

Supplement 2

Meeker D, Linder JA, Fox CR, et al. Effect of behavioral interventions on inappropriate antibiotic prescribing among primary care practices: a randomized clinical trial. *JAMA*. doi:10.1001/jama.2016.0275.

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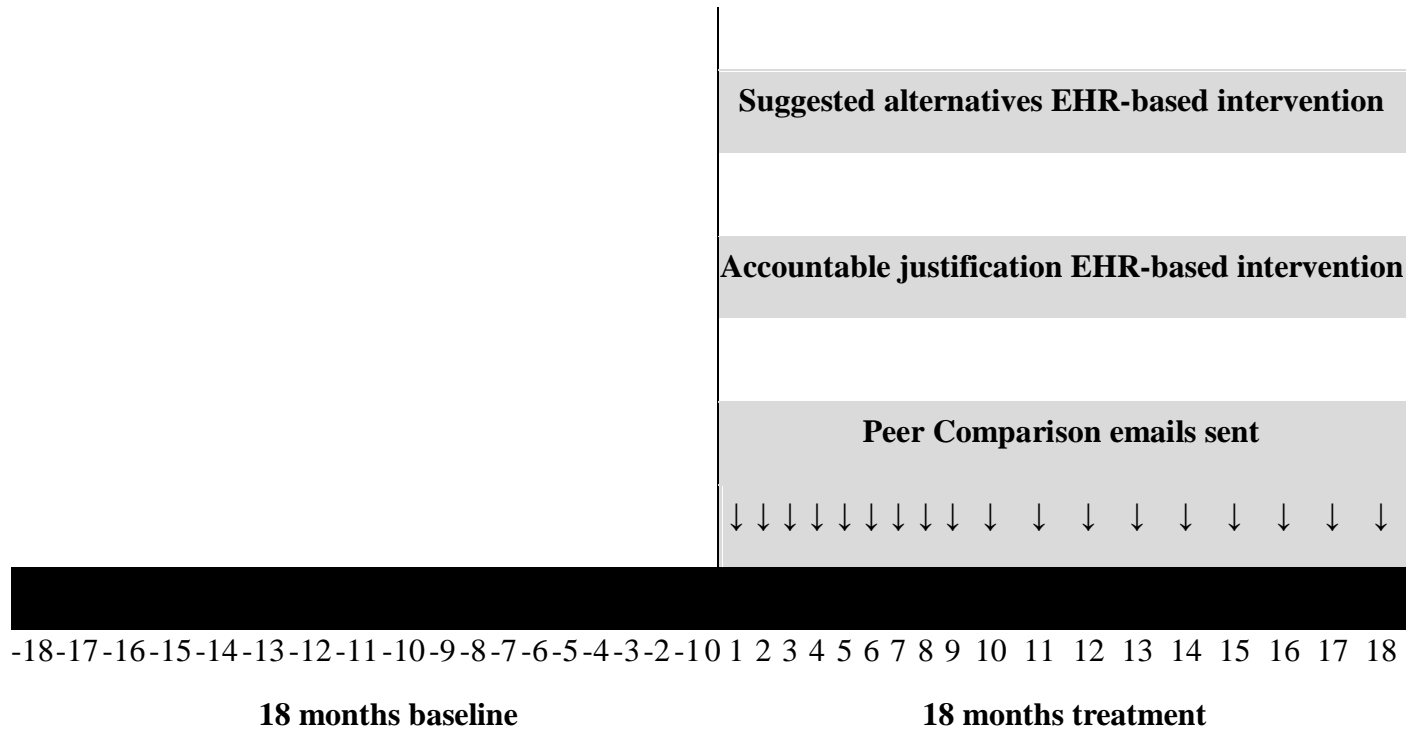
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This supplementary material has been provided by the authors to give readers additional information about their work.

