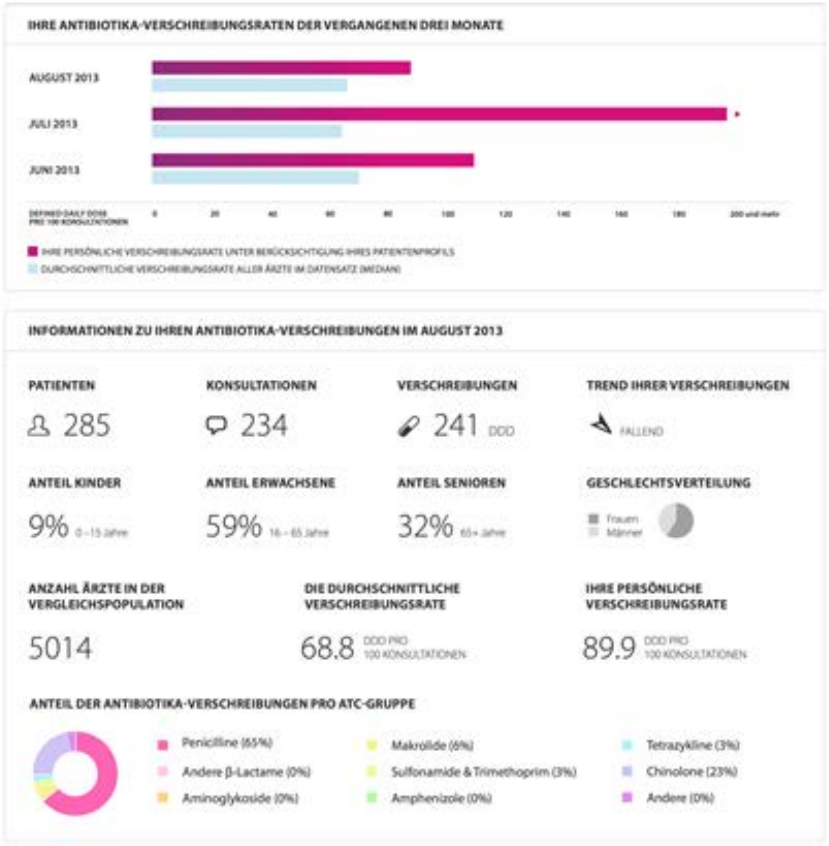
Supplementary Online Content

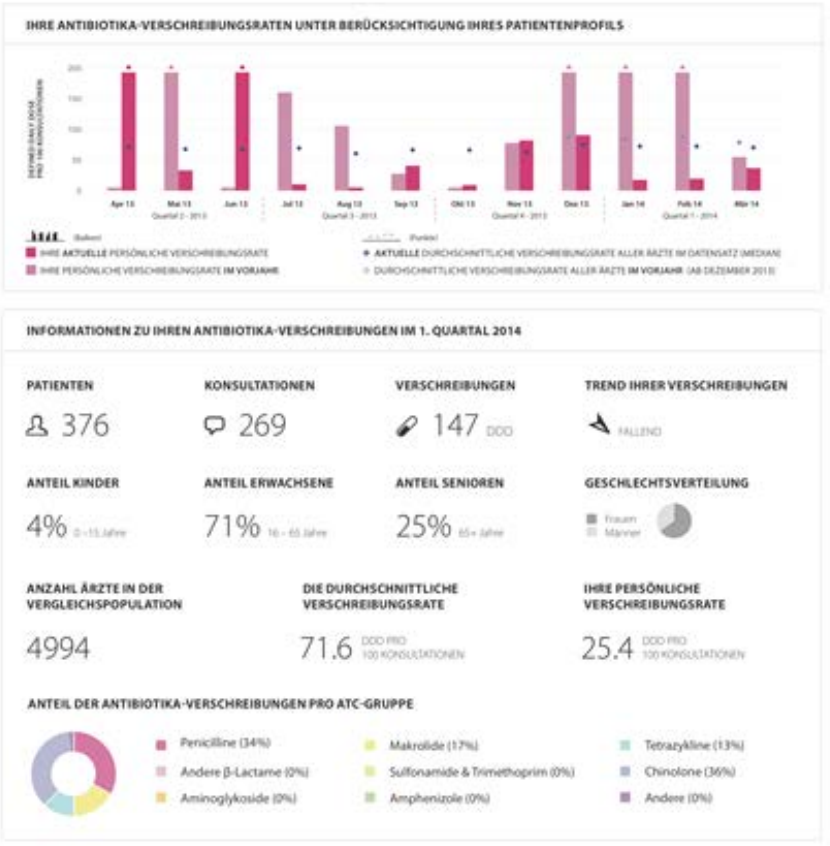
Hemkens LG, Saccilotto R, Reyes SL, et al. Personalized prescription feedback using routinely collected data to reduce antibiotic use in primary care: a randomized clinical trial [published online December 27, 2016]. *JAMA Intern Med*. doi:10.1001/jamainternmed.2016.8040

