SDC 1. Supplementary notes to Methods

Settings

Groote Schuur Hospital is a 975-bed urban academic hospital situated in Cape Town, in the Western Cape province, which provides secondary and tertiary level care, serves as a referral centre for approximately half of the province's population (2011 population: 5.8 million)[1] and is associated with the University of Cape Town. At this hospital we surveyed the general medical wards during May and June 2013. We did not survey the sub-speciality wards (dermatology, neurology, cardiology, respiratory medicine and nephrology), the oncology wards, or the high care / intensive care units. Restricting the survey to general medical wards was done partly due to resource limitations but also to allow the patients at this site to be reasonably comparable to those at other sites, which did not have sub-specialist wards. In 2009, the crude inpatient mortality in the medical wards of Groote Schuur Hospital was shown to be 573/3465 patients (17%)[2] and the 12-month post-discharge mortality to be 145/415 (35%).[3]

Edendale Hospital is a 900-bed peri-urban regional teaching hospital situated near Pietermaritzburg, in the KwaZulu-Natal province (2011 population: 10.3 million).[1] It provides care to the peri-urban community and serves as a referral centre for several district hospitals in the surrounding rural area. It is located at the epicentre of the HIV, tuberculosis and multidrug resistant tuberculosis epidemics in South Africa: a post-mortem study in 2008-2009 found that 94% of decedents in the medical wards of Edendale Hospital were HIV-seropositive, 50% had culture-positive tuberculosis at the time of death and 17% of these cultures were resistant to isoniazid and rifampicin.[4] At Edendale Hospital, we surveyed the medical wards over 30 days during July and August of 2013. We did not survey the intensive care unit, and there were no high care unit or sub-speciality wards at the time of this survey.

Cecilia Makiwane Hospital, situated in the large peri-urban community of Mdantsane in the Eastern Cape province, and Frere Hospital, situated in the city of East London, are co-managed as the East London Hospital Complex and provide secondary and tertiary-level care. These hospitals also serve as referral centres for a significant part of the province (2011 population: 6.6 million).[1] At these two teaching hospitals, we surveyed the general medical wards, as well as the high care and intensive care units, over 30 days during August and September 2013; there were no sub-speciality wards at the time of this survey. The burden of disease in the medical wards of these hospitals has not previously been published.

All four hospitals are public sector facilities. In the overburdened public health sector of South Africa, even at tertiary centres, elective medical admissions are rare and virtually all admissions to the medical wards occurred as emergencies via the emergency department or via primary care facilities.

Identification of new admissions

We identified all newly admitted patients using hospital administrative records. When possible, we cross-referenced administrative records with lists of admissions kept by the medical team on intake. We included in our survey all patients whom the medical team decided to admit, regardless of their actual admission status; thus, we included those patients who were discharged from or died in the emergency unit while still awaiting transfer to a ward. We collected data on weekdays; thus we identified newly admitted patients and collected the initial dataset within three days from the date of admission.

Multidisciplinary case review panels

We constituted two case review panels to review the causality, severity and preventability of cases identified as potential adverse drug reactions (ADRs). The first panel, consisting of a clinical pharmacist, a clinical pharmacologist, and one to three physicians / internists, reviewed the cases of patients who died during the 30-day survey period. (For these patients,

we had more detailed information in the form of a copy of their hospital folder, as well as a narrative case summary, prepared by the first author.) This panel's primary aim was to identify deaths in which ADRs played a causal or contributory role; results have been previously published.[5] For the purposes of our previous paper, the panel assessed the deaths of 105 patients: 28 of those were not included in the denominator of the current survey, as they were admitted prior to the current paper's 30-day survey period, and a further 48 patients' deaths were unrelated to ADRs, or related to ADRs that were not present on admission but developed in-hospital, or related to ADRs that were present on admission but did not form the main reason for admission. Those 48 cases are thus not included in the current study's numerator, but do form part of the current study's denominator. The remaining 29 patient folders which were assessed by the first case review panel fulfilled the inclusion criteria of the previous[5] and the current survey (i.e., were admitted due to an ADR and died during the 30-day survey period), and have thus been included in both studies' analyses.

The second panel, who assessed the suspected ADR-related admissions of patients alive at the end of the 30-day period, consisted of a research pharmacist, a clinical pharmacist, a general practitioner (GP), a second GP / medical epidemiologist, two clinical pharmacologists, and a physician. This panel performed their assessments in two rounds. In the first round, two GP-pharmacist pairs reviewed all 196 suspected ADR-related admissions, with the pairs reviewing the case independently from one another. Cases in which the two pairs disagreed on the WHO-UMC causality rating of any drug-event association were forwarded to the second round; cases where the two pairs agreed on the WHO-UMC causality rating of all drug-event associations were not forwarded to the second round. (In cases not forwarded to the second round, disagreements regarding preventability or severity were resolved through discussion by the panel members.) All seven panel members participated in the second round of assessment, during which the causality, preventability and severity of 132 cases were discussed until consensus was reached.

Three authors reconciled the data generated by the two assessment panels, as some methodological differences existed between their assessments: in the event of one ADR being attributed to multiple drug causes, the first panel (who assessed cases of patients who died) performed their causality assessment on each drug suspect individually. For the purposes of the current paper, however, we distinguish between Type A and Type B ADRs in our approach to causality assessment of these cases with multiple drug suspects, as described in the manuscript.

Presumptions and exceptions on Anatomic-Therapeutic-Chemical (ATC) coding

We presumed all aspirin to have been used for inhibition of platelet aggregation (and not for analgesia), and thus coded it to the ATC code B01AC06.

We presumed all bronchodilators and corticosteroids to have been inhaled, unless specifically documented to have been used systemically.

We coded antiretroviral and antituberculosis fixed drug combinations to the two, three, or four component drugs. We did not code other combinations to their components, but instead arbitrarily increased a patient's drug count with one unit for every combination drug recorded.

In the event that the precise drug was not known, but the class was, we coded the drug to the lowest level possible. For example, unspecified antihypertensive therapy was coded as C ('Cardiovascular system'). All insulins were recorded and reported as A10A ('Insulin and analogues').Where the fourth-level drug code (class) exploded down to only one fifth-level code (drug), we reported the drug name. (For example, the fourth-level (class) code C03CA 'high-ceiling diuretics: sulfonamides, plain' had only one member, the fifth-level (drug) code C03CA01 'furosemide'. For the purpose of this paper, we reported it as 'C03CA furosemide'.)

Reporting of ADRs

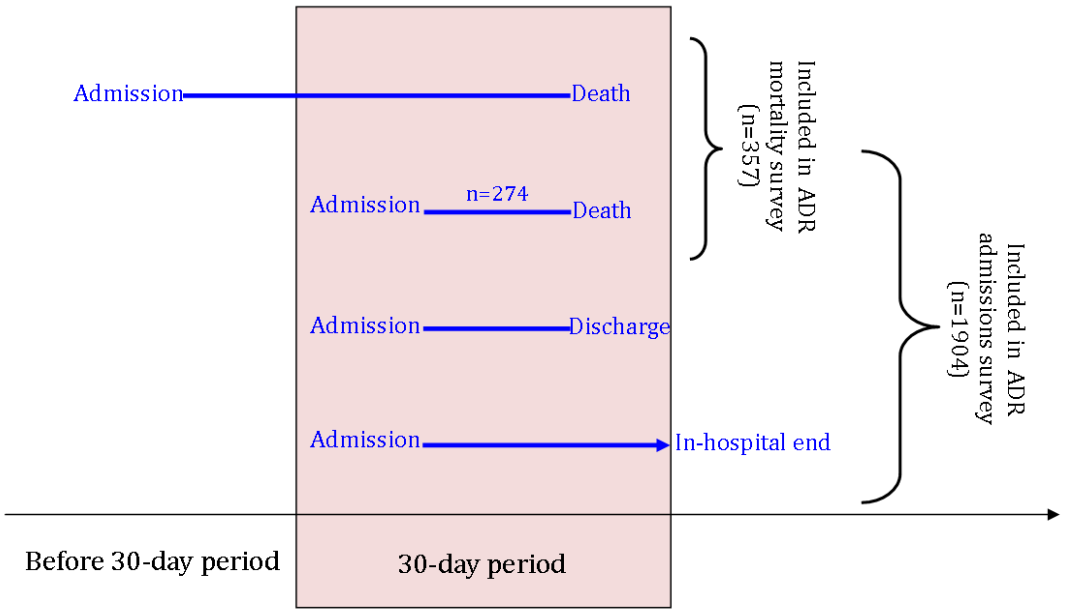
MedDRA® is a multiaxial classification system, with lower-level terms not mapping on a one-to-one basis to higher-level terms. For reporting purposes, we grouped MedDRA® 'preferred terms' as follows:

Reported ADR	**MedDRA® 'preferred terms' included in the reported ADR**
Blood dyscrasias	Anaemia, Anaemia macrocytic, Anaemia normochromic normocytic, Aplastic anaemia, Pancytopenia, Thrombocytopenia, Leukopenia, Neutropenia
Drug-induced liver injury (DILI)	Cholestatic liver injury, Hepatocellular liver injury, Mixed liver injury, Hepatorenal failure[a]
Renal impairment	Renal failure acute, Renal failure, Hepatorenal failure[a]
Haemorrhage	Gingival bleeding, Gastric haemorrhage, Gastrointestinal haemorrhage, Gastritis haemorrhagic, Lower gastrointestinal haemorrhage, Haemoptysis, Epistaxis, Haemarthrosis, Haematuria, Retroperitoneal haemorrhage, Menorrhagia, Cerebral haemorrhage, Haemorrhage intracranial, Subarachnoid haemorrhage

(a) Hepatorenal failure was reported under two grouped terms.

