

Supplementary data

Antibiotics in primary care in England: which antibiotics are prescribed and for which conditions?

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A. Linking diagnostic codes to prescriptions

We developed a hierarchical system to link systemic antibiotic prescriptions to diagnostic codes (Read codes), both of which are recorded in the THIN primary care database. Diagnostic codes that were included in the hierarchical system were selected in an iterative process (see Figure S1) and optimized for sensitivity (i.e., even rather non-specific or fuzzy codes were included if they were of help to understand why an antibiotic was prescribed) rather than specificity.

As depicted in Figure S1, we assembled initial lists of diagnostic codes that were based on codes used in published literature on antibiotic prescribing in primary care and amended with further codes we found necessary / helpful for capturing indications for antibiotic prescribing. These initial lists were reviewed by clinical prescribing experts regarding their meaningfulness and subsequently revised by us. The revised lists were applied to an extract from THIN that contained all systemic antibiotic prescriptions (years 2013-2015) recorded in THIN (i.e., it was checked whether one or more of the listed diagnostic codes co-occurred with an antibiotic prescription). For prescriptions that did not co-occur with the listed diagnostic codes, we extracted the diagnostic codes that did co-occur with the prescription and discussed for each of these codes individually, whether they were potentially explaining the antibiotic prescription and helpful in understanding antibiotic prescribing. Codes that were (potentially) related to the antibiotic prescription were included in the revised lists (2nd revision), obviously unrelated codes still excluded. The so revised lists were, again, reviewed by clinical experts and final lists were generated based on the experts' input.

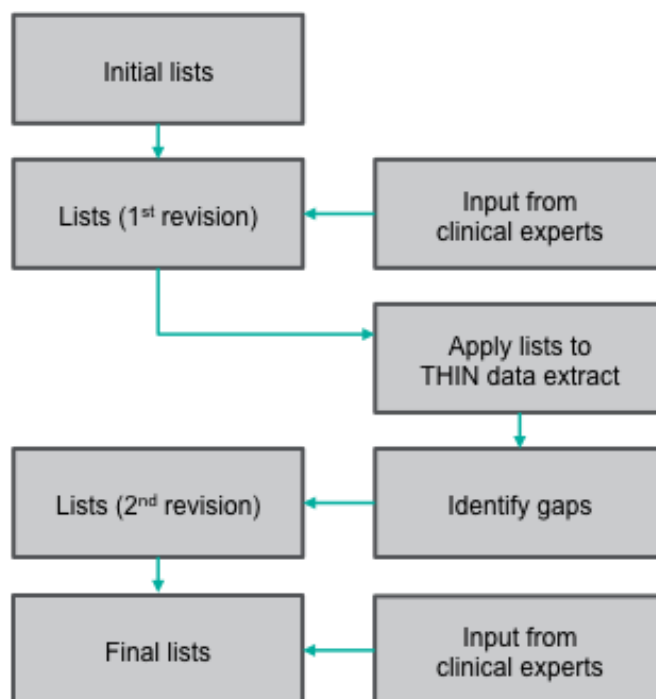


Figure S1 Iterative process for selecting diagnostic codes (Read codes).

The highest hierarchical level in the system of diagnostic codes was the level of body systems (similar to the ones used in the British National Formulary; see Figure S2).