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

eFigure: Example of Prescription Feedback



A] Year 1



B] Year 2

eTable 1: Intention To Treat Analysis

	Year 1				Year 2				Change Year 1 vs Year 2
Prescriptions per year (DDD/100c, all antibiotic types)	**Intervention group physicians (n=1406)**	**Control group physicians (n=1408)**	**Change from Baseline (between-group difference)**	**p-value**	**Intervention group physicians (n=1406)**	**Control group physicians (n=1408)**	**Change from Baseline (between-group difference)**	**p-value**	**p-value**
All patients	90.46 (71.22, 119.08)	90.32 (71.81, 121.22)	0.81% (-2.56%, 4.30%)	0.64	91.03 (70.26, 121.69)	92.66 (71.54, 128.33)	-1.73% (-5.07%, 1.72%)	0.32	0.15
▪ ≤ 5 years	89.48 (47.66, 166.67)	82.94 (48.66, 164.71)	1.53% (-9.39%, 13.77%)	0.79	80 (46.65, 156.07)	84.38 (46.35, 160)	-2.03% (-13.11%, 10.45%)	0.74	0.57
▪ 6 - 18 years	97.15 (60.42, 156.86)	105 (65.79, 164.21)	-8.61% (-14.87%, -1.90%)	0.01	101.51 (63.26, 163.72)	105.89 (63.93, 172.14)	-4.10% (-10.78%, 3.07%)	0.25	0.20
▪ 19 - 65 years	94.39 (73.14, 126.85)	95.36 (71.50, 129.17)	-0.17% (-3.58%, 3.36%)	0.93	92.8 (68.78, 128.02)	97.67 (70.87, 137.99)	-4.59% (-7.91%, -1.16%)	<.01	0.01
▪ > 65 years	81.43 (62.07, 113.21)	80.29 (60.26, 113.69)	1.13% (-2.75%, 5.16%)	0.57	83.69 (61.39, 118.64)	83.55 (61.15, 122.43)	-2.53% (-6.33%, 1.42%)	0.21	0.07
▪ Women	93.22 (71.86, 124.49)	91.44 (70.37, 126.24)	1.45% (-2.07%, 5.09%)	0.42	93.31 (71.13, 129.59)	95.57 (70.04, 136.05)	-1.01% (-4.49%, 2.60%)	0.58	0.18
▪ Men	86.21 (63.84, 115.39)	86.65 (65.30, 119.32)	-1.37% (-5.02%, 2.42%)	0.47	85.82 (62.91, 118.45)	88.94 (65.84, 123.66)	-3.46% (-7.09%, 0.31%)	0.07	0.28
Prescriptions per year (DDD/100c, all patients)									
▪ Penicillins (beta-Lactams)	37.59 (26.50, 50.60)	36.64 (25.89, 50.71)	1.42% (-2.65%, 5.65%)	0.5	37.84 (26.74, 53.75)	38.82 (26.49, 56.90)	-1.98% (-5.97%, 2.18%)	0.35	0.09
▪ Other beta-Lactams	6.58 (2.35, 15.82)	6.87 (2.43, 16.53)	-0.04% (-7.80%, 8.37%)	0.99	6.22 (2.15, 16.09)	7.16 (2.25, 17.88)	-3.55% (-11.15%, 4.70%)	0.39	0.39
▪ Quinolones	16.24 (10.96, 23.90)	15.48 (10.17, 22.98)	-0.82% (-5.42%, 4.00%)	0.73	15.12 (9.57, 23.34)	14.32 (9.36, 22.42)	-1.00% (-5.67%, 3.91%)	0.68	0.94
▪ Macrolides, Lincosamides, StGr	11.8 (6.76, 19.89)	12.41 (6.96, 20.97)	-1.39% (-6.58%, 4.07%)	0.61	12.48 (7.03, 21.35)	13.61 (7.52, 23.28)	-5.71% (-10.75%, -0.38%)	0.04	0.09
▪ Tetracyclines	4.91 (2.46, 9.64)	5.08 (2.28, 9.56)	4.77% (-3.78%, 14.08%)	0.28	5.05 (2.50, 9.51)	4.92 (2.52, 9.45)	2.81% (-5.91%, 12.34%)	0.54	0.67
▪ Sulfonamides/Trimethoprim	2.12 (0.88, 4.39)	2.02 (0.85, 4.49)	5.68% (-4.29%, 16.70%)	0.27	1.95 (0.76, 4.34)	2.12 (0.82, 4.45)	4.94% (-5.42%, 16.44%)	0.36	0.89
▪ Aminoglycosides	0.09 (0.02, 0.96)	3.21 (0.64, 4.80)	12.89% (-64.10%, 255.0%)	0.83	0.17 (0.05, 3.11)	1.35 (0.40, 3.00)	-43.59% (-84.51%, 105.4%)	0.37	0.19
▪ Other	2.81 (1.09, 7.80)	2.92 (1.08, 7.78)	0.31% (-8.86%, 10.40%)	0.95	3.44 (1.13, 8.81)	3.5 (1.26, 9.04)	-4.21% (-13.07%, 5.56%)	0.39	0.32