References

1. Statistics South Africa. *Census 2011. Statistical release P0301.4 (Revised)*. Pretoria: Statistics South Africa; 2012.
2. Myer L, Smith E, Mayosi BM. Medical inpatient mortality at Groote Schuur Hospital, Cape Town, South Africa, 2002-2009. *S Afr Med J*. 2013;103(1):28–31.
3. Stuart-Clark H, Vorajee N, Zuma S, et al. Twelve-month outcomes of patients admitted to the acute general medical service at Groote Schuur Hospital. *S Afr Med J*. 2012;102(6):549–53.
4. Cohen T, Murray M, Wallengren K, Alvarez GG, Samuel EY, Wilson D. The prevalence and drug sensitivity of tuberculosis among patients dying in hospital in KwaZulu-Natal, South Africa: a postmortem study. *PLoS Med*. 2010;7(6):e1000296.
5. Mouton JP, Mehta U, Parrish AG, et al. Mortality from adverse drug reactions in adult medical inpatients at four hospitals in South Africa: a cross-sectional survey. Br J Clin Pharmacol. 2015;80(4):818–826.



SDC 2. Schematic representation of overlap in the denominator of the current survey (n=1904) and a previously published survey (n=357) on ADR-related mortality.[1] There were 274 patients who were included in the denominator of both surveys.

1. Mouton JP, Mehta U, Parrish AG, et al. Mortality from adverse drug reactions in adult medical inpatients at four hospitals in South Africa: a cross-sectional survey. Br J Clin Pharmacol. 2015;80(4):818-826.

SDC 3. List of triggers used to identify suspected adverse drug reactions.

Event triggers	Drug order triggers	Laboratory result triggers	Suspected ADR
• Angioedema • Bronchospasm • Lip swelling • Rash or ulceration	• Adrenaline/epinephrine • Antihistamine • Corticosteroid • Promethazine for HSR		**Hypersensitivity reaction**
	• Flumazenil • Naloxone	• Amikacin peak > 30 or trough > 2 mg/L • Carbamazepine > 45 µmol/L • Digoxin > 1.5 nmol/L • Gentamicin peak > 8 or trough > 1 mg/L • Phenobarbital > 160 µmol/L • Phenytoin > 80 µmol/L • Theophylline >110 µmol/L • Tobramycin peak > 8 or trough > 1 mg/L • Valproic acid > 700 µmol/L • Vancomycin > 20 mg/L • Other toxic drug concentration • Paracetamol concentration done	**Toxic drug effect**
• Fracture • Osteonecrosis			**Drug-induced bone disease**
• Bone marrow biopsy	• GCSF/meropenem	• Haemoglobin <8 g/dL • Pancytopenia • Platelets < 50 x 10^9/L • White blood cell count < 1.5 x 10^9/L	**Drug-induced bone marrow suppression**
• New arrhythmia • New cardiac failure • New hypotension • Torsades de pointes	• Atropine • Magnesium sulphate		**Drug-induced cardiovascular problem**
• Ataxia • Decreased LOC • Delirium • Dizziness • Dyskinesia • Dystonia • Falls • Lethargy • Oversedation • Seizure(s) • Torticollis	• Biperidin • Diazepam for EPSE • Diazepam for seizure • Lorazepam stat for seizure • Phenytoin for seizure • Promethazine for EPSE		**Drug-induced central nervous system problem**
• Bleeding	• Fresh frozen plasma • Protamine sulphate • Vitamin K	• International normalised ratio (INR) >5 • Partial thromboplastin time (PTT) > 100 seconds	**Drug-induced coagulation problem**
	• Calcium gluconate • Insulin with glucose • Polystyrene sulfate	• Potassium <3.5 mmol/L • Potassium >5.5 mmol/L	**Drug-induced electrolyte disturbance**
• Gastroscopy • Nausea and vomiting	• Antidiarrhoeals • Antiemetic • Metoclopramide	• *Clostridium difficile* after antibiotics	**Drug-induced gastrointestinal problem**
	• Dextrose 50%	• Glucose < 3 mmol/L	**Drug-induced hypoglycaemia**
• New jaundice • Liver biopsy		• Alanine transaminase (ALT) > 3x ULN • Bilirubin > 2x ULN	**Drug-induced liver injury**
• Renal biopsy		• eGFR worsening / single new low • CrCl worsening / single new low • Creatinine rising / single new high	**Drug-induced renal impairment**
• Abrupt drug stop • HCW suspects ADR • Transfer to higher level of care			**Event suggests ADR**

ADR: adverse drug reaction; CrCl: creatinine clearance; eGFR: estimated glomerular filtration rate; EPSE: extrapyramidal side effects; GCSF: granulocyte colony stimulating factor; HCW: healthcare worker; HSR: hypersensitivity reaction; LOC: level of consciousness; ULN: upper limit of normal

SDC 4. Prevalence of comorbidities, according to ICD-10 classification, over the 4-week period prior to patients' first admission (n=1904 patients).

ICD-10 Chapter / Diagnostic Block	Count	Proportion
A00-B99 CERTAIN INFECTIOUS AND PARASITIC DISEASES	**645**	**34%**
A00-A09 Intestinal infectious diseases	41	2.1%
A15-A19 Tuberculosis	200	11%
A30-A49 Other bacterial diseases	18	<1%
A50-A64 Infections with a predominantly sexual mode of transmission	6	<1%
A80-A89 Viral infections of the central nervous system	2	<1%
B00-B09 Viral infections characterized by skin and mucous membrane lesions	6	<1%
B15-B19 Viral hepatitis	5	<1%
B20-B24 Human immunodeficiency virus [HIV] disease[a]	559	29%
B25-B34 Other viral diseases	2	<1%
B35-B49 Mycoses	57	2.9%
B50-B64 Protozoal diseases	3	<1%
B85-B89 Pediculosis, acariasis and other infestations	1	<1%
B90-B94 Sequelae of infectious and parasitic diseases	2	<1%
C00-D48 NEOPLASMS	**50**	**2.6%**
C15-C26 Malignant neoplasms: Digestive organs	7	<1%
C30-C39 Malignant neoplasms: Respiratory and intrathoracic organs	3	<1%
C40-C41 Malignant neoplasms: Bone and articular cartilage	1	<1%
C45-C49 Malignant neoplasms: Mesothelial and soft tissue	7	<1%
C50-C50 Malignant neoplasms: Breast	5	<1%
C51-C58 Malignant neoplasms: Female genital organs	2	<1%
C60-C63 Malignant neoplasms: Male genital organs	4	<1%
C64-C68 Malignant neoplasms: Urinary tract	2	<1%
C69-C72 Malignant neoplasms: Eye, brain and other parts of central nervous system	3	<1%
C76-C80 Malignant neoplasms of ill-defined, secondary and unspecified sites	3	<1%
C81-C96 Malignant neoplasms of lymphoid, haematopoietic and related tissue	7	<1%
D00-D09 In situ neoplasms	1	<1%
D10-D36 Benign neoplasms	4	<1%
D37-D48 Neoplasms of uncertain or unknown behaviour	5	<1%
D50-D89 DISEASES OF THE BLOOD AND HAEMOPOIESIS; CERTAIN DISORDERS OF THE IMMUNE SYSTEM	**171**	**9.0%**
D50-D53 Nutritional anaemias	30	1.6%
D55-D59 Haemolytic anaemias	1	<1%
D60-D64 Aplastic and other anaemias	114	6.0%
D65-D69 Coagulation defects, purpura and other haemorrhagic conditions	33	1.7%
D70-D77 Other diseases of blood and blood-forming organs	11	<1%
D80-D89 Certain disorders involving the immune mechanism	1	<1%
E00-E90 ENDOCRINE, NUTRITIONAL AND METABOLIC DISEASES	**585**	**31%**
E00-E07 Disorders of thyroid gland	35	1.8%
E10-E14 Diabetes mellitus	343	18%
E15-E16 Other disorders of glucose regulation and pancreatic internal secretion	15	<1%
E20-E35 Disorders of other endocrine glands	2	<1%
E40-E46 Malnutrition	2	<1%
E50-E64 Other nutritional deficiencies	7	<1%
E65-E68 Obesity and other hyperalimentation	59	3.1%
E70-E90 Metabolic disorders	257	13%
F00-F99 MENTAL AND BEHAVIOURAL DISORDERS	**134**	**7.0%**
F00-F09 Organic, including symptomatic, mental disorders	44	2.3%
F10-F19 Mental and behavioural disorders due to psychoactive substance use	30	1.6%
F20-F29 Schizophrenia, schizotypal and delusional disorders	18	<1%
F30-F39 Mood [affective] disorders	21	1.1%
F40-F48 Neurotic, stress-related and somatoform disorders	5	<1%
F50-F59 Behavioural syndromes associated with physiological disturbances and physical factors	1	<1%
F70-F79 Mental retardation	14	<1%
F99-F99 Unspecified mental disorder	8	<1%
G00-G99 DISEASES OF THE NERVOUS SYSTEM	**123**	**6.5%**
G00-G09 Inflammatory diseases of the central nervous system	7	<1%
G10-G14 Systemic atrophies primarily affecting the central nervous system	3	<1%