eFigure 1. Study Timeline (See excel spreadsheet for original version)



eTable 1. Qualifying Revisit Diagnostic Codes

ICD 9 code	description	category
390-392	Acute rheumatic fever code family	acute rheumatic fever
528.3	Cellulitis and abscess--Cellulitis of mouth (floor), Ludwig's angina	Head and Neck Abscess
324	Intracranial abscess	Head and Neck Abscess
475	Peritonsillar abscess	Head and Neck Abscess
682.1	Other cellulitis and abscess, neck	Head and Neck Abscess
478.21	Cellulitis of pharynx or nasopharynx	Head and Neck Abscess
478.22	Parapharyngeal abscess	Head and Neck Abscess
478.24	Retropharyngeal abscess	Head and Neck Abscess
478.71	Cellulitis and perichondritis of larynx	Head and Neck Abscess
478.29	Other Abscess of pharynx or nasopharynx	Head and Neck Abscess
478.9	Abscess of trachea	Head and Neck Abscess
325	Phlebitis and thrombophlebitis of intracranial venous sinuses	Head and Neck Abscess
324	Intracranial Abscess	Head and Neck Abscess
040.3	Necrobacillosis	Lemierre's Syndrome
383	Acute mastoiditis	Mastoiditis
383	Acute mastoiditis without complications	Mastoiditis
383.01	Subperiosteal abscess of mastoid	Mastoiditis
383.02	Acute mastoiditis with other complications	Mastoiditis/Gradenigo's syndrome
320	Bacterial meningitis	meningitis
320	Hemophilus meningitis	meningitis
320.1	Pneumococcal meningitis	meningitis
320.2	Streptococcal meningitis	meningitis
320.3	Staphylococcal meningitis	meningitis

eTable 1. Qualifying Revisit Diagnostic Codes, Continued

ICD 9 code	description	category
320.8	Bacterial meningitis nec	meningitis
320.81	Anaerobic meningitis	meningitis
320.89	Meningitis oth spcf bact	meningitis
320.9	Bacterial meningitis nos	meningitis
321	Other organism meningitis	meningitis
322	Meningitis, unspecified	meningitis
322	Nonpyogenic meningitis	meningitis
322.9	Meningitis not otherwise specified	meningitis
376.01	Orbital cellulitis	cellulitis eye
073	Ornithosis pneumonia	pneumonia
481	Pneumococcal pneumonia	pneumonia
482	Other bacterial pneumonia	pneumonia
482	K. pneumoniae pneumonia	pneumonia
482.1	Pseudomonal pneumonia	pneumonia
482.2	H. influenzae pneumonia	pneumonia
482.3	Streptococcal pneumonia	pneumonia
482.31	Pneumonia strptococcus a	pneumonia
482.32	Pneumonia strptococcus b	pneumonia
482.39	Pneumonia oth strep	pneumonia
482.4	Staphylococcal pneumonia	pneumonia
482.49	Staph pneumonia nec	pneumonia
482.8	Bacterial pneumonia nec	pneumonia
482.81	Pneumonia anaerobes	pneumonia
482.82	Pneumonia e coli	pneumonia

eTable 1. Qualifying Revisit Diagnostic Codes, Continued

ICD 9 code	description	category
482.89	Pneumonia oth spcf bact	pneumonia
482.9	Bacterial pneumonia nos	pneumonia
483	pneumonia: organism nec	pneumonia
483	Pneu mycplsm pneumoniae	pneumonia
483.1	Pneumonia d/t chlamydia	pneumonia
484.3	Pneumonia in whoop cough	pneumonia
484.5	Pneumonia in anthrax	pneumonia
485	Bronchopneumonia org nos	pneumonia
486	pneumonia, organism nos	pneumonia
487	influenza with pneumonia	pneumonia
997.31	ventltr assoc pneumonia	pneumonia
771.81	nb septicemia [sepsis]	sepsis
995.91	sepsis	sepsis
995.92	severe sepsis	sepsis

