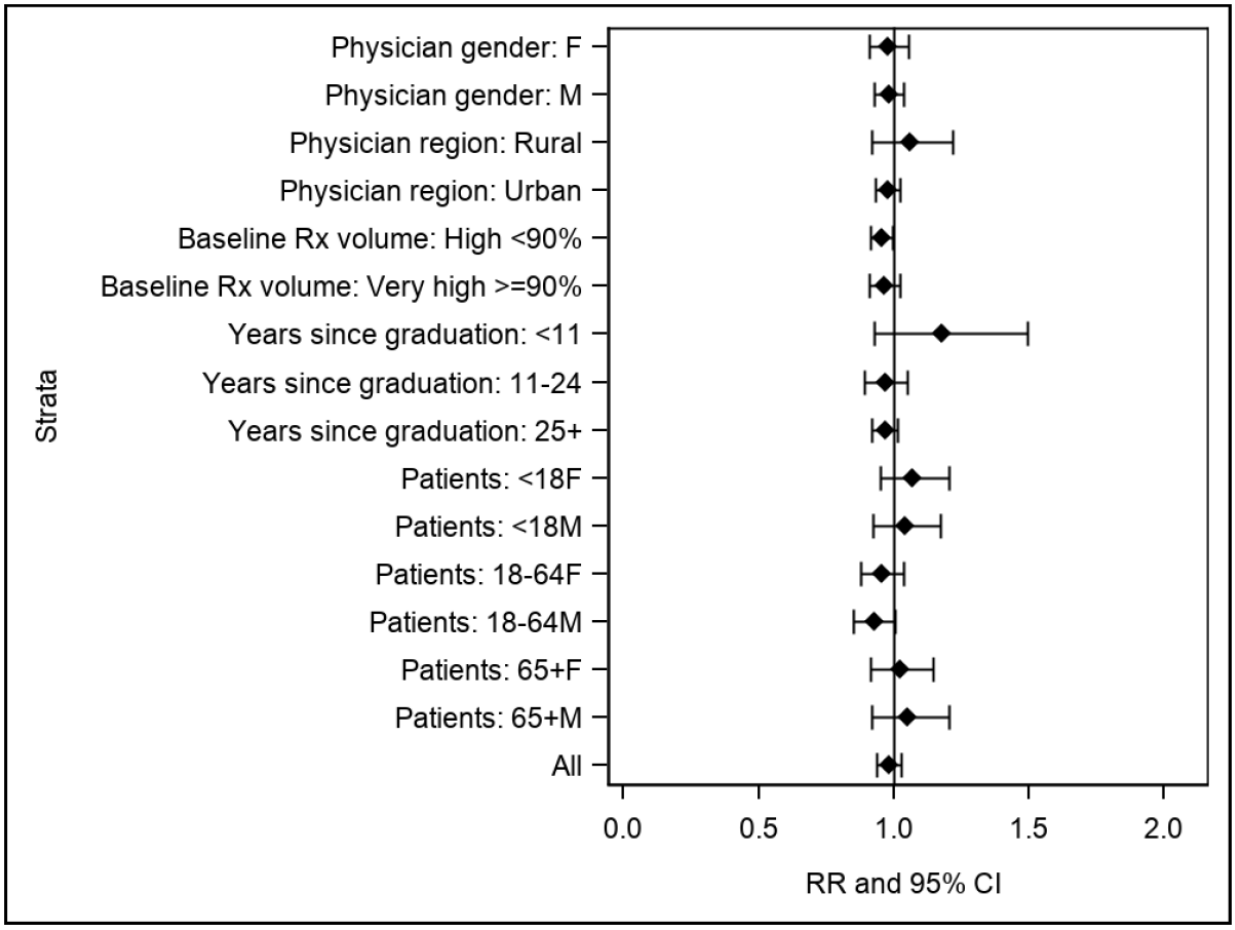
eFigure 5: Forest plot showing subgroup analysis of the *duration* letter compared to the *initiation* letter for the outcome of total antibiotic use. Rx=antibiotic prescriptions, F=female, M=male; *$p_{interaction}$<0.05



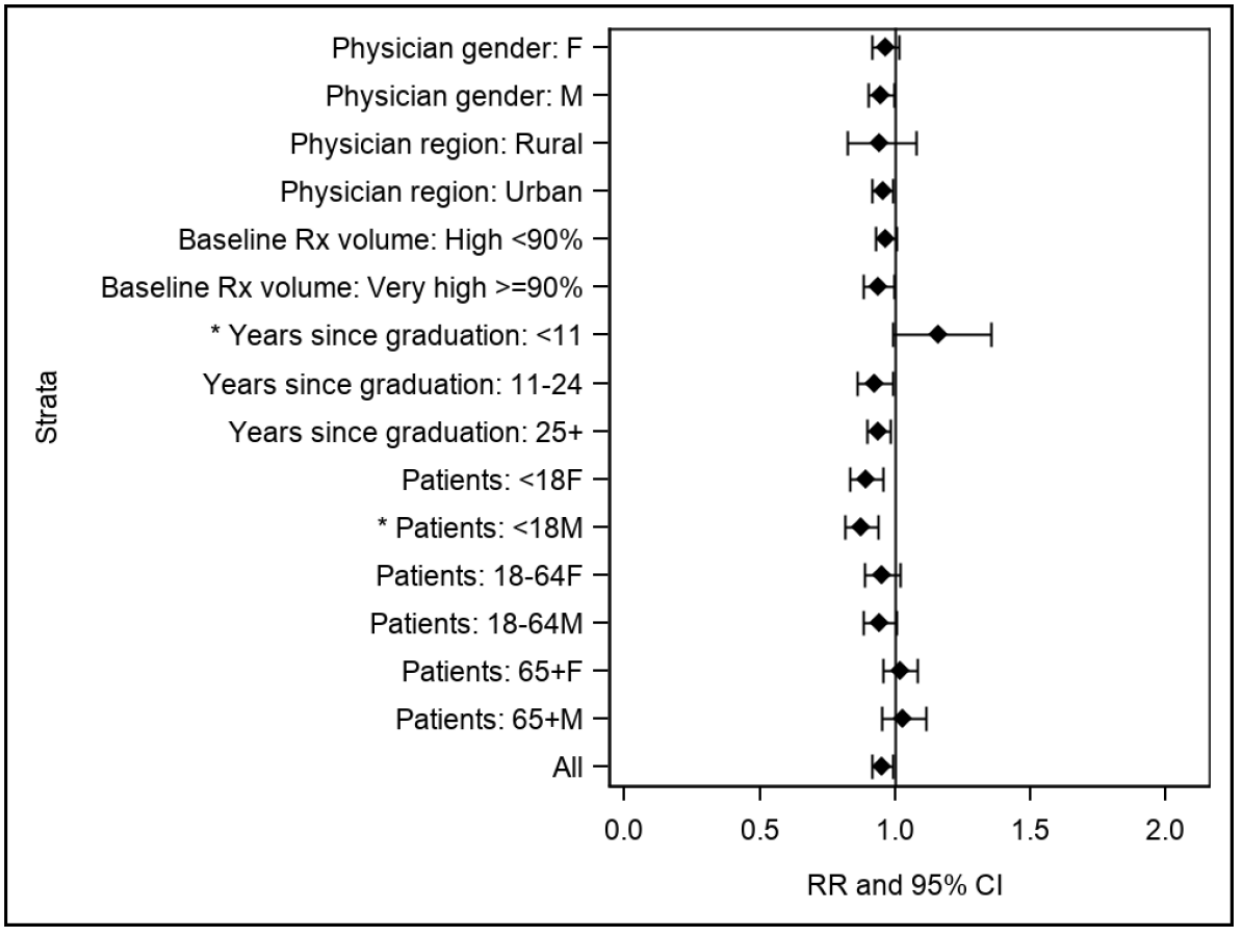