Supplementary data

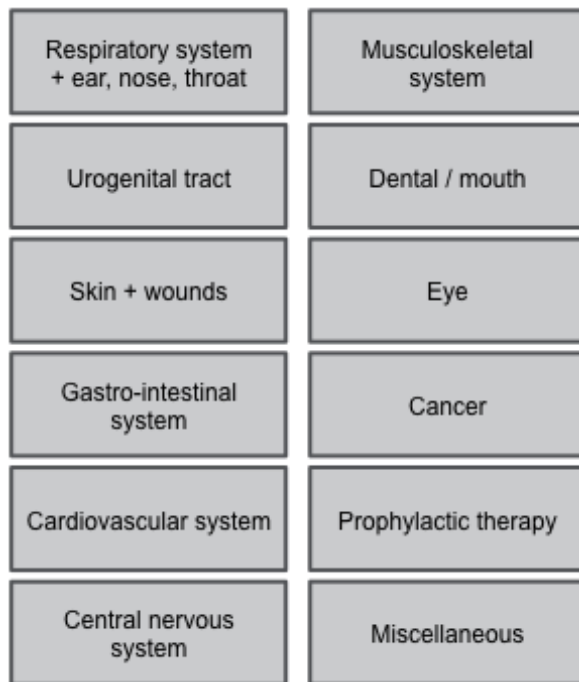


Figure S2 Body systems included in the analysis

Diagnostic codes within a body system were then further subdivided into diagnostic codes for concrete diagnoses (see, e.g., Figure S3) and less concrete diagnostic codes indicating symptoms, specific tests or examinations (Figure S4), but no concrete diagnosis.

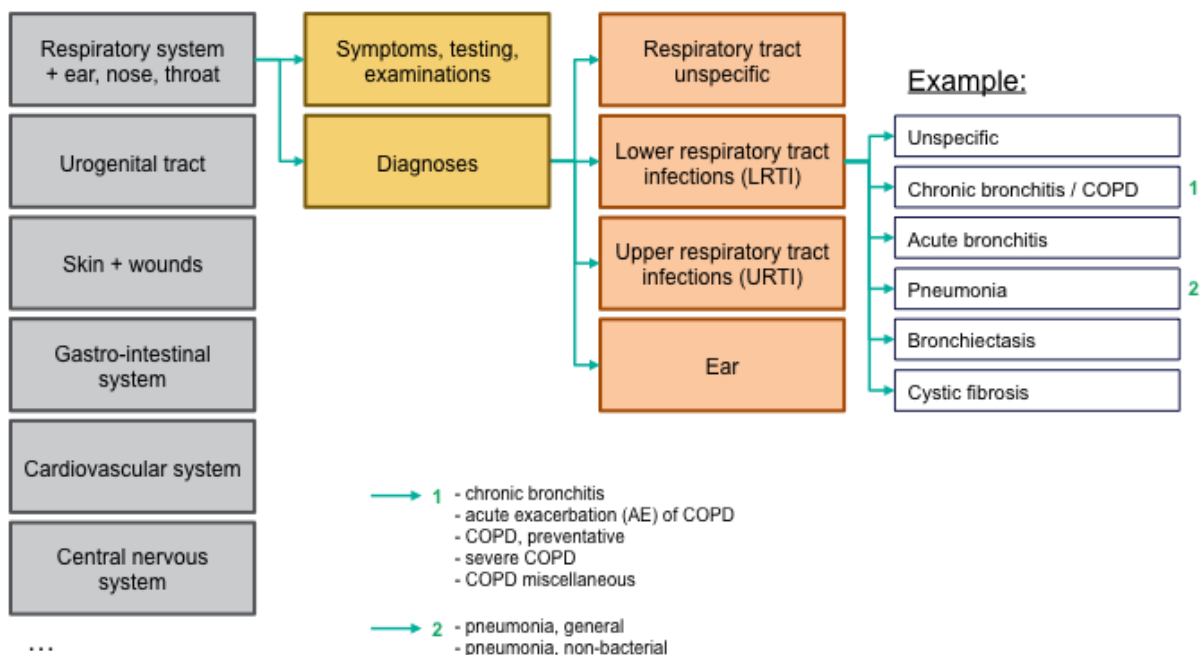


Figure S3 Subdivision of diagnostic codes into groups of and concrete diagnoses, here for the respiratory system (including ear, nose, throat).