eTable 2. Sample Characteristics During the 18-Month Baseline Period

Patient characteristics	Overall	Control	Suggested Alternatives	Accountable Justification	Peer Comparison	Suggested Alternatives + Accountable Justification	Suggested Alternatives + Peer Comparison	Accountable Justification + Peer Comparison	Suggested Alternatives + Accountable Justification + Peer Comparison
Mean age, years (SD)	47 (17)	48 (16)	47 (17)	54 (17)	47 (16)	46 (16)	48 (16)	48 (17)	43 (17)
Male sex, No. (%)	4644 (31)	669 (36)	594 (28)	583 (39)	385 (31)	523 (26)	418 (28)	780 (33)	692 (32)
Race, No. (%)*									
White	12192 (87)	1397 (82)	1654 (82)	1324 (91)	1018 (87)	1648 (87)	1298 (87)	2068 (91)	1785 (88)
Black	566 (4)	60 (4)	115 (6)	51 (4)	50 (4)	69 (4)	84 (6)	46 (2)	91 (5)
Asian	545 (4)	55 (3)	60 (3)	32 (2)	65 (6)	88 (5)	40 (3)	110 (5)	95 (4)
Other Race/Unknown	761 (5)	201 (12)	195 (10)	47 (3)	37 (3)	93 (5)	70 (5)	58 (3)	60 (3)
Hispanic or Latino ethnicity, No. (%)	6460 (44)	883 (47)	738 (35)	492 (33)	459 (37)	758 (38)	787 (52)	1099 (47)	1244 (57)
Insurance type, No (%)*									
Medicare	1585 (14)	187 (13)	209 (13)	204 (20)	111 (12)	207 (13)	133 (12)	321 (17)	213 (13)
State or county subsidized**	4306 (39)	627 (43)	554 (36)	172 (17)	351 (37)	652 (42)	480 (42)	727 (39)	743 (46)

Table 2, Sample Characteristics During the 18-Month Baseline Period, Continued

Patient characteristics	Overall	Control	Suggested Alternatives	Accountable Justification	Peer Comparison	Suggested Alternatives + Accountable Justification	Suggested Alternatives + Peer Comparison	Accountable Justification + Peer Comparison	Suggested Alternatives + Accountable Justification + Peer Comparison
Private	4921 (44)	619 (43)	775 (50)	534 (51)	454 (48)	658 (43)	471 (41)	771 (42)	639 (39)
Self-pay or other	327 (3)	22 (1)	18 (1)	217 (12)	22 (2)	22 (2)	58 (5)	23 (1)	35 (2)
Number of qualifying visits	14753	1866	2132	1491	1236	1977	1511	2362	2178

*Cell counts may not sum to total due to missing values

**Includes Medicaid and other public payers

eTable 3. Coefficient Estimates From Main Hierarchical Logistic Model to Estimate Intervention Effects on Inappropriate Antibiotic Prescribing Trajectories

Variable	Coefficient	SE	(95% CI)	z	P value
Suggested alternatives	-0.025	0.235	(-0.485,0.435)	-0.11	0.916
Accountable justification	0.105	0.236	(-0.358,0.567)	0.44	0.658
Peer comparison	-0.284	0.242	(-0.758,0.189)	-1.18	0.240
Months in treatment	-0.010	0.008	(-0.025,0.005)	-1.35	0.176
Suggested alternatives × Months in treatment	-0.003	0.006	(-0.015,0.009)	-0.45	0.655
Accountable justification × Months in treatment	-0.029	0.006	(-0.041,-0.017)	-4.72	< 0.001
Peer comparison × Months in treatment	-0.047	0.006	(-0.060,-0.035)	-7.37	< 0.001
Time (months)	-0.031	0.004	(-0.038,-0.024)	-8.81	< 0.001
Constant	-1.145	0.235	(-1.607,-0.683)	-4.86	< 0.001

Note: These coefficient estimates are from the same model used to generate Figure 2.

eTable 4A. Coefficient Estimates for the Fully Interacted Logistic Model Estimated With Robust Standard Errors to Estimate Intervention Effects on Inappropriate Antibiotic Prescribing Trajectories, for Wald Test

Variable	Coefficient	Robust SE*	95% CI	z	P value
Suggested Alternatives	0.506	0.493	(-0.461,1.471)	1.03	0.304
Accountable Justification	-0.205	0.455	(-1.101,0.691)	-0.45	0.652
Peer Comparison	-0.082	0.612	(-1.281,1.121)	-0.13	0.893
Suggested Alternatives × Accountable Justification	-0.389	0.558	(-1.481,0.701)	-0.7	0.485
Suggested Alternatives × Peer Comparison	-1.079	0.693	(-2.441,0.281)	-1.56	0.119
Accountable Justification × Peer Comparison	0.212	0.801	(-1.361,1.781)	0.26	0.792
Suggested Alternatives × Accountable Justification × Peer Comparison	0.539	0.884	(-1.191,2.271)	0.61	0.542
Months in Treatment	-0.012	0.025	(-0.061,0.041)	-0.48	0.628
Suggested Alternatives × Months in Treatment	-0.018	0.033	(-0.081,0.051)	-0.55	0.579
Accountable Justification × Months in Treatment	-0.025	0.029	(-0.081,0.031)	-0.86	0.389
Suggested Alternatives × Accountable Justifications × Months in Treatment	-0.001	0.038	(-0.081,0.071)	-0.02	0.981
Peer Comparison × Months in Treatment	-0.025	0.033	(-0.091,0.041)	-0.76	0.45
Suggested Alternatives × Peer Comparison × Months in Treatment	-0.056	0.048	(-0.151,0.041)	-1.17	0.241
Accountable Justification × Peer Comparison × Months in Treatment	-0.040	0.049	(-0.141,0.061)	-0.82	0.413