eFigure 6: Forest plot showing subgroup analysis of *duration* letter compared to the *initiation* letter for the outcome of prolonged antibiotic duration. Rx=antibiotic prescriptions, F=female, M=male; *$p_{interaction}$<0.05



eFigure 7: Forest plot showing subgroup analysis of the *initiation* letter compared to control for the outcome of total antibiotic use. Rx=antibiotic prescriptions, F=female, M=male; *$p_{interaction}$<0.05



eFigure 8: Forest plot showing subgroup analysis of *initiation* letter compared to control for the outcome of prolonged antibiotic duration. Rx=antibiotic prescriptions, F=female, M=male; *$p_{interaction}$<0.05



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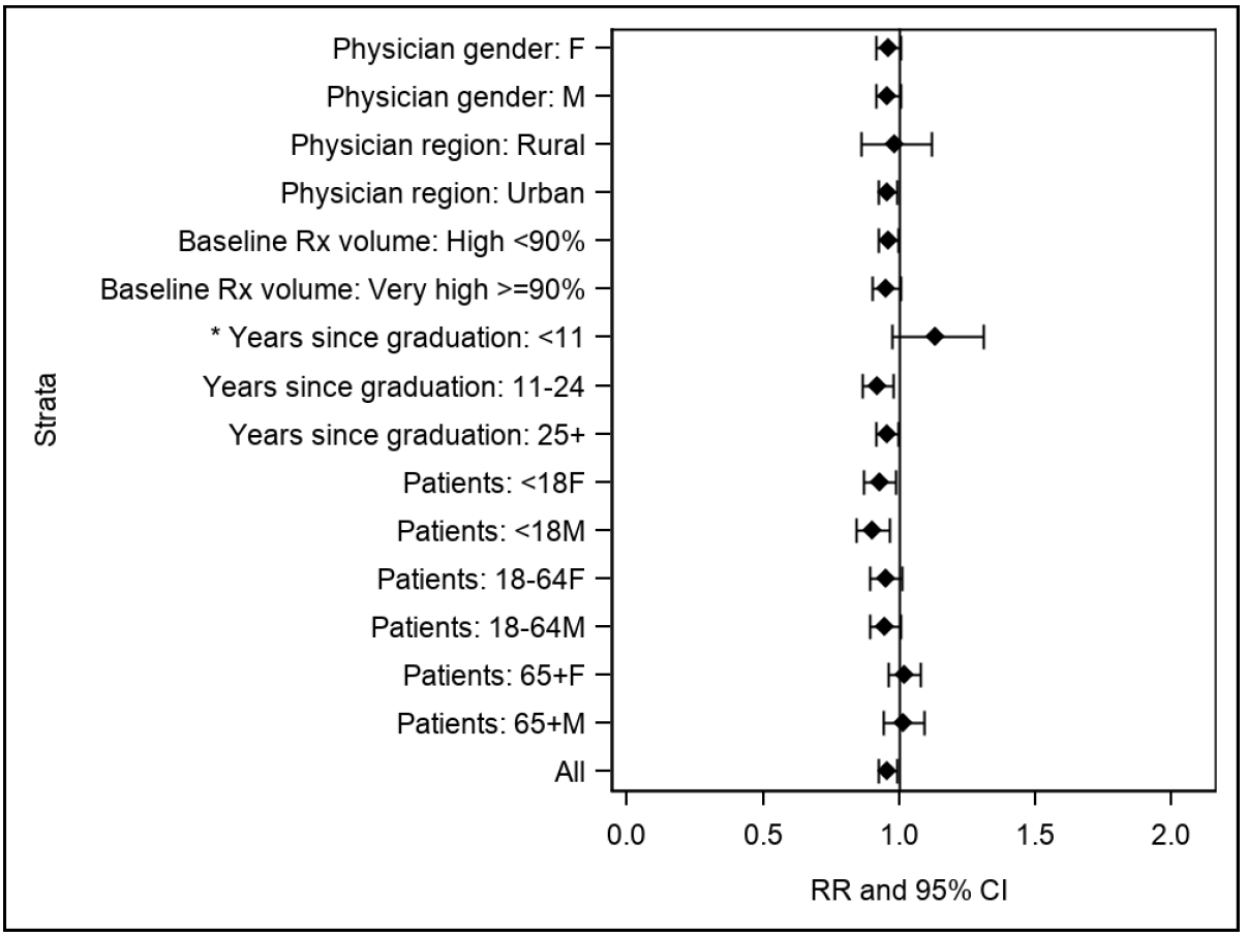

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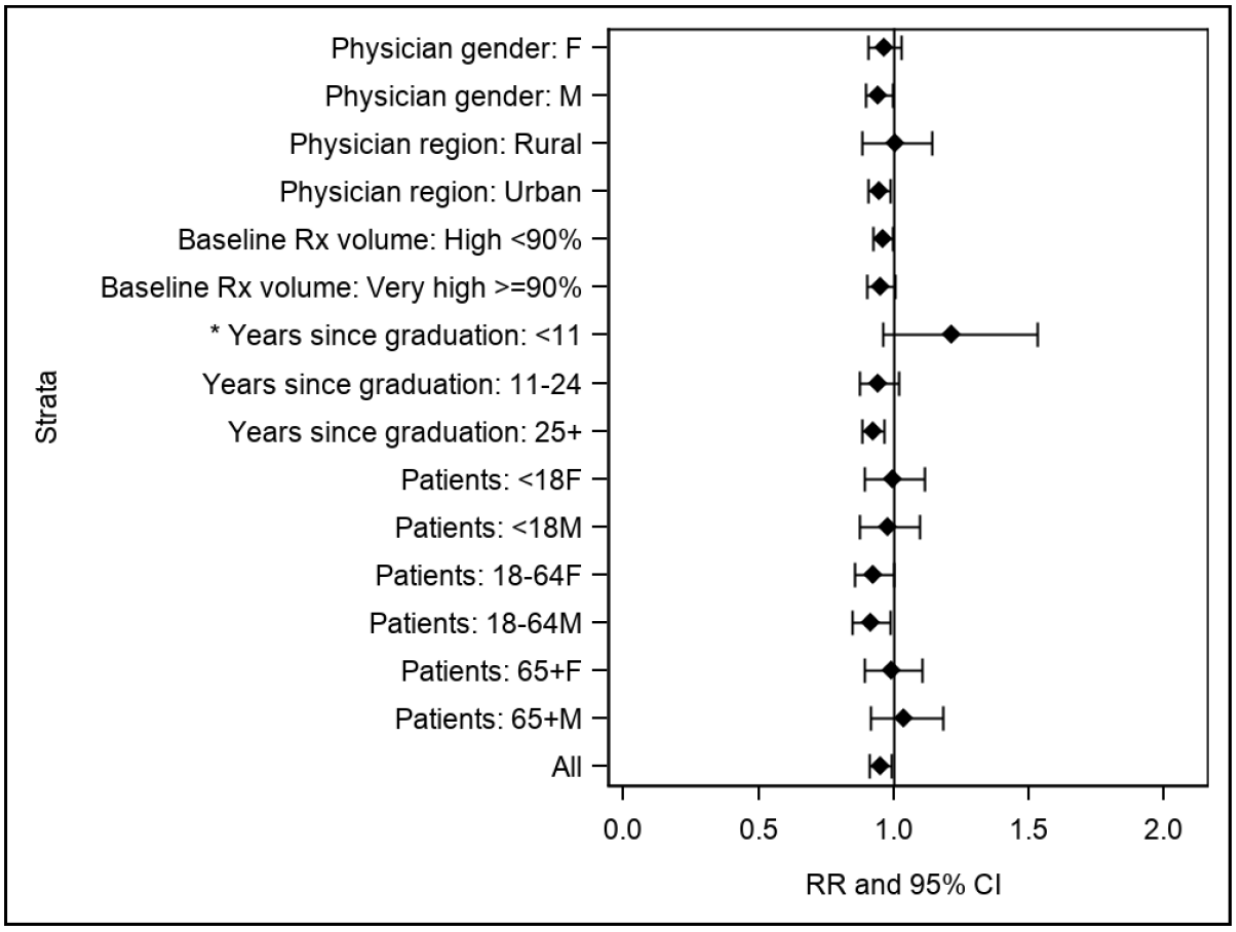

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