Supplementary data

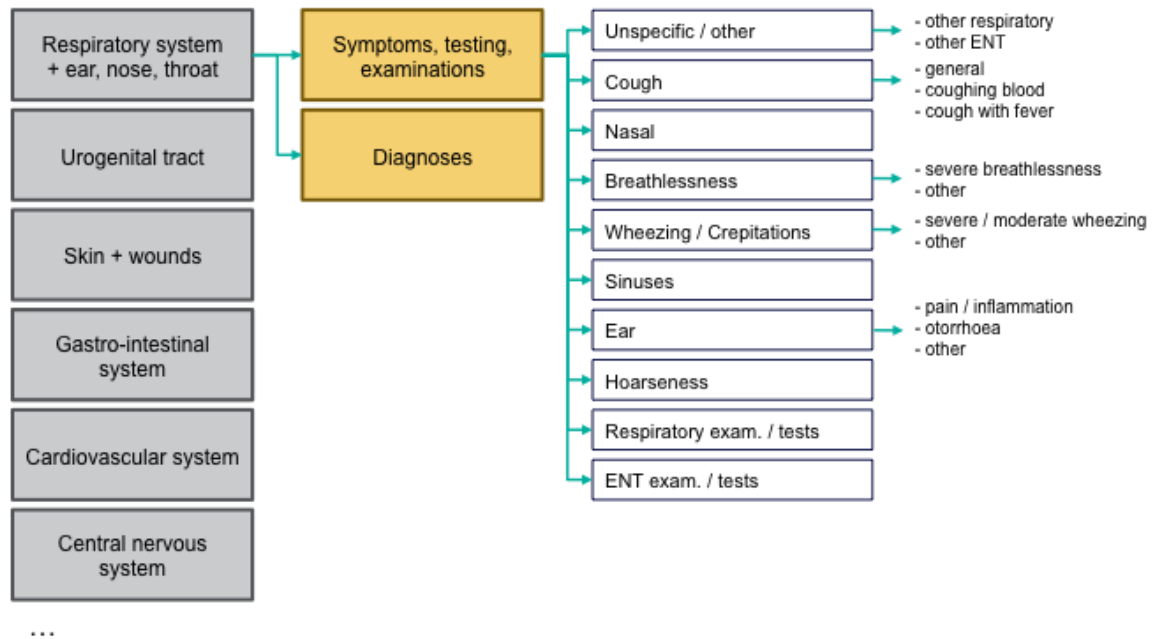


Figure S4 Subdivision of diagnostic codes into symptoms, tests, and examinations; here for the respiratory system (including ear, nose, throat).

The structure of the hierarchical system is provided subsequently.

B. Hierarchical system

All Read codes were mapped into a hierarchical system and attributed to (i) a body system and (ii) a diagnosis, symptom or examination within a specific body system.

1 Gastro-intestinal system

1.1 Symptoms / testing / examinations

- 1.1.1 Diarrhea
- 1.1.2 Constipation
- 1.1.3 Nausea / Vomiting
- 1.1.4 Misc. symptoms
- 1.1.5 Testing and examinations

1.2 Diagnoses

- 1.2.1 Gastro-enteritis and gastritis
 - 1.2.1.1 General
 - 1.2.1.2 Bacterial / treated w. abx
 - 1.2.1.3 Non-bacterial / non-infectious
 - 1.2.1.4 Gastritis
- 1.2.2 Campylobacter enteritis
- 1.2.3 Salmonella (non-typhoid)
- 1.2.4 Shigellosis
- 1.2.5 Typhoid fever
- 1.2.6 Clostridium difficile infection
- 1.2.7 Biliary-tract
 - 1.2.7.1 Biliary-tract infection
 - 1.2.7.2 Biliary-tract (likely no infect.)
- 1.2.8 Peritonitis
- 1.2.9 Helicobacter pylori

Supplementary data

- 1.2.10 Diverticulitis /-osis
 - 1.2.10.1 Diverticulitis
 - 1.2.10.2 Diverticulosis (non-infectious)
- 1.2.11 Reflux
- 1.2.12 Misc.