eTable 4A, Continued

Variable	Coefficient	Robust SE*	95% CI	z	P value
Suggested Alternatives × Accountable Justification × Peer Comparison × Months in Treatment	0.091	0.063	(-0.031,0.211)	1.44	0.149
Time (months)	-0.023	0.009	(-0.041,-0.011)	-2.59	0.01
Constant	-0.789	0.368	(-1.511,-0.071)	-2.14	0.032

*Robust Standard errors were used in this approach because for the Wald test, the fully interacted hierarchical mixed effects model did not converge

eTable 4B. Coefficient Estimates for the Main Effects Only Logistic Model Estimated With Robust Standard Errors to Estimate Intervention Effects on Inappropriate Antibiotic Prescribing Trajectories, for Wald Test

Variable	Coefficient	Robust SE	95% CI	z	P value
Suggested Alternatives	-0.053	0.257	(-0.557, 0.450)	-0.21	0.835
Accountable Justifications	-0.172	0.244	(-0.651, 0.307)	-0.7	0.481
Peer Comparisons	-0.381	0.241	(-0.853, 0.091)	-1.58	0.114
Months in Treatment	-0.023	0.010	(-0.043, -0.004)	-2.4	0.017
Suggested Alternatives X Months in Treatment	-0.010	0.019	(-0.046, 0.027)	-0.52	0.604
Accountable Justifications X Months in Treatment	-0.035	0.017	(-0.067, -0.002)	-2.1	0.036
Peer Comparisons X Months in Treatment	-0.047	0.019	(-0.084, -0.009)	-2.45	0.014
Time (months)	-0.012	0.018	(-0.048, 0.023)	-0.68	0.499
Constant	-0.593	0.261	(-1.104, -0.083)	-2.28	0.023

The Wald test comparing this fully interacted model to the main effects-only model showed no statistically significant improvement in explanatory power associated with inclusion of the interaction terms (P=0.168).

eTable 5. Coefficient Estimates From Sensitivity Analysis: Simplified Hierarchical Logistic Model to Estimate Intervention Effects on Inappropriate Antibiotic Prescribing Rates, Comparing 18-Month Baseline to 18-Month Intervention Period

Variable	Coefficient	SE	(95% CI)	z	P value
Suggested alternatives	-.018	.235	(-.480, .443)	-0.08	0.939
Accountable justification	.095	.236	(-.368, .559)	0.40	0.688
Peer comparison	-.329	.242	(-.805, .146)	-1.36	0.175
Treatment period	-.806	.060	(-.924, -.688)	-13.39	0.001
Suggested alternatives × Treatment period	-.009	.063	(-.133, .114)	-0.15	0.884
Accountable justification × Treatment period	-.215	.064	(-.341, -.089)	-3.36	0.001
Peer comparison × Treatment period	-.211	0.64	(-.338, -.084)	-3.26	0.001
Constant	-.801	.235	(-1.26, -.340)	-3.41	0.001

eTable 6. Coefficient Estimates From Logistic Model to Estimate Intervention Effects on Proportion of all Acute Respiratory Infections Coded as Antibiotic-Appropriate Diagnoses

Variable	Coefficient	Robust SE*	(95% CI)	z	P value
Suggested alternatives	0.274	0.145	(-0.011, 0.559)	1.89	0.059
Accountable justification	-0.123	0.164	(-0.445, 0.198)	-0.75	0.451
Peer comparison	0.065	0.170	(-0.269, 0.400)	0.38	0.701
Months in treatment	-0.020	0.008	(-0.036, -0.004)	-2.42	0.015
Suggested alternatives x Months in treatment	-0.007	0.006	(-0.018, 0.004)	-1.28	0.202
Accountable justification x Months in treatment	0.005	0.006	(-0.008, 0.017)	0.74	0.457
Peer comparison x Months in treatment	0.005	0.007	(-0.008, 0.018)	0.78	0.434
Time (months)	0.008	0.005	(-0.002, 0.017)	1.59	0.112
Constant	0.044	0.122	(-0.195, 0.283)	0.36	0.72