G20-G26 Extrapyramidal and movement disorders	8	<1%
G30-G32 Other degenerative diseases of the nervous system	2	<1%
G35-G37 Demyelinating diseases of the central nervous system	2	<1%
G40-G47 Episodic and paroxysmal disorders	87	4.6%
G50-G59 Nerve, nerve root and plexus disorders	3	<1%
G60-G64 Polyneuropathies and other disorders of the peripheral nervous system	6	<1%
G70-G73 Diseases of myoneural junction and muscle	1	<1%
G80-G83 Cerebral palsy and other paralytic syndromes	7	<1%
G90-G99 Other disorders of the nervous system	4	<1%
H00-H59 DISEASES OF THE EYE AND ADNEXA	**32**	**1.7%**
H15-H22 Disorders of sclera, cornea, iris and ciliary body	2	<1%
H25-H28 Disorders of lens	4	<1%
H30-H36 Disorders of choroid and retina	6	<1%
H40-H42 Glaucoma	8	<1%
H46-H48 Disorders of optic nerve and visual pathways	2	<1%
H53-H54 Visual disturbances and blindness	12	<1%
H55-H59 Other disorders of eye and adnexa	1	<1%
H60-H95 DISEASES OF THE EAR AND MASTOID PROCESS	**13**	**<1%**
H65-H75 Diseases of middle ear and mastoid	1	<1%
H80-H83 Diseases of inner ear	1	<1%
H90-H95 Other disorders of ear	11	<1%
I00-I99 DISEASES OF THE CIRCULATORY SYSTEM	**845**	**44%**
I00-I02 Acute rheumatic fever	2	<1%
I05-I09 Chronic rheumatic heart diseases	22	1.2%
I10-I15 Hypertensive diseases	691	36%
I20-I25 Ischaemic heart diseases	123	6.5%
I26-I28 Pulmonary heart disease and diseases of pulmonary circulation	39	2.0%
I30-I52 Other forms of heart disease	194	10%
I60-I69 Cerebrovascular diseases	112	5.9%
I70-I79 Diseases of arteries, arterioles and capillaries	21	1.1%
I80-I89 Diseases of veins, lymphatic vessels and lymph nodes, not elsewhere classified	18	<1%
I95-I99 Other and unspecified disorders of the circulatory system	5	<1%
J00-J99 DISEASES OF THE RESPIRATORY SYSTEM	**283**	**15%**
J00-J06 Acute upper respiratory infections	3	<1%
J09-J18 Influenza and pneumonia	38	2.0%
J20-J22 Other acute lower respiratory infections	43	2.3%
J30-J39 Other diseases of upper respiratory tract	5	<1%
J40-J47 Chronic lower respiratory diseases	167	8.8%
J60-J70 Lung diseases due to external agents	7	<1%
J80-J84 Other respiratory diseases principally affecting the interstitium	12	<1%
J85-J86 Suppurative and necrotic conditions of lower respiratory tract	2	<1%
J90-J94 Other diseases of pleura	16	<1%
J95-J99 Other diseases of the respiratory system	17	<1%
K00-K93 DISEASES OF THE DIGESTIVE SYSTEM	**133**	**7.0%**
K00-K14 Diseases of oral cavity, salivary glands and jaws	3	<1%
K20-K31 Diseases of oesophagus, stomach and duodenum	54	2.8%
K35-K38 Diseases of appendix	1	<1%
K40-K46 Hernia	2	<1%
K50-K52 Noninfective enteritis and colitis	4	<1%
K55-K64 Other diseases of intestines	40	2.1%
K65-K67 Diseases of peritoneum	3	<1%
K70-K77 Diseases of liver	19	<1%
K80-K87 Disorders of gallbladder, biliary tract and pancreas	7	<1%
K90-K93 Other diseases of the digestive system	13	<1%
L00-L99 DISEASES OF THE SKIN AND SUBCUTANEOUS TISSUE	**44**	**2.3%**
L00-L08 Infections of the skin and subcutaneous tissue	12	<1%
L10-L14 Bullous disorders	1	<1%
L20-L30 Dermatitis and eczema	5	<1%
L40-L45 Papulosquamous disorders	7	<1%
L60-L75 Disorders of skin appendages	2	<1%
L80-L99 Other disorders of the skin and subcutaneous tissue	18	<1%

M00-M99 DISEASES OF THE MUSCULOSKELETAL SYSTEM AND CONNECTIVE TISSUE	**101**	**5.3%**
M00-M03 Arthropathies: Infectious arthropathies	1	<1%
M05-M14 Arthropathies: Inflammatory polyarthropathies	51	2.7%
M15-M19 Arthropathies: Arthrosis	17	<1%
M20-M25 Arthropathies: Other joint disorders	6	<1%
M30-M36 Systemic connective tissue disorders	8	<1%
M40-M43 Dorsopathies: Deforming dorsopathies	2	<1%
M45-M49 Dorsopathies: Spondylopathies	2	<1%
M50-M54 Dorsopathies: Other dorsopathies	8	<1%
M60-M63 Soft tissue disorders: Disorders of muscles	3	<1%
M70-M79 Soft tissue disorders: Other soft tissue disorders	7	<1%
M80-M85 Osteopathies and chondropathies: Disorders of bone density and structure	2	<1%
N00-N99 DISEASES OF THE GENITOURINARY SYSTEM	**373**	**20%**
N00-N08 Glomerular diseases	6	<1%
N10-N16 Renal tubulo-interstitial diseases	4	<1%
N17-N19 Renal failure	323	17%
N20-N23 Urolithiasis	1	<1%
N25-N29 Other disorders of kidney and ureter	2	<1%
N30-N39 Other diseases of urinary system	33	1.7%
N40-N51 Diseases of male genital organs	14	<1%
N60-N64 Disorders of breast	1	<1%
N70-N77 Inflammatory diseases of female pelvic organs	5	<1%
N80-N98 Noninflammatory disorders of female genital tract	7	<1%
O00-O99 PREGNANCY, CHILDBIRTH AND THE PUERPERIUM	**6**	**<1%**
O10-O16 Oedema, proteinuria and hypertensive disorders in pregnancy, childbirth, puerperium	3	<1%
O30-O48 Maternal care related to the fetus and amniotic cavity and possible delivery problems	1	<1%
O80-O84 Delivery	3	<1%
Q00-Q99 CONGENITAL MALFORMATIONS, DEFORMATIONS AND CHROMOSOMAL ABNORMALITIES	**7**	**<1%**
Q00-Q07 Congenital malformations of the nervous system	1	<1%
Q30-Q34 Congenital malformations of the respiratory system	1	<1%
Q38-Q45 Other congenital malformations of the digestive system	1	<1%
Q60-Q64 Congenital malformations of the urinary system	1	<1%
Q80-Q89 Other congenital malformations	3	<1%
S00-T98 INJURY, POISONING AND CERTAIN OTHER CONSEQUENCES OF EXTERNAL CAUSES	**20**	**1.1%**
S00-S09 Injuries to the head	2	<1%
S20-S29 Injuries to the thorax	1	<1%
S40-S49 Injuries to the shoulder and upper arm	1	<1%
S50-S59 Injuries to the elbow and forearm	1	<1%
S70-S79 Injuries to the hip and thigh	4	<1%
S80-S89 Injuries to the knee and lower leg	1	<1%
S90-S99 Injuries to the ankle and foot	1	<1%
T08-T14 Injuries to unspecified parts of trunk, limb or body region	1	<1%
T20-T32 Burns and corrosions	1	<1%
T36-T50 Poisoning by drugs, medicaments and biological substances	1	<1%
T51-T65 Toxic effects of substances chiefly nonmedicinal as to source	1	<1%
T66-T78 Other and unspecified effects of external causes	1	<1%
T80-T88 Complications of surgical and medical care, not elsewhere classified	3	<1%
T90-T98 Sequelae of injuries, of poisoning and of other consequences of external causes	1	<1%
V01-Y98 EXTERNAL CAUSES OF MORBIDITY AND MORALITY	**11**	**<1%**
V80-V89 Accidents: Transport accidents: Other land transport accidents	1	<1%
W00-W19 Accidents: Other external causes of accidental injury: Falls	1	<1%
X60-X84 Intentional self-harm	3	<1%
X85-Y09 Assault	2	<1%
Y60-Y69 Complications of care: Misadventures	1	<1%
Y83-Y84 Complications of care: Without mention of misadventure	1	<1%
Y90-Y98 Supplementary factors related to causes of morbidity and mortality	2	<1%
Z00-Z99 FACTORS INFLUENCING HEALTH STATUS AND CONTACT WITH HEALTH SERVICES	**318**	**17%**
Z00-Z13 Persons encountering health services for examination and investigation	1	<1%
Z20-Z29 Persons with potential health hazards related to communicable diseases	4	<1%
Z30-Z39 Persons encountering health services in circumstances related to reproduction	1	<1%
Z40-Z54 Persons encountering health services for specific procedures and health care	1	<1%

Z55-Z65 Potential health hazards related to socioeconomic and psychosocial circumstances	6	<1%
Z70-Z76 Persons encountering health services in other circumstances	65	3.4%
Z80-Z99 Persons with potential health hazards related to family and personal history	275	14%

(a) HIV infection diagnosed during hospital admission was considered to have been present in the four weeks prior to the admission and to therefore be a comorbid condition.

SDC 5. Prevalence of drug use, according to ATC-classification, over the 4-week period prior to patients' first admission (n=1904 patients).