2 Respiratory system (with ENT)

2.1 Symptoms / testing / examinations

- 2.1.0 Unspecific
 - 2.1.0.1 Unspecific / misc. respiratory
 - 2.1.0.2 Unspecific / misc. ENT
- 2.1.1 Cough
 - 2.1.1.1 general
 - 2.1.1.2 Coughing blood
 - 2.1.1.3 Cough w. fever
 - 2.1.1.4 Chronic cough
- 2.1.2 Nasal
 - 2.1.2.1 Nasal (misc.)
 - 2.1.2.2 Nosebleed
- 2.1.3 Breathlessness
 - 2.1.3.1 Severe Breathlessness
 - 2.1.3.2 General Breathlessness
- 2.1.4 Wheezing / Crepitations
 - 2.1.4.1 Severe-moderate wheezing
 - 2.1.4.2 General
- 2.1.5 Sinuses
- 2.1.6 Ear
 - 2.1.6.1 Ear pain / inflammation
 - 2.1.6.2 Otorrhoea & complicating factors
 - 2.1.6.3 Ear other symptoms
- 2.1.7 Hoarseness
- 2.1.8 Respiratory testing and examinations
- 2.1.9 ENT testing and examinations

2.2 Diagnoses

- 2.2.1 Diagnoses RT (misc.)
 - 2.2.1.1 Diagnoses RTI (unspecific)
 - 2.2.1.2 Allergic condition of RT
 - 2.2.1.3 Asthma
 - 2.2.1.4 Misc.
- 2.2.2 Diagnoses LRTI
 - 2.2.2.1 Unspecific / misc. LRTI
 - 2.2.2.2 Chronic bronchitis / COPD: acute exacerbations
 - 2.2.2.2.1 Chronic bronchitis
 - 2.2.2.2.2 COPD / related conditions
 - 2.2.2.2.2.1 Clear indication
 - 2.2.2.2.2.2 Preventative
 - 2.2.2.2.2.3 Severe COPD
 - 2.2.2.2.2.4 Misc.
 - 2.2.2.3 Acute / unspecific bronchitis
 - 2.2.2.4 Pneumonia
 - 2.2.2.4.1 General
 - 2.2.2.4.2 Non-bacterial
 - 2.2.2.5 Bronchiectasis

Supplementary data

- 2.2.2.6 Cystic Fibrosis
- 2.2.3 Diagnoses URTI
 - 2.2.3.1 Unspecific URTI / misc.
 - 2.2.3.1.1 URTI (narrow sense)
 - 2.2.3.1.2 Tonsil-related
 - 2.2.3.2 Haemophilus influenzae epiglottitis
 - 2.2.3.3 Sinusitis
 - 2.2.3.3.1 Acute sinusitis
 - 2.2.3.3.2 Chronic sinusitis
 - 2.2.3.4 Common cold / nasopharyngitis
 - 2.2.3.5 Influenza / ILI
 - 2.2.3.6 Pharyngitis / tonsillitis / sore throat
 - 2.2.3.6.1 general & acute
 - 2.2.3.6.2 bacterial
 - 2.2.3.6.3 non-bacterial
 - 2.2.3.6.4 chronic / recurrent
 - 2.2.3.7 Laryngitis / tracheitis
 - 2.2.3.7.1 Acute
 - 2.2.3.7.2 Chronic
 - 2.2.3.8 Parotitis
- 2.2.4 Diagnoses Ear
 - 2.2.4.1 Unspecific / misc.
 - 2.2.4.2 Otitis externa
 - 2.2.4.2.1 general
 - 2.2.4.2.2 non-bacterial
 - 2.2.4.2.3 Malignant otitis externa
 - 2.2.4.3 Otitis media
 - 2.2.4.3.1 Acute
 - 2.2.4.3.1.1 Discharge / bilateral
 - 2.2.4.3.1.2 Other
 - 2.2.4.3.2 Chronic
 - 2.2.4.4 Mastoiditis

3 Urogenital tract

3.1 Urinary / genital distinction not possible

- 3.1.1 Symptoms / testing / examinations
- 3.1.2 Diagnoses (misc.)

