Supplementary Material

Appendix 1. Summary counts of infection-related hospital admission types as recorded as hospital admission codes in the primary care records.

Table S1. Summary counts of distribution of infection-related complications based on hospital admission codes in CPRD-HES. Table shows counts from CPRD-HES by sex and age for multiple infection-related complications.

CPRD-HES	All	Male	Female	Age 0-17	Age 18-39	Age 40-59	Age 60-74	Age 75+
Cough/Cold	103	60	43	96	<5	<5	<5	<5
LRTI/Pneumonia	13543	6026	7527	2515	877	1681	2418	6056
Otitis externa	67	29	38	12	18	16	10	10
Otitis media	432	223	209	236	64	64	47	18
Sinusitis	46	16	31	7	7	15	14	<5
Sore Throat	2000	1066	932	481	1085	357	58	17
URTI	695	375	319	509	47	42	36	62
UTI	112	39	73	<5	36	12	27	38
Sepsis	397	183	214	16	16	31	85	249
Meningitis	45	18	27	13	11	10	5	6
Infection-related complication, protocol defined	17810	8234	9580	3673	2226	2464	2890	6562
Any hospitalisation, not infection specific	77704	34050	43695	8196	7865	11990	18640	31030

Note 1: the sum of specific infections does not add up to sum of infection-related complications protocol defined due to a subset of patients having multiple infection-related complication admission codes. Note 2: the sum of Male and Female, and the sum of the age categories may not add up to the sum of 'All' due to some missingness in gender or year-of-birth registration in the patient's medical records.

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Appendix 2. Sensitivity analysis of continuous antibiotic prescribing rate

A sensitivity analysis was performed to determine if treating the antibiotic prescribing rate continuously is justified. The rate of infection-related hospital admission and antibiotic prescribing rate was modelled with negative binomial regression. The antibiotic prescribing rate was decile ranked to create 10 equally sized subsections. These deciles were modelled in the exact same way as the main analyses presented in this paper. First, second, and third degree polynomials were fitted on the deciled antibiotic rate and evaluated against the IRRs for infection-related complication as recorded by the GP ('A', 'B', 'C') and for infection-related hospital admission ('D', 'E', 'F'). For both outcomes the first order polynomials were the preferred models. Figure S1 Plot A shows a strong linear trend for between low prescribing at deciles 1 to 3 and high prescribing at deciles 8 to 10. Although the error bars of each point estimate overlap a downward linear trend is observable. Creating categories of the antibiotic prescribing rate may hide significant variability within each specific category. Treating the antibiotic prescribing rate continuously ensures that each GP practice is analysed separately against the outcomes of interest.

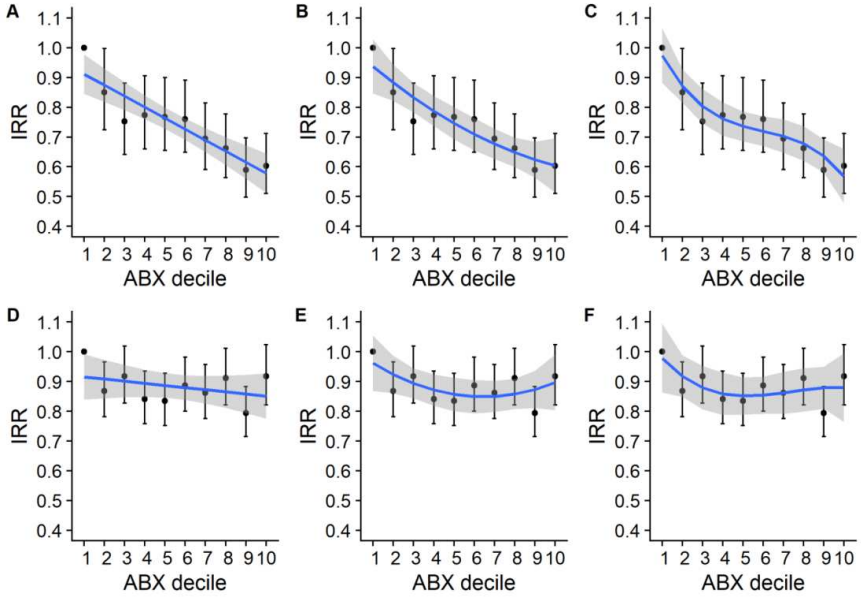

Figure s1. First (left), second (middle), and third (right) degree polynomials fitted on the deciled antibiotic prescribing rate. Plot A, B, and C model outcome infection-related complication as recorded by the GP. Plot D, E, and F model outcome infection-related hospital admission.

Appendix 3. Sensitivity analysis of paired infection-related complication with common infection

A sensitivity analysis was performed where antibiotic prescribing for URTI and for LRTI was linked with three adverse outcomes: 1) Pneumonia GP diagnosed (CPRD), 2) LRTI hospital admission (CPRD-HES), and 3) Pneumonia hospital admission (CPRD-HES).

Table S2. Adjusted IRRs from paired analysis of infection-related complications after a common infection with URTI or LRTI.

Common infection / infection-related complication	Adjusted IRR (95% CI)	IQR
URTI / Pneumonia (CPRD)	0.801 (0.743 - 0.864)	15.48
URTI / LRTI (CPRD-HES)	0.928 (0.868 - 0.992)	14.92
URTI / Pneumonia (CPRD-HES)	0.888 (0.805 - 0.978)	14.92
LRTI / Pneumonia (CPRD)	0.842 (0.787 - 0.902)	9.07
LRTI / LRTI (CPRD-HES)	0.820 (0.765 - 0.879)	8.67
LRTI / Pneumonia (CPRD-HES)	0.917 (0.834 - 1.011)	8.67

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