Drug class / Drug	Count	Proportion
A ALIMENTARY TRACT AND METABOLISM	**448**	**24%**
A02 Drugs for acid-related disorders	97	5.1%
A02A Antacids	9	<1%
A02AA Magnesium compounds	1	<1%
A02AA05 Magnesium silicate	1	<1%
A02AB Aluminium compounds	1	<1%
A02AB01 Aluminium hydroxide	1	<1%
A02AH Antacids with sodium bicarbonate	2	<1%
Unspecified antacids	6	<1%
A02B Drugs for peptic ulcer and gastro-oesophageal reflux disease	93	4.9%
A02BA H2-receptor antagonists	10	<1%
A02BA01 Cimetidine	3	<1%
A02BA02 Ranitidine	5	<1%
Unspecified H2-receptor antagonists	2	<1%
A02BC Proton pump inhibitors	81	4.3%
A02BC01 Omeprazole	74	3.9%
A02BC02 Pantoprazole	5	<1%
A02BC03 Lansoprazole	2	<1%
A02BC05 Esomeprazole	1	<1%
A02BX Other drugs for peptic ulcer and gastro-oesophageal reflux disease	2	<1%
Unspecified drugs for peptic ulcer and gastro-oesophageal reflux disease	1	<1%
A03 Drugs for functional gastrointestinal disorders	43	2.3%
A03B Belladonna and derivatives, plain	12	<1%
A03BA Belladonna alkaloids, tertiary amines	1	<1%
A03BA01 Atropine	1	<1%
A03BB Belladonna alkaloids, semisynthetic, quaternary ammonium compounds	11	<1%
A03BB01 Butylscopolamine	11	<1%
A03F Propulsives	37	1.9%
A03FA Propulsives	37	1.9%
A03FA01 Metoclopramide	36	1.9%
A03FA03 Domperidone	1	<1%
A04 Antiemetics and antinauseants	1	<1%
A04A Antiemetics and antinauseants	1	<1%
A04AA Serotonin (5HT3) antagonists	1	<1%
A04AA01 Ondansetron	1	<1%
A04AA02 Granisetron	1	<1%
A05 Bile and liver therapy	1	<1%
A05A Bile therapy	1	<1%
A05AA Bile acid preparations	1	<1%
A05AA02 Ursodeoxycholic acid	1	<1%
A06 Laxatives	29	1.5%
A06A Laxatives	29	1.5%
A06AA Softeners, emollients	1	<1%
A06AA01 Liquid paraffin	1	<1%
A06AB Contact laxatives	8	<1%
A06AB02 Bisacodyl	2	<1%
A06AB06 Senna glycosides	7	<1%
A06AD Osmotically acting laxatives	18	<1%
A06AD11 Lactulose	15	<1%
A06AD18 Sorbitol	2	<1%
Unspecified osmotically acting laxatives	1	<1%
Unspecified laxatives	3	<1%
A07 Antidiarrhoeals, intestinal anti-inflammatory / anti-infective agents	28	1.5%
A07A Intestinal anti-infectives	7	<1%
A07AA Antibiotics	7	<1%
A07AA02 Nystatin	7	<1%

A07B Intestinal adsorbents	3	<1%
A07BA Charcoal preparations	3	<1%
A07BA01 Medicinal charcoal	3	<1%
A07C Electrolytes with carbohydrates	2	<1%
A07CA Oral rehydration salt formulations	2	<1%
A07D Antipropulsives	12	<1%
A07DA Antipropulsives	12	<1%
A07DA03 Loperamide	12	<1%
A07E Intestinal anti-inflammatory agents	5	<1%
A07EC Aminosalicylic acid and similar agents	5	<1%
A07EC01 Sulfasalazine	3	<1%
A07EC02 Mesalazine	2	<1%
Unspecified antidiarrhoeals	2	<1%
A09 Digestives, incl. enzymes	1	<1%
A09A Digestives, incl. enzymes	1	<1%
A09AA Enzyme preparations	1	<1%
A09AA02 Multienzymes (lipase, protease etc.)	1	<1%
A10 Drugs used in diabetes	321	17%
A10A Insulins and analogues	130	6.8%
A10AB Insulins and analogues, fast-acting	16	<1%
A10AC Insulins and analogues, intermediate-acting	18	<1%
A10AD Insulins and analogues, intermediate-acting combined with fast-acting	78	4.1%
A10AE Insulins and analogues, long-acting	1	<1%
Insulin, type unspecified	30	1.6%
A10B Oral blood glucose lowering drugs	225	12%
A10BA Biguanides	190	10%
A10BA02 Metformin	190	10%
A10BB Sulfonamides, urea derivatives	109	5.7%
A10BB01 Glibenclamide	43	2.3%
A10BB09 Gliclazide	66	3.5%
Unspecified oral blood glucose lowering drugs	11	<1%
Unspecified treatment for diabetes	18	<1%
A11 – A12 Vitamin and mineral supplements	212	11%
B BLOOD AND BLOOD FORMING ORGANS	**370**	**19%**
B01 Antithrombotic agents	305	16%
B01A Antithrombotic agents	305	16%
B01AA Vitamin K antagonists	57	3.0%
B01AA03 Warfarin	57	3.0%
B01AB Heparin group	36	1.9%
B01AB01 Heparin	13	<1%
B01AB05 Enoxaparin	23	1.2%
B01AC Platelet aggregation inhibitors, excl. heparins	238	13%
B01AC04 Clopidogrel	10	<1%
B01AC06 Acetylsalicylic acid	238	13%
B01AD Enzymes	7	<1%
B01AD01 Streptokinase	7	<1%
B02 Antihaemorrhagics	9	<1%
B02A Antifibrinolytics	4	<1%
B02AA Amino acids	4	<1%
B02AA02 Tranexamic acid	4	<1%
B02B Vitamin K and other haemostatics	5	<1%
B02BA Vitamin K	5	<1%
B02BA01 Phytomenadione	5	<1%
B03 Anti-anaemic preparations	77	4.0%
B03A Iron preparations	55	2.9%
B03AA Iron bivalent, oral preparations	54	2.8%
B03AA07 Ferrous sulfate	54	2.8%
B03AD Iron in combination with folic acid	2	<1%
B03AD02 Ferrous fumarate	2	<1%
B03B Vitamin B12 and folic acid	51	2.7%
B03BA Vitamin B12 (cyanocobalamin and analogues)	3	<1%

B03BA01 Cyanocobalamin	3	<1%
B03BB Folic acid and derivatives	48	2.5%
B03BB01 Folic acid	48	2.5%
B03X Other anti-anaemic preparations	2	<1%
B03XA Other anti-anaemic preparations	2	<1%
B03XA01 Erythropoietin	2	<1%
B05 Blood substitutes and perfusion solutions	12	<1%
B05B IV solutions	5	<1%
B05BA Solutions for parenteral nutrition	5	<1%
B05BA03 Carbohydrate solutions for parenteral nutrition	5	<1%
B05C Irrigating solutions	4	<1%
B05CX Other irrigating solutions	4	<1%
B05CX01 Glucose	4	<1%
B05X IV Solution additives	4	<1%
B05XA Electrolyte solutions	4	<1%
B05XA01 Potassium chloride	2	<1%
B05XA02 Sodium bicarbonate	2	<1%
C CARDIOVASCULAR SYSTEM	**765**	**40%**
C01 Cardiac therapy	133	7.0%
C01A Cardiac glycosides	40	2.1%
C01AA Digitalis glycosides	40	2.1%
C01AA05 Digoxin	40	2.1%
C01B Anti-arrhythmics, class I and III	7	<1%
C01BA Anti-arrhythmics, class Ia	1	<1%
C01BA03 Disopyramide	1	<1%
C01BD Anti-arrhythmics, class III	6	<1%
C01BD01 Amiodarone	6	<1%
C01C Cardiac stimulants, excl. cardiac glycosides	2	<1%
C01CA Adrenergic and dopaminergic agents	2	<1%
C01CA24 Epinephrine	2	<1%
C01D Vasodilators used in cardiac diseases	85	4.5%
C01DA Organic nitrates	85	4.5%
C01DA02 Glyceryl trinitrate	5	<1%
C01DA08 Isosorbide dinitrate	67	3.5%
C01DA14 Isosorbide mononitrate	26	1.4%
Unspecified nitrates	2	<1%
C01E Other cardiac preparations	2	<1%
C01EB Other cardiac preparations	2	<1%
C01EB10 Adenosine	1	<1%
C01EB17 Ivabradine	1	<1%
C02 Antihypertensives	35	1.8%
C02A Antiadrenergic agents, centrally acting	2	<1%
C02AB Methyldopa	2	<1%
C02AB01 Methyldopa (levorotatory)	2	<1%
C02C Antiadrenergic agents, peripherally acting	17	<1%
C02CA Alpha-adrenoreceptor antagonists	17	<1%
C02CA01 Prazosin	3	<1%
C02CA04 Doxazosin	14	<1%
C02D Arteriolar smooth muscle, agents acting on	22	1.2%
C02DB Hydrazinophthalazine derivatives	21	1.1%
C02DB02 Hydralazine	21	1.1%
C02DC Pyrimidine derivatives	1	<1%
C02DC01 Minoxidil	1	<1%
C03 Diuretics	559	29%
C03A Low-ceiling diuretics, thiazides	262	14%
C03AA Thiazides, plain	260	14%
C03AA03 Hydrochlorothiazide	260	14%
C03AB Thiazides and potassium in combination	2	<1%
C03AB03 Hydrochlorothiazide and potassium	2	<1%
C03B Low-ceiling diuretics, excl. thiazides	1	<1%
C03BA Sulfonamides, plain	1	<1%
C03BA11 Indapamide	1	<1%