3.2 Urinary tract

- 3.2.1 Symptoms / testing / examinations
 - 3.2.1.1 Symptoms
 - 3.2.1.1.1 Haematuria
 - 3.2.1.1.2 Urination-related symptoms
 - 3.2.1.1.2.1 Cloudy urine
 - 3.2.1.1.2.2 Other
 - 3.2.1.1.3 Other symptoms
 - 3.2.1.2 Tests and examinations
- 3.2.2 Diagnoses
 - 3.2.2.1 Diagnoses (unspecific re site)
 - 3.2.2.1.1 Recurrent / chronic UTI
 - 3.2.2.1.2 UTI in pregnancy
 - 3.2.2.1.3 Misc.
 - 3.2.2.2 Lower UTI
 - 3.2.2.2.1 Cystitis

Supplementary data

- 3.2.2.2.1.1 general
- 3.2.2.2.1.2 non-bacterial / non-infectious
- 3.2.2.2.1.3 chronic / recurrent
- 3.2.2.2.1.4 in pregnancy
- 3.2.2.2.2 Prostatitis: acute
- 3.2.2.2.2.1 general
- 3.2.2.2.2.2 non-bacterial
- 3.2.2.3 Upper UTI
- 3.2.2.3.1 Pyelonephritis: acute / infections of kidney

3.3 Genital system

- 3.3.1 Symptoms / testing / examinations
- 3.3.2 Diagnoses
 - 3.3.2.1 Bacterial vaginosis / vaginitis
 - 3.3.2.1.1 Bacterial vaginosis
 - 3.3.2.1.2 Vaginitis
 - 3.3.2.2 Chlamydial infection / non-gonococcal urethritis / non-specific genital infection
 - 3.3.2.2.1 at-risk of / suspected
 - 3.3.2.2.2 diagnosed
 - 3.3.2.3 Gonorrhoea
 - 3.3.2.4 Pelvic inflammatory disease
 - 3.3.2.5 Syphilis
 - 3.3.2.6 Syphilis contact
 - 3.3.2.7 Non-bacterial genital tract infection
 - 3.3.2.8 Balanitis

4 Skin and wounds

4.1 Skin

- 4.1.1 Symptoms / testing / examinations
 - 4.1.1.1 Unspecific / misc.
 - 4.1.1.1.2 Rash / itch
 - 4.1.1.3 Tests, procedures and referrals
- 4.1.2 Diagnoses
 - 4.1.2.0 Unspecific skin infection / misc.
 - 4.1.2.0.1 Unspecific infection (pot req AB)
 - 4.1.2.0.2 Psoriasis
 - 4.1.2.0.3 Misc.
 - 4.1.2.1 Impetigo
 - 4.1.2.1.1 general
 - 4.1.2.1.2 chronic
 - 4.1.2.2 Erysipelas
 - 4.1.2.3 Cellulitis
 - 4.1.2.4 Animal and human bites
 - 4.1.2.5 Mastitis
 - 4.1.2.6 Boil / cyst / abscess
 - 4.1.2.7 Dermatitis / eczema
 - 4.1.2.7.1 Infected
 - 4.1.2.7.2 Rest
 - 4.1.2.8 Ulcers / diabetic foot
 - 4.1.2.8.1 Diabetic foot
 - 4.1.2.8.2 Infected ulcer
 - 4.1.2.8.3 Other
 - 4.1.2.9 Fungal / viral infections
 - 4.1.2.10 Ingrowing / infected nail