* Robust Standard errors were used in model because the hierarchical mixed effects model failed to converge.

eTable 7. Rate of Return Visit With Diagnosis of Concern, When Antibiotics Were Not Prescribed at the Index Visit, by Study Arm

Study arm	Number of intervention-qualifying ARI encounters*	Number of intervention-qualifying ARI encounters where antibiotics were not prescribed†	Number of intervention-qualifying ARI encounters where antibiotics were not prescribed <u>and</u> with a RETURN visit within 30 days with a Diagnosis of Concern‡	Rate of RETURN Visit with Diagnosis of Concern§	95% Confidence Intervals	P value**
Control	4667	3245	14	0.43%	(0.24%, 0.70%)	Reference
Suggested alternatives only	6383	4579	16	0.35%	(0.20%, 0.55%)	0.718
Accountable justification only	5815	4622	16	0.35%	(0.20%, 0.54%)	0.727
Peer comparison only	4781	3781	13	0.34%	(0.19%, 0.57%)	0.722
Accountable justification + Peer comparison	4321	3398	48	1.41%	(1.05%, 1.85%)	<0.001

eTable 7, Continued

Study arm	Number of intervention-qualifying ARI encounters*	Number of intervention-qualifying ARI encounters where antibiotics were not prescribed†	Number of intervention-qualifying ARI encounters where antibiotics were not prescribed <u>and</u> with a RETURN visit within 30 days with a Diagnosis of Concern‡	Rate of RETURN Visit with Diagnosis of Concern§	95% Confidence Intervals	P value**
Accountable justification + Suggested alternatives	7212	5717	22	0.38%	(0.24%, 0.57%)	0.631
Peer comparison + Suggested alternatives	7363	5993	23	0.38%	(0.25%, 0.56%)	0.635
Accountable justification + Peer comparison + Suggested alternatives	4990	4164	15	0.36%	(0.21%, 0.57%)	0.687

*Intervention-qualifying acute respiratory infections (ARI) encounters include all ARI visits eligible for the suggested alternatives and accountable justification interventions (not limited to the antibiotic-inappropriate ARI diagnoses that define the primary outcome).

†Subset of the intervention-qualifying ARI encounters for which no antibiotics were prescribed

‡Diagnosis of Concern (DoC): based on ICD9 codes of concern at revisit (See Table S6 in the Supplementary Appendix)

eTable 7, Continued

§Rate of RETURN Visit with DoC: # of qualifying ARI encounters where antibiotics were not prescribed and with a RETURN visit within 30 days with a Diagnosis of Concern / # of total qualifying ARI encounters where antibiotics were not prescribed

**P values computed using difference between proportions (z value). With Bonferroni correction, the critical p is 0.007 (0.05/7).

*Standard approaches for calculating confidence intervals of proportions were not valid for the safety analysis because these were very rare events. Therefore, we calculated Jeffrey's interval for rare events, an equal-tailed 95% confidence interval obtained when using noninformative prior for the binomial proportion p. The interval assumes an a prior Beta distribution with parameters Beta(1/2, 1/2). After observing x successes in n trials, the confidence interval is computed as a posterior Beta distribution with parameters(x + 1/2, n - x + 1/2).

Jeffreys, H. (1946, September). An invariant form for the prior probability in estimation problems. In Proceedings of the Royal Society of London A: Mathematical, Physical and Engineering Sciences (Vol. 186, No. 1007, pp. 453-461). The Royal Society.

Brown, L. D., Cai, T. T., & DasGupta, A. (2001). Interval estimation for a binomial proportion. Statistical science, 101-117.

eTable 8. Specific Diagnoses of Concern Associated With Return Visits for Which Antibiotics Might Have Been Helpful in the Initial Visit

Diagnosis of concern	Pneumonia	Otitis media	Pneumonia and otitis media
Suggested alternatives only	2	0	0
Accountable justification only	1	0	0
Peer comparison only	0	1	0
Accountable justification + Peer comparison	4	0	1
Accountable justification + Suggested alternatives	0	0	0
Peer comparison + Suggested alternatives	2	0	0
Accountable justification + Peer comparison + Suggested alternatives	2	0	0