C03C High-ceiling diuretics	327	17%
C03CA Sulfonamides, plain	327	17%
C03CA01 Furosemide	327	17%
C03D Potassium-sparing agents	80	4.2%
C03DA Aldosterone antagonists	79	4.1%
C03DA01 Spironolactone	79	4.1%
C03DB Other potassium-sparing agents	1	<1%
C03DB01 Amiloride	1	<1%
Unspecified diuretics	2	<1%
C05 Vasoprotectives	1	<1%
C05A Anti-haemorrhoidals for topical use	1	<1%
C05AX Other anti-haemorrhoidals for topical use	1	<1%
C05AX02 Bismuth preparations, combinations	1	<1%
C07 Beta-blocking agents	186	9.8%
C07A Beta-blocking agents	186	9.8%
C07AA Beta-blocking agents, non-selective	6	<1%
C07AA05 Propranolol	6	<1%
C07AB Beta-blocking agents, selective	134	7.0%
C07AB03 Atenolol	132	6.9%
C07AB07 Bisoprolol	2	<1%
C07AG Alpha- and beta-blocking agents	48	2.5%
C07AG02 Carvedilol	48	2.5%
C08 Calcium channel blockers	240	13%
C08C Selective calcium channel blockers with mainly vascular effects	230	12%
C08CA Dihydropyridine derivatives	230	12%
C08CA01 Amlodipine	187	9.8%
C08CA05 Nifedipine	44	2.3%
C08D Selective calcium channel blockers with direct cardiac effects	10	<1%
C08DA Phenylalkylamine derivatives	9	<1%
C08DA01 Verapamil	9	<1%
C08DB Benzothiazepine derivatives	1	<1%
C08DB01 Diltiazem	1	<1%
C09 Agents acting on the renin-angiotensin system	386	20%
C09A ACE-inhibitors, plain	369	19%
C09AA ACE-inhibitors, plain	369	19%
C09AA01 Captopril	6	<1%
C09AA02 Enalapril	246	13%
C09AA04 Perindopril	117	6.1%
C09B ACE-inhibitors, combinations	4	<1%
C09BA ACE-inhibitors and diuretics	4	<1%
C09BA03 Lisinopril and diuretics	1	<1%
C09BA04 Perindopril and diuretics	3	<1%
C09C Angiotensin II antagonists, plain	14	<1%
C09CA Angiotensin II antagonists, plain	14	<1%
C09CA01 Losartan	13	<1%
C09CA03 Valsartan	1	<1%
C09D Angiotensin II antagonists, combinations	1	<1%
C09DA Angiotensin II antagonists and diuretics	1	<1%
C09DA07 Telmisartan and diuretics	1	<1%
C10 Serum lipid reducing agents	223	12%
C10A Cholesterol and triglyceride reducers	220	12%
C10AA HMG-coA reductase inhibitors	217	11%
C10AA01 Simvastatin	208	11%
C10AA05 Atorvastatin	6	<1%
Unspecified statins	3	<1%
C10AB Fibrates	1	<1%
C10AB02 Bezafibrate	1	<1%
C10AC Bile acid sequestrants	2	<1%
C10AC01 Cholestyramine	2	<1%
Unspecified lipid reducing agents	3	<1%
Unspecified cardiovascular agents (*)	71	3.7%

D DERMATOLOGICALS	**14**	**<1%**
D01 Antifungals for dermatological use	5	<1%
D01A Antifungals for topical use	3	<1%
D01AC Imidazole and triazole derivatives	2	<1%
D01AC01 Clotrimazole	2	<1%
D01AE Other antifungals for topical use	1	<1%
D01AE02 Methylrosaniline (Gentian violet)	1	<1%
D01B Antifungals for systemic use	2	<1%
D01BA Antifungals for systemic use	2	<1%
D01BA01 Griseofulvin	2	<1%
D02 Emollients and protectives	3	<1%
D02A Emollients and protectives	3	<1%
D02AB Zinc products	1	<1%
D02AX Other emollients and protectives	2	<1%
D07 Corticosteroids, dermatological preparations	4	<1%
D07A Corticosteroids, plain	4	<1%
D07AA Corticosteroids, weak (Group I)	1	<1%
D07AA02 Hydrocortisone	1	<1%
D07AC Corticosteroids, potent (Group III)	3	<1%
D07AC01 Betamethasone	3	<1%
D07AD Corticosteroids, very potent (Group IV)	1	<1%
D07AD01 Clobetasol	1	<1%
D08 Antiseptics and disinfectants	2	<1%
D08A Antiseptics and disinfectants	2	<1%
D08AG Iodine products	1	<1%
D08AG02 Povidone-iodine	1	<1%
D08AX Other antiseptics and disinfectants	1	<1%
D08AX06 Potassium permanganate	1	<1%
G GENITO-URINARY SYSTEM AND SEX HORMONES	**21**	**1.1%**
G02 Other gynaecologicals	2	<1%
G02A Oxytocics	1	<1%
G02AB Ergot alkaloids	1	<1%
G02AB03 Ergometrine	1	<1%
G02C Other gynaecologicals	1	<1%
G02CB Prolactine inhibitors	1	<1%
G02CB01 Bromocriptine	1	<1%
G03 Sex hormones and modulators of the genital system	10	<1%
G03A Hormonal contraceptives for systemic use	9	<1%
G03AA Progestogens and oestrogens, fixed combinations	2	<1%
G03AA07 Levonorgestrel and oestrogen	2	<1%
G03AC Progestogens	5	<1%
G03AC01 Norethisterone	1	<1%
G03AC06 Medroxyprogesterone	4	<1%
Unspecified hormonal contraceptives	2	<1%
Unspecified sex hormones	1	<1%
G04 Urologicals	9	<1%
G04B Other urologicals, incl. antispasmodics	3	<1%
G04BD Urinary antispasmodics	3	<1%
G04BD04 Oxybutynin	3	<1%
G04C Drugs used in benign prostatic hypertrophy	8	<1%
G04CA Alpha-adrenoreceptor antagonists	8	<1%
G04CA02 Tamsulosin	8	<1%
H SYSTEMIC HORMONAL PREPARATIONS, EXCL. SEX HORMONES AND INSULINS	**142**	**7.5%**
H01 Pituitary and hypothalamic hormones and analogues	1	<1%
H01C Hypothalamic hormones	1	<1%
H01CB Antigrowth hormone	1	<1%
H01CB01 Somatostatin	1	<1%

H02 Corticosteroids for systemic use	118	6.2%
H02A Corticosteroids for systemic use, plain	118	6.2%
H02AB Glucocorticoids	118	6.2%
H02AB01 Betamethasone	1	<1%
H02AB02 Dexamethasone	4	<1%
H02AB04 Methylprednisolone	3	<1%
H02AB06 Prednisolone	4	<1%
H02AB07 Prednisone	97	5.1%
H02AB09 Hydrocortisone	23	1.2%
H03 Thyroid therapy	27	1.4%
H03A Thyroid preparations	23	1.2%
H03AA Thyroid hormones	23	1.2%
H03AA01 Levothyroxine sodium	23	1.2%
H03AA03 Combinations of levothyroxine and liothyronine	1	<1%
H03B Antithyroid preparations	4	<1%
H03BB Sulfur-containing imidazole derivatives	4	<1%
H03BB01 Carbimazole	4	<1%
J ANTI-INFECTIVES FOR SYSTEMIC USE	**559**	**29%**
J01 Antibacterials for systemic use	240	13%
J01A Tetracyclines	11	<1%
J01AA Tetracyclines	11	<1%
J01AA02 Doxycycline	11	<1%
J01C Beta-lactam antibacterials, penicillins	101	5.3%
J01CA Penicillins with extended spectrum	59	3.1%
J01CA01 Ampicillin	6	<1%
J01CA04 Amoxicillin	52	2.7%
J01CA12 Piperacillin	1	<1%
J01CE Beta-lactamase sensitive penicillins	6	<1%
J01CE01 Benzylpenicillin	4	<1%
J01CE02 Phenoxymethylpenicillin	2	<1%
J01CF Beta-lactamase resistant penicillins	8	<1%
J01CF02 Cloxacillin	4	<1%
J01CF05 Flucloxacillin	4	<1%
J01CG Beta-lactamase inhibitors	1	<1%
J01CG02 Tazobactam	1	<1%
J01CR Combinations of penicillins, incl. beta-lactamase inhibitors	39	2.0%
J01CR02 Amoxicillin and enzyme inhibitor	39	2.0%
J01CR05 Piperacillin and enzyme inhibitor	1	<1%
Unspecified penicillins	1	<1%
J01D Other beta-lactam antibacterials	57	3.0%
J01DC Second-generation cephalosporins	5	<1%
J01DC02 Cefuroxime	5	<1%
J01DD Third-generation cephalosporins	52	2.7%
J01DD01 Cefotaxime	1	<1%
J01DD04 Ceftriaxone	50	2.6%
J01DD08 Cefixime	1	<1%
J01DH Carbapenems	1	<1%
J01DH03 Ertapenem	1	<1%
J01E Sulfonamides and trimethoprim	68	3.6%
J01EE Combinations of sulfonamides and trimethoprim, incl. derivatives	68	3.6%
J01EE01 Sulfamethoxazole and trimethoprim	68	3.6%
J01F Macrolides, lincosamides and streptogramins	15	<1%
J01FA Macrolides	13	<1%
J01FA01 Erythromycin	6	<1%
J01FA09 Clarithromycin	4	<1%
J01FA10 Azithromycin	3	<1%
J01FA15 Telithromycin	1	<1%
J01FF Lincosamides	2	<1%
J01FF01 Clindamycin	2	<1%
J01G Aminoglycoside antibacterials	8	<1%
J01GB Other aminoglycosides	8	<1%
J01GB03 Gentamicin	4	<1%