Supplementary data

4.1.2.11 Acne

4.1.2.11.1 Severe forms of acne

4.1.2.11.2 Rest

4.2 Wounds and surgery

4.2.1 Wounds and burns

4.2.1.1 general

4.2.1.2 Infected wound

4.2.2 Post-surgery (incl. childbirth)

4.2.2.1 general

4.2.2.2 Infected surgical wound

5 Cardiovascular system

5.1 Symptoms / testing / examinations

5.2 Diagnoses

5.2.1 Endocarditis

5.2.2 Phlebitis / arteritis

5.2.3 Pericarditis

6 Central nervous system

6.1 Symptoms / testing / examinations

6.2 Diagnoses

6.2.1 Meningitis

7 Musculoskeletal system

7.1 Symptoms / testing / examinations [here non-infectious]

7.2 Diagnoses

7.2.1 Osteomyelitis

7.2.2 Arthritis

7.2.2.1 Septic arthritis

7.2.2.2 Evidence supp. abx use

7.2.2.3 General / other

8 Dental / mouth

8.1 Symptoms / testing / procedures

8.2 Diagnoses

8.2.1 Diagnoses combined

8.2.2 Oral thrush

8.2.3 Herpes

9 Eye

9.1 Symptoms

9.2 Diagnoses

11 Cancer

12 Prophylactic therapy

X Miscellaneous

X.1 Symptoms / testing / examinations

- X.1.1 Unwell / ill
- X.1.2 Fever
- X.1.3 Pain
 - X.1.3.1 Back pain
 - X.1.3.2 Abdominal pain
 - X.1.3.3 Chest pain
 - X.1.3.4 Facial pain
 - X.1.3.5 Arm / hand / finger pain
 - X.1.3.6 Leg / foot / toe pain
 - X.1.3.7 Other pain
- X.1.4 Swelling
- X.1.5 Lymph node enlargement / infection
- X.1.8 Infection-specific testing
- X.1.9 Other symptoms / testing / examinations

X.2 Infections / conditions

- X.2.1 Unspecific infection (general)
- X.2.2 Unspecific / misc. infection (viral)
- X.2.3 E. coli
- X.2.4 Streptococcus
- X.2.5 Staphylococcus
- X.2.6 Pseudomonas
- X.2.7 Scarlet fever
- X.2.8 Thrush
- X.2.9 Chickenpox / Shingles
- X.2.10 Hand, foot and mouth disease
- X.2.11 Lyme
- X.2.12 Whooping cough
- X.2.13 Other bacterial infection

X.3 Misc.

- X.3.1 Severe unspecific / other
- X.3.2 Misc.

C. Results of using a more extensive algorithm

The baseline algorithm linked prescriptions to Read codes (i) entered on the same day as the prescription and/or (ii) with the same consultation identifier, given that the diagnoses were coded on or before the date of the prescription.

For the prescriptions that could not be linked to any Read code using the above algorithm, a more extensive algorithm was created. This second algorithm used consultation and prescribing data in three ways in the following order: (i) if a prescription was part of a sequence of repeat prescriptions, it was linked to any Read code with the same date as the first antibiotic prescribed in the sequence; (ii) otherwise, any Read code coinciding with the

Supplementary data

same antibiotic prescribed within 30 days prior was used; (iii) and lastly, if no diagnosis could be found in the previous steps, any diagnosis dated <8 days before the prescription was used to capture delayed prescribing.

Use of the second algorithm increased the proportion of prescriptions that could be linked to a Read code in our system to 75.3% compared to 69.0% for the baseline algorithm.

However, the distribution of the prescriptions over the body systems remained similar. (Table S1)

Body system	Baseline Algorithm			Second algorithm		
	Prescriptions	% of mapped	% of total	Prescriptions	% of mapped	% of total
Respiratory tract	1450757	46.0%	31.7%	1533377	44.5%	33.5%
Urogenital tract	716795	22.7%	15.7%	751161	21.8%	16.4%
Skin & Wounds	515270	16.3%	11.3%	582573	16.9%	12.7%
Other bodysystems	324060	10.3%	7.1%	407949	11.8%	8.9%
Multiple bodysystems	149625	4.7%	3.2%	168608	5.0%	3.8%
not mapped	821307		18.0%	759567		16.6%
no code	596559		13.0%	371138		8.1%

Table S1 Prescriptions that could be linked to a Read code in the hierarchical system by body system