Median (interquartile range) if not stated otherwise. DDD: Defined daily doses. DDD/100c: DDD per 100 consultations. StGr: Streptogramins

eTable 2: On-intervention/Per-Protocol Analysis

	Year 1				Year 2				Change Year 1 vs Year 2
Prescriptions per year (DDD/100c, all antibiotic types)	**Intervention group physicians (n=1025)**	**Control group physicians (n=1173)**	**Change from Baseline (between-group difference)**	**p-value**	**Intervention group physicians (n=1025)**	**Control group physicians (n=1173)**	**Change from Baseline (between-group difference)**	**p-value**	**p-value**
All patients	95.25 (78.00, 122.70)	97.18 (77.03, 127.91)	-1.20% (-4.74%, 2.46%)	0.51	96.52 (75.99, 127.71)	99.44 (79.09, 136.61)	-4.06% (-7.53%, -0.45%)	0.03	0.12
▪ ≤ 5 years	99.29 (52.94, 173.91)	87.11 (55.56, 166.67)	5.43% (-7.11%, 19.66%)	0.41	84.97 (48.90, 164.08)	93.33 (52.30, 171.25)	-6.32% (-18.04%, 7.08%)	0.34	0.09
▪ 6 - 18 years	103.55 (66.57, 159.79)	114.06 (73.83, 172.09)	-11.13% (-17.91%, -3.80%)	<.01	106.97 (68.75, 170)	113.54 (71.43, 183.16)	-6.90% (-14.09%, 0.88%)	0.08	0.26
▪ 19 - 65 years	98.56 (78.49, 129.98)	103.32 (78.35, 136.62)	-1.17% (-4.91%, 2.72%)	0.55	99.25 (75.21, 131.70)	106 (78.81, 146.64)	-5.21% (-8.85%, -1.43%)	<.01	0.04
▪ > 65 years	87.26 (67.01, 119.00)	84.3 (65.64, 121.59)	-0.51% (-4.69%, 3.85%)	0.82	89.18 (66.33, 123.68)	90.29 (67.82, 131.39)	-4.26% (-8.33%, -0.01%)	0.05	0.08
▪ Women	97.85 (77.52, 130.93)	98 (77.03, 133.54)	-0.20% (-3.99%, 3.74%)	0.92	99.14 (76.95, 134.04)	102.86 (77.70, 146.52)	-3.27% (-6.98%, 0.59%)	0.10	0.12