J01GB04 Kanamycin	4	<1%
J01M Quinolone antibacterials	23	1.2%
J01MA Fluoroquinolones	23	1.2%
J01MA01 Ofloxacin	1	<1%
J01MA02 Ciprofloxacin	17	<1%
J01MA14 Moxifloxacin	5	<1%
J01X Other antibacterials	1	<1%
J01XB Polymyxins	1	<1%
J01XB01 Colistin	1	<1%
Unspecified antibacterials	13	<1%
J02 Antimycotics for systemic use	26	1.4%
J02A Antimycotics for systemic use	26	1.4%
J02AC Triazole derivatives	26	1.4%
J02AC01 Fluconazole	25	1.3%
J02AC02 Itraconazole	1	<1%
J04 Antimycobacterials	198	10%
J04A Drugs for treatment of tuberculosis	197	10%
J04AB Antibiotics	179	9.4%
J04AB02 Rifampicin	179	9.4%
J04AC Hydrazides	187	9.8%
J04AC01 Isoniazid	187	9.8%
J04AD Thiocarbamide derivatives	4	<1%
J04AD03 Ethionamide	4	<1%
J04AK Other drugs for treatment of tuberculosis	138	7.2%
J04AK01 Pyrazinamide	134	7.0%
J04AK02 Ethambutol	134	7.0%
J04AK03 Terizidone	4	<1%
Unspecified treatment for tuberculosis	4	<1%
J04B Drugs for treatment of lepra	1	<1%
J04BA Drugs for treatment of lepra	1	<1%
J04BA02 Dapsone	1	<1%
J05 Antivirals for systemic use	320	17%
J05A Direct-acting antivirals	320	17%
J05AB Nucleosides and nucleotides, excl. reverse transcriptase inhibitors	6	<1%
J05AB01 Aciclovir	6	<1%
J05AE Protease inhibitors	20	1.1%
J05AE08 Atazanavir	1	<1%
J05AE30 Lopinavir-ritonavir	19	<1%
J05AF Nucleoside and nucleotide reverse transcriptase inhibitors	278	15%
J05AF01 Zidovudine	28	1.5%
J05AF02 Didanosine	1	<1%
J05AF04 Stavudine	37	1.9%
J05AF05 Lamivudine	213	11%
J05AF06 Abacavir	9	<1%
J05AF07 Tenofovir disoproxil	207	11%
J05AF09 Emtricitabine	62	3.3%
J05AG Non-nucleoside reverse transcriptase inhibitors	255	13%
J05AG01 Nevirapine	15	<1%
J05AG03 Efavirenz	240	13%
J05AX Other antivirals	1	<1%
J05AX08 Raltegravir	1	<1%
Unspecified antiretroviral therapy	41	2.2%
J07 Vaccines	1	<1%
J07B Viral vaccines	1	<1%
J07BB Influenza vaccines	1	<1%
L ANTINEOPLASTIC AND IMMUNOMODULATING AGENTS	**27**	**1.4%**
L01 Antineoplastic agents	6	<1%
L01A Alkylating agents	1	<1%
L01AA Nitrogen mustard analogues	1	<1%
L01AA02 Chlorambucil	1	<1%
L01X Other antineoplastic agents	2	<1%

L01XE Protein kinase inhibitors	2	<1%
L01XE01 Imatinib	2	<1%
Unspecified antineoplastic agents	3	<1%
L02 Endocrine therapy	2	<1%
L02B Hormone antagonists and related agents	2	<1%
L02BA Anti-oestrogens	2	<1%
L02BA01 Tamoxifen	2	<1%
L04 Immunosuppressive agents	19	<1%
L04A Immunosuppressive agents	19	<1%
L04AA Selective immunosuppressive agents	1	<1%
L04AA06 Mycophenolic acid	1	<1%
L04AD Calcineurin inhibitors	3	<1%
L04AD01 Ciclosporin	1	<1%
L04AD02 Tacrolimus	2	<1%
L04AX Other immunosuppressive agents	16	<1%
L04AX01 Azathioprine	5	<1%
L04AX03 Methotrexate	11	<1%
M MUSCULO-SKELETAL SYSTEM	**79**	**4.1%**
M01 Anti-inflammatory and antirheumatic products	49	2.6%
M01A Anti-inflammatory and antirheumatic products, non-steroids	49	2.6%
M01AB Acetic acid derivatives and related substances	21	1.1%
M01AB01 Indometacin	6	<1%
M01AB05 Diclofenac	16	<1%
M01AE Propionic acid derivatives	22	1.2%
M01AE01 Ibuprofen	20	1.1%
M01AE02 Naproxen	1	<1%
M01AE51 Ibuprofen, combinations	2	<1%
M01AG Fenamates	1	<1%
M01AG01 Mefenamic acid	1	<1%
M01AH Coxibs	2	<1%
M01AH01 Celecoxib	1	<1%
M01AH04 Parecoxib	1	<1%
Unspecified non-steroidal anti-inflammatories	6	<1%
M02 Topical products for joint and muscular pain	7	<1%
M02A Topical products for joint and muscular pain	7	<1%
M02AA Anti-inflammatory preparations, non-steroids for topical use	1	<1%
M02AA13 Ibuprofen	1	<1%
M02AC Preparations with salicylic acid derivatives	5	<1%
Unspecified topical products for joint and muscular pain	1	<1%
M03 Muscle relaxants	4	<1%
M03A Muscle relaxants, peripherally acting agents	1	<1%
M03AB Choline derivatives	1	<1%
M03AB01 Suxamethonium	1	<1%
M03B Muscle relaxants, centrally acting agents	3	<1%
M03BX Other centrally acting agents	3	<1%
M03BX01 Baclofen	3	<1%
M04 Antigout preparations	22	1.2%
M04A Antigout preparations	22	1.2%
M04AA Preparations inhibiting uric acid production	18	<1%
M04AA01 Allopurinol	18	<1%
M04AC Preparations with no effect on uric acid metabolism	7	<1%
M04AC01 Colchicine	7	<1%
Unspecified antigout preparations	1	<1%
M05 Drugs for treatment of bone diseases	2	<1%
M05B Drugs affecting bone structure and mineralization	2	<1%
M05BA Bisphosphonates	2	<1%
M05BA04 Alendronic acid	2	<1%
N NERVOUS SYSTEM	**427**	**22%**

N02 Analgesics	228	12%
N02A Opioids	90	4.7%
N02AA Natural opium alkaloids	32	1.7%
N02AA01 Morphine	30	1.6%
N02AA08 Dihydrocodeine	2	<1%
N02AB Phenylpiperidine derivatives	2	<1%
N02AB02 Pethidine	2	<1%
N02AX Other opioids	65	3.4%
N02AX02 Tramadol	63	3.3%
N02AX52 Tramadol, combinations	2	<1%
N02B Other analgesics and antipyretics	185	9.7%
N02BE Anilides	185	9.7%
N02BE01 Paracetamol	160	8.4%
N02BE51 Paracetamol, combinations excl. psycholeptics	31	1.6%
N02BE71 Paracetamol, combinations with psycholeptics	2	<1%
Unspecified analgesics	6	<1%
N03 Anti-epileptics	139	7.3%
N03A Anti-epileptics	139	7.3%
N03AA Barbiturates and derivatives	3	<1%
N03AA02 Phenobarbital	3	<1%
N03AB Hydantoin derivatives	55	2.9%
N03AB02 Phenytoin	55	2.9%
N03AE Benzodiazepine derivatives	19	<1%
N03AE01 Clonazepam	19	<1%
N03AF Carboxamide derivatives	26	1.4%
N03AF01 Carbamazepine	26	1.4%
N03AG Fatty acid derivatives	60	3.2%
N03AG01 Valproic acid	60	3.2%
N03AX Other anti-epileptics	5	<1%
N03AX09 Lamotrigine	5	<1%
Unspecified anti-epileptics	7	<1%
N04 Anti-Parkinson drugs	23	1.2%
N04A Anticholinergic agents	18	<1%
N04AB Ethers chemically close to antihistamines	18	<1%
N04AB02 Orphenadrine	18	<1%
N04B Dopaminergic agents	5	<1%
N04BA Dopa and dopa derivatives	5	<1%
N04BA02 Levodopa and decarboxylase inhibitor	5	<1%
N05 Psycholeptics	100	5.3%
N05A Antipsychotics	67	3.5%
N05AA Phenothiazines with aliphatic side-chain	6	<1%
N05AA01 Chlorpromazine	6	<1%
N05AB Phenothiazines with piperazine structure	7	<1%
N05AB02 Fluphenazine	3	<1%
N05AB04 Prochlorperazine	4	<1%
N05AD Butyrophenone derivatives	33	1.7%
N05AD01 Haloperidol	33	1.7%
N05AF Thioxanthene derivatives	6	<1%
N05AF01 Flupentixol	2	<1%
N05AF05 Zuclopenthixol	4	<1%
N05AH Diazepines, oxazepines and thiazepines	6	<1%
N05AH02 Clozapine	2	<1%
N05AH04 Quetiapine	4	<1%
N05AN Lithium	1	<1%
N05AN01 Lithium	1	<1%
N05AX Other antipsychotics	11	<1%
N05AX08 Risperidone	11	<1%
Unspecified antipsychotics	4	<1%
N05B Anxiolytics	40	2.1%
N05BA Benzodiazepine derivatives	40	2.1%
N05BA01 Diazepam	24	1.3%
N05BA04 Oxazepam	4	<1%
N05BA06 Lorazepam	13	<1%

N05C Hypnotics and sedatives	9	<1%
N05CD Benzodiazepine derivatives	4	<1%
N05CD08 Midazolam	4	<1%
N05CF Benzodiazepine-related drugs	5	<1%
N05CF01 Zopiclone	4	<1%
N05CF02 Zolpidem	1	<1%
N06 Psychoanaleptics	63	3.3%
N06A Antidepressants	63	3.3%
N06AA Non-selective monoamine reuptake inhibitors	45	2.4%
N06AA09 Amitriptyline	42	2.2%
Unspecified non-selective monoamine reuptake inhibitors	3	<1%
N06AB Selective serotonin reuptake inhibitors	13	<1%
N06AB03 Fluoxetine	9	<1%
N06AB04 Citalopram	5	<1%
N06AX Other antidepressants	3	<1%
N06AX03 Mianserin	2	<1%
N06AX16 Venlafaxine	1	<1%
Unspecified antidepressants	2	<1%
N07 Other nervous system drugs	1	<1%
N07A Parasympathomimetics	1	<1%
N07AA Anticholinesterases	1	<1%
N07AA02 Pyridostigmine	1	<1%
Unspecified drugs acting on the nervous system	3	<1%
P ANTIPARASITIC PRODUCTS, INSECTICIDES AND REPELLENTS	**36**	**1.9%**
P01 Antiprotozoals	35	1.8%
P01A Agents against amoebiasis and other protozoal diseases	26	1.4%
P01AB Nitroimidazole derivatives	26	1.4%
P01AB01 Metronidazole	26	1.4%
P01B Antimalarials	9	<1%
P01BA Aminoquinolines	9	<1%
P01BA01 Chloroquine	9	<1%
P03 Ectoparasiticides, incl. scabicides, insecticides and repellents	1	<1%
P03A Ectoparasiticides, incl. scabicides	1	<1%
P03AA Sulfur-containing products	1	<1%
Monosulfiram	1	<1%
R RESPIRATORY SYSTEM	**219**	**12%**
R01 Nasal preparations	7	<1%
R01A Decongestants and other nasal preparations for topical use	7	<1%
R01AA Sympathomimetics, plain	1	<1%
R01AA05 Oxymetazoline	1	<1%
R01AD Corticosteroids	6	<1%
R01AD01 Beclometasone	6	<1%
R02 Throat preparations	2	<1%
R02A Throat preparations	2	<1%
R02AA Antiseptics	2	<1%
R02AA20 Various throat antiseptics	2	<1%
R03 Drugs for obstructive airway	194	10%
R03A Adrenergics, inhalants	149	7.8%
R03AA Alpha- and beta-adrenoreceptor agonists	1	<1%
R03AA01 Epinephrine	1	<1%
R03AC Selective beta-2-adrenoreceptor agonists	148	7.8%
R03AC02 Salbutamol	144	7.6%
R03AC04 Fenoterol	5	<1%
R03AC12 Salmeterol	3	<1%
R03AC13 Formoterol	8	<1%
Unspecified beta-adrenergic inhalant	1	<1%
R03AK Adrenergics and other drugs for obstructive airway diseases	1	<1%
R03AK06 Salmeterol and other drugs for obstructive airway diseases	1	<1%

R03B Other drugs for obstructive airway diseases, inhalants	103	5.4%
R03BA Glucocorticoids	88	4.6%
R03BA01 Beclometasone	16	<1%
R03BA02 Budesonide	74	3.9%
Unspecified inhaled corticosteroid	1	<1%
R03BB Anticholinergics	36	1.9%
R03BB01 Ipratropium bromide	35	1.8%
R03BB04 Tiotropium bromide	1	<1%
R03C Adrenergics for systemic use	3	<1%
R03CC Selective beta-2-adrenoreceptor agonists	3	<1%
R03CC02 Salbutamol	3	<1%
R03D Other systemic drugs for obstructive airway diseases	67	3.5%
R03DA Xanthines	67	3.5%
R03DA04 Theophylline	64	3.4%
R03DA05 Aminophylline	2	<1%
R03DA54 Theophylline, combinations excl. psycholeptics	2	<1%
Unspecified treatment for obstructive airway diseases	28	1.5%
R05 Cough and cold preparations	5	<1%
Unspecified cough and cold preparations	5	<1%
R06 Antihistamines for systemic use	29	1.5%
R06A Antihistamines for systemic use	29	1.5%
R06AA Aminoalkyl ethers	3	<1%
R06AA02 Diphenhydramine	3	<1%
R06AB Substituted alkylamines	14	<1%
R06AB04 Chlorphenamine	14	<1%
R06AD Phenothiazine derivatives	6	<1%
R06AD02 Promethazine	6	<1%
R06AE Piperazine derivatives	8	<1%
R06AE03 Cyclizine	2	<1%
R06AE07 Cetirizine	6	<1%
R06AX Other antihistamines for systemic use	1	<1%
R06AX13 Loratadine	1	<1%
Unspecified systemic antihistamines	1	<1%
S SENSORY ORGANS	**8**	**<1%**
S01 Ophthalmologicals	8	<1%
S01C Anti-inflammatory agents and anti-infectives in combination	1	<1%
S01CA Corticosteroids and anti-infectives in combination	1	<1%
S01CA01 Dexamethasone and anti-infectives	1	<1%
S01E Antiglaucoma preparations and miotics	3	<1%
S01EA Sympathomimetics in glaucoma therapy	1	<1%
S01EA05 Brimonidine	1	<1%
S01ED Beta-blocking agents	2	<1%
S01ED02 Betaxolol	1	<1%
S01ED51 Timolol, combinations	1	<1%
S01K Surgical aids	1	<1%
S01KA Viscoelastic substances	1	<1%
S01KA02 Hypromellose	1	<1%
S01X Other ophthalmologicals	1	<1%
S01XA Other ophthalmological	1	<1%
S01XA20 Artificial tears and other indifferent preparations	1	<1%
Unspecified ophthalmologicals	4	<1%
V VARIOUS	**4**	**<1%**
V03 All Other therapeutic products	4	<1%
V03A All Other therapeutic products	4	<1%
V03AE Drugs for treatment of hyperkalaemia and hyperphosphataemia	4	<1%
V03AE01 Polystyrene sulfonate	4	<1%
ANY HERBAL PREPARATION	**10**	**<1%**

SDC 6. Reason for admission, according to ICD-10 classification (n=1951 admissions).

ICD-10 Chapter / Code block	Count	Proportion
ADVERSE DRUG REACTIONS	**164**	**8.4%**
(various codes) Adverse drug reactions	164	8.4%
CERTAIN INFECTIOUS AND PARASITIC DISEASES	**285**	**15%**
A00-A09 Intestinal infectious diseases	49	2.5%
A15-A19 Tuberculosis	155	7.9%
A30-A49 Other bacterial diseases	16	<1%
A50-A64 Infections with a predominantly sexual mode of transmission	2	<1%
A80-A89 Viral infections of the central nervous system	6	<1%
B00-B09 Viral infections characterized by skin and mucous membrane lesions	1	<1%
B15-B19 Viral hepatitis	5	<1%
B20-B24 Human immunodeficiency virus [HIV] disease	12	<1%
B35-B49 Mycoses	30	1.5%
B50-B64 Protozoal diseases	8	<1%
B65-B83 Helminthiases	1	<1%
NEOPLASMS	**53**	**2.7%**
C15-C26 Malignant neoplasms of digestive organs	8	<1%
C30-C39 Malignant neoplasms of respiratory and intrathoracic organs	19	<1%
C45-C49 Malignant neoplasms of mesothelial and soft tissue	2	<1%
C50-C50 Malignant neoplasm of breast	1	<1%
C69-C72 Malignant neoplasms of eye, brain and other parts of the central nervous system	2	<1%
C73-C75 Malignant neoplasms of thyroid and other endocrine glands	1	<1%
C76-C80 Malignant neoplasms of ill-defined, secondary and unspecified sites	14	<1%
C81-C96 Malignant neoplasms, stated or presumed to be primary, of lymphoid, haematopoietic and related tissue	4	<1%
D00-D09 In situ neoplasms	1	<1%
D10-D36 Benign neoplasms	1	<1%
DISEASES OF THE BLOOD AND BLOOD-FORMING ORGANS; CERTAIN DISORDERS INVOLVING THE IMMUNE MECHANISM	**35**	**1.8%**
D50-D53 Nutritional anaemias	6	<1%
D55-D59 Haemolytic anaemias	2	<1%
D60-D64 Aplastic and other anaemias	18	<1%
D65-D69 Coagulation defects, purpura and other haemorrhagic conditions	7	<1%
D70-D77 Other diseases of blood and blood-forming organs	1	<1%
D80-D89 Certain disorders involving the immune mechanism	1	<1%
ENDOCRINE, NUTRITIONAL AND METABOLIC DISEASES	**87**	**4.5%**
E00-E07 Disorders of thyroid gland	1	<1%
E10-E14 Diabetes mellitus	62	3.2%
E15-E16 Other disorders of glucose regulation	4	<1%
E70-E90 Metabolic disorders	20	1.0%
MENTAL AND BEHAVIOURAL DISORDERS	**106**	**5.4%**
F00-F09 Organic, including symptomatic, mental disorders	26	1.3%
F10-F19 Mental and behavioural disorders due to psychoactive substance use	25	1.3%
F20-F29 Schizophrenia, schizotypal and delusional disorders	41	2.1%
F30-F39 Mood [affective] disorders	5	<1%
F40-F48 Neurotic, stress-related and somatoform disorders	9	<1%
DISEASES OF THE NERVOUS SYSTEM	**115**	**5.9%**
G00-G09 Inflammatory diseases of the central nervous system	19	<1%
G10-G14 Systemic atrophies primarily affecting the central nervous system	1	<1%
G20-G26 Extrapyramidal and movement disorders	1	<1%
G35-G37 Demyelinating diseases of the central nervous system	2	<1%
G40-G47 Episodic and paroxysmal disorders	68	3.5%
G50-G59 Nerve, nerve root and plexus disorders	1	<1%
G60-G64 Polyneuropathies and other disorders of the peripheral nervous system	3	<1%
G80-G83 Cerebral palsy and other paralytic syndromes	14	<1%
G90-G99 Other disorders of the nervous system	6	<1%