▪ Men	90.87 (70.85, 117.81)	94.49 (71.14, 125.80)	-2.36% (-6.33%, 1.79%)	0.26	91.37 (67.06, 125.20)	94.51 (72.20, 129.99)	-4.28% (-8.22%, -0.16%)	0.04	0.36
Prescriptions per year (DDD/100c, all patients)									
▪ Penicillins (beta-Lactams)	39.08 (28.08, 51.77)	39.35 (27.90, 54.65)	-0.43% (-4.70%, 4.03%)	0.85	39.69 (28.40, 56.03)	41.12 (29.12, 59.57)	-3.48% (-7.67%, 0.91%)	0.12	0.17
▪ Other beta-Lactams	7.33 (2.68, 17.30)	7.68 (2.85, 18.35)	0.17% (-8.34%, 9.47%)	0.97	6.97 (2.46, 17.27)	7.98 (2.6, 20.34)	-2.78% (-11.15%, 6.38%)	0.54	0.52
▪ Quinolones	17.4 (11.58, 24.85)	16.67 (11.13, 24.53)	-2.11% (-7.10%, 3.14%)	0.42	16.2 (10.50, 24.43)	15.57 (10.46, 23.66)	-3.27% (-8.27%, 2.00%)	0.22	0.66
▪ Macrolides, Lincosamides, StGr	12.5 (7.36, 21.32)	13.24 (7.41, 22.75)	-1.52% (-7.19%, 4.50%)	0.61	13.45 (7.58, 23.31)	14.47 (8.05, 24.56)	-4.75% (-10.31%, 1.16%)	0.11	0.28
▪ Tetracyclines	4.82 (2.50, 9.49)	5.18 (2.51, 9.99)	2.98% (-6.31%, 13.20%)	0.54	5.08 (2.52, 9.64)	5.25 (2.58, 9.71)	1.86% (-7.64%, 12.33%)	0.71	0.83
▪ Sulfonamides/Trimethoprim	2.08 (0.91, 4.39)	2.03 (0.85, 4.56)	4.76% (-6.21%, 17.00%)	0.41	1.93 (0.74, 4.25)	2.06 (0.83, 4.54)	-0.34% (-11.18%, 11.82%)	0.95	0.40
▪ Aminoglycosides	0.07 (0.02, 0.31)	3.63 (1.04, 4.78)	-52.70% (-91.64%, 167.6%)	0.38	0.12 (0.05, 0.41)	1.66 (1.24, 3.00)	-58.37% (-93.81%, 180.1%)	0.35	0.88
▪ Other	2.91 (1.12, 8.43)	3.19 (1.20, 8.69)	-1.11% (-11.09%, 10.00%)	0.84	3.59 (1.16, 9.11)	3.94 (1.38, 10.25)	-5.71% (-15.31%, 4.99%)	0.28	0.38

Median (interquartile range). DDD: Defined daily drugs. DDD/100c: DDD per 100 consultations. StGr: Streptogramins

eTable 3: Subgroup and Sensitivity Analyses

Prescriptions per year (DDD/100c, all antibiotic types)	**Year 1** Change from Baseline (between-group difference)	p-value	**Year 2** Change from Baseline (between-group difference)	p-value
Subgroup analyses				
Dispensing method [a]				
▪ Physicians self-dispensing (n=1081)	1.61% (-3.80%, 7.33%)	0.57	-1.43% (-6.78%, 4.23%)	0.61
▪ Physicians non-self-dispensing (n=1281)	0.05% (-4.81%, 5.17%)	0.98	-1.67% (-6.51%, 3.42%)	0.51
Patient-mix type [a]				
▪ Physicians prescribing medications for many comorbidities (n=894)	-0.35% (-6.15%, 5.81%)	0.91	-2.84% (-8.59%, 3.27%)	0.91
▪ Physicians prescribing medication for fewer comorbidities (n=1920)	1.31% (-2.79%, 5.58%)	0.54	-1.11% (-5.18%, 3.13%)	0.60
Sensitivity analyses				
Different outcome definition: Prescribed packages of antibiotics per 100 consultations (n=2814)	0.47% (-2.70%, 3.76%)	0.77	-2.77% (-5.90%, 0.46%)	0.09
Physicians who opted out from the study excluded (n=2620) [b]	-1.40% (-4.80%, 2.13%)	0.43	-3.35% (-6.73%, 0.15%)	0.06
Model without baseline covariates (n=2842) [c]	0.64% (-2.71%, 4.11%)	0.71	-1.69% (-5.02%, 1.75%)	0.33
Physicians with incomplete antibiotic prescription data at any time-point excluded (n=2543) [d]	-0.57% (-3.88%, 2.86%)	0.74	-2.78% (-6.03%, 0.58%)	0.10
Physicians with outliers for antibiotic prescription data at any time-point excluded (n=2747) [e]	-0.41% (-2.67%, 1.91%)	0.73	-2.73% (-4.98%, -0.43%)	0.02

Wilcoxon test results on changes in medians between intervention and control: p=0.96 (first year, n=2766, 7 physicians with zero prescriptions included) and p= 0.14 (second year, n=2643, 6 physicians with zero prescriptions included)

Analyses are based on the main model (intention-to-treat analyses; n=2814) with modifications as specified, if not otherwise stated.

a) p-value for interaction = 0.90 in both cases
b) 211 physicians excluded who declined receiving feedback (opting out); 17 of them were already excluded for other reasons from the main analysis.
c) The 28 physicians (intervention group: 11; control group: 17) with missing or outlying baseline covariate information (i.e. number of patients at baseline, dispensing method, or patient-mix type as derived from cluster analysis), data errors for baseline covariates, or very atypical combination of values for baseline covariates indicating group practices were included in this analysis.
d) Incomplete antibiotic prescription data for 271 physicians (intervention group: 137; control group: 134). Of note, only in this analysis were physicians excluded because of incomplete antibiotic prescription data.
e) Outliers for antibiotic prescription data for 67 physicians (intervention group: 33; control group: 34). Of note, only in this analysis were physicians excluded because of outliers for antibiotic prescription data.

Webappendix: Search strategy for "Research in Context"

We searched for randomized controlled trials (RCTs), including cluster RCTs, evaluating antibiotic prescription feedback interventions in primary care which are implementable on a system level, i.e. not involving direct physician contact, and without combined patient directed interventions. We searched PubMed from inception to 2016 for systematic reviews on antibiotic prescription feedback interventions. The two most recent relevant reviews were perused for eligible RCTs. For the time-period not covered by these reviews, we directly queried PubMed for RCTs (i.e. from 1 January 2012 to 28 September 2016). We combined MeSH headings and text terms for "antibiotics" and "feedback" and used the PubMed standard filter for systematic reviews and a Cochrane standard filter for RCTs.

Search	Query	Items found
#1	(((systematic[sb]) AND ("feedback"[tiab] OR "Feedback"[Mesh]))) AND (("antibiotic*"[tiab] OR "antimicrobial*"[tiab] OR "Anti-Bacterial Agents"[Mesh]))	48

Search date: 28 September 2016; Interface: PubMed

Search	Query	Items found
#4	(#1 AND #2 AND #3) Filters: Publication date from 2012/01/01	43
#3	randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR "clinical trials as topic"[MeSH Terms:noexp] OR randomly[tiab] OR trial[ti] NOT ("animals"[MeSH Terms] NOT "humans"[MeSH Terms])	970063
#2	"antibiotic*"[tiab] OR "antimicrobial*"[tiab] OR "Anti-Bacterial Agents"[Mesh]	458294
#1	"feedback"[tiab] OR "Feedback"[Mesh] OR "peer comparison"[tiab]	123978

Search date: 28 September 2016; Interface: PubMed