DISEASES OF THE EYE AND ADNEXA	**3**	**<1%**
H40-H42 Glaucoma	1	<1%
H46-H48 Disorders of optic nerve and visual pathways	1	<1%
H53-H54 Visual disturbances and blindness	1	<1%
DISEASES OF THE EAR AND MASTOID PROCESS	**1**	**<1%**
H65-H75 Diseases of middle ear and mastoid	1	<1%
DISEASES OF THE CIRCULATORY SYSTEM	**496**	**25%**
I05-I09 Chronic rheumatic heart diseases	2	<1%
I10-I15 Hypertensive diseases	30	1.5%
I20-I25 Ischaemic heart diseases	91	4.7%
I26-I28 Pulmonary heart disease and diseases of the pulmonary circulation	31	1.6%
I30-I52 Other forms of heart disease	151	7.7%
I60-I69 Cerebrovascular diseases	152	7.8%
I70-I79 Diseases of arteries, arterioles and capillaries	2	<1%
I80-H89 Diseases of veins, lymphatic vessels and lymph nodes	36	1.9%
I95-I99 Other and unspecified disorders of the cardiovascular system	1	<1%
DISEASES OF THE RESPIRATORY SYSTEM	**313**	**16%**
J00-J06 Acute upper respiratory infections	3	<1%
J09-J18 Influenza and pneumonia	117	6.0%
J20-J22 Other acute lower respiratory infections	40	2.1%
J40-J47 Chronic lower respiratory diseases	98	5.0%
J60-J70 Lung diseases due to external agents	2	<1%
J80-J84 Other respiratory diseases principally affecting the interstitium	23	1.2%
J85-J86 Suppurative and necrotic conditions of the lower respiratory tract	6	<1%
J90-J94 Other diseases of pleura	18	<1%
J95-J99 Other diseases of the respiratory system	6	<1%
DISEASES OF THE DIGESTIVE SYSTEM	**39**	**2.0%**
K00-K14 Diseases of oral cavity, salivary glands and jaws	1	<1%
K20-K31 Diseases of oesophagus, stomach and duodenum	6	<1%
K55-K64 Other diseases of intestines	9	<1%
K65-K67 Diseases of peritoneum	4	<1%
K70-K77 Diseases of liver	13	<1%
K80-K87 Disorders of gallbladder, biliary tract and pancreas	2	<1%
K90-K93 Other diseases of the digestive	4	<1%
DISEASES OF THE SKIN AND SUBCUTANEOUS TISSUE	**7**	**<1%**
L00-L08 Infections of the skin and subcutaneous tissue	5	<1%
L10-L14 Bullous disorders	1	<1%
L80-L99 Other disorders of the skin and subcutaneous tissue	1	<1%
DISEASES OF THE MUSCULOSKELETAL SYSTEM AND CONNECTIVE TISSUE	**10**	**<1%**
M15-M19 Arthropathies: Arthrosis	1	<1%
M20-M25 Arthropathies: Other joint disorders	1	<1%
M30-M36 Systemic connective tissue disorders	3	<1%
M50-M54 Dorsopathies: Other dorsopathy	2	<1%
M70-M79 Soft tissue disorders: Other soft tissue disorders	2	<1%
M91-M94 Osteopathies and chondropathies: chondropathies	1	<1%
DISEASES OF THE GENITOURINARY SYSTEM	**61**	**3.1%**
N00-N08 Glomerular diseases	7	<1%
N10-N16 Renal tubulo-interstitial diseases	4	<1%
N17-N19 Renal failure	30	1.5%
N20-N23 Urolithiasis	1	<1%
N30-N39 Other diseases of urinary system	19	<1%
PREGNANCY, CHILDBIRTH AND THE PUERPERIUM	**2**	**<1%**
O00-O08 Pregnancy with abortive outcome	1	<1%
O10-O16 Oedema, proteinuria and hypertensive disorders in pregnancy, childbirth and puerperium	1	<1%
CONGENITAL MALFORMATIONS, DEFORMATIONS AND CHROMOSOMAL ABNORMALITIES	**3**	**<1%**
Q20-Q28 Congenital malformations of the circulatory system	2	<1%
Q60-Q64 Congenital malformations of the urinary system	1	<1%

SYMPTOMS, SIGNS AND ABNORMAL CLINICAL AND LABORATORY FINDINGS	**94**	**4.8%**
R00-R09 Symptoms and signs involving the circulatory and respiratory systems	18	<1%
R10-R19 Symptoms and signs involving the digestive system and abdomen	13	<1%
R40-R46 Symptoms and signs involving cognition, perception, emotional state and behaviour	16	<1%
R50-R69 General symptoms and signs	39	2.0%
R70-R79 Abnormal findings on examination of blood, without diagnosis	2	<1%
R90-R94 Abnormal findings on diagnostic imaging and on function studies, without diagnosis	6	<1%
INJURY, POISONING AND CERTAIN OTHER CONSEQUENCES OF EXTERNAL CAUSES	**5**	**<1%**
S00-S09 Injuries to the head	1	<1%
S70-S79 Injuries to the hip and thigh	2	<1%
T80-T88 Complications of surgical and medical care	2	<1%
EXTERNAL CAUSES OF MORBIDITY AND MORTALITY	**65**	**3.3%**
X40-X49 Accidents: Other external causes	1	<1%
X60-X84 Intentional self-harm	64	3.3%
FACTORS INFLUENCING HEALTH STATUS AND CONTACT WITH HEALTH SERVICES	**7**	**<1%**
Z00-Z13 Persons encountering health services for examination and investigation	1	<1%
Z40-Z54 Persons encountering health services for specific procedures and health care	4	<1%
Z70-Z76 Persons encountering health services in other circumstances	2	<1%
TOTAL	**1951**	**100%**

SDC 7. Summary of presentation of patients admitted for drug-induced renal impairment.

Case	Age, sex	HIV (CD4)	Presentation	Implicated drugs (duration of exposure)	Causality	Preventable
1†	40 M	Pos (70)	Creat = 1026, K = 6.8; baseline creat = 145 (3m ago). Urinary tract infection.	Tenofovir (unk)	Possible	Yes
2	56 F	Neg	Creat = 360, K = 4.0; no baseline available. Hypertension and previous CVA.	Spironolactone (>3w), enalapril (>3w), and furosemide (>3w)	Possible	Yes
3†	25 M	Pos (297)	Creat = 139, K = 5.5 and hypocalcaemia; baseline creat = 65 (2m ago). Kaposi sarcoma, pulmonary TB and chronic gastroenteritis.	Tenofovir (3m)	Possible	Yes
4	41 F	Pos (416)	Creat = 268, K = 3.2 and proteinuria; baseline creat = 67 (4m ago). Biopsy: mild HIVAN, central sclerosing variant. Pulmonary TB.	Tenofovir (4m)	Possible	Yes
5†	49 M	Unk	Creat = 1038, K = 6.7; baseline not recorded, but known with chronic kidney disease, hypertension and diabetes.	Acetylsalicylic acid (unk), furosemide (unk), perindopril and HCTZ (unk), and valsartan (unk)	Possible	Yes
6†	30 M	Pos (unk)	Creat = 647, K = 5.0; no baseline available. Gastroenteritis, dehydration, lower respiratory tract infection	Tenofovir (2m or more)	Possible	No
7	42 M	Neg	Creat = 614, K = 4.5 and proteinuria. Biopsy: diabetic nodular glomerulosclerosis.	Enalapril (3d)	Probable	No
8	22 F	Pos (140)	Creat = 1337, K = 7.3 and proteinuria; baseline creat = 39 (3w ago). Suspected sepsis (raised inflammatory markers).	Tenofovir (3w)	Possible	No
9†	36 M	Pos (84)	Creat = 2300, K = 8.9 and proteinuria; baseline creat = 818 (5w ago). Chronic kidney disease previously attributed to HIVAN.	Captopril (4w), furosemide (2.5w), and HCTZ (2w)	Probable	Yes
10	32 M	Pos (31)	Creat = 303, K = 4.1 and proteinuria; baseline creat = 63 (3m ago). Pulmonary TB and chronic gastroenteritis.	Tenofovir (2m)	Possible	No
11†	65 F	Unk	Creat = 1541, K = 4.5; baseline creat = 350 (14m ago). Hypertension, diabetes, previous CVA, cardiac failure, gastroenteritis.	Enalapril (>1y)	Possible	Yes
12	56 F	Unk	Creat = 360, K = 4.0; no baseline available. Gastroenteritis and dehydration.	Amlodipine (>5y), atenolol (>5y), enalapril (>5y), furosemide (>2y), HCTZ (>5y), and hydralazine (>2y)	Possible	No
13	34 F	Pos (137)	Creat = 171, K = 2.2, phosphate low, chloride high, normal anion gap, acidosis; baseline creat = 68 (4m ago). TB meningitis.	Tenofovir (unk)	Possible	Yes
14†	43 F	Pos (103)	Creat = 1356, K = 5.2; no baseline available. Chronic gastroenteritis, dehydration.	Tenofovir (3m)	Possible	No
15	48 M	Unk	Creat = 807, K = 6.7 and proteinuria; baseline creat = 179 (18m ago). Type 2 diabetes, chronic kidney disease, gastroenteritis.	Spironolactone (unk), enalapril (unk), and furosemide (unk)	Possible	Yes
16	69 M	Neg	Creat = 1249, K = 5.7 and proteinuria; baseline creat = 72 (1m ago). Biopsy: acute tubular necrosis on background mild diabetic changes. Pulmonary TB.	Rifampicin (4w)	Possible	No
				Enalapril (unk)	Possible	No
17†	31 F	Pos (700)	Creat = 822, K = 4.6; no baseline available. Epilepsy, schizophrenia, urinary tract infection.	Co-amoxiclav (5d)	Possible	No
				Ibuprofen (5d)	Possible	No
18	28 F	Pos (218)	Creat = 605, K = 2.8; baseline creat = 112 (10d ago). Pulmonary TB.	Co-trimoxazole (unk)	Possible	No
				Tenofovir (for 2w, stopped 1m ago)	Possible	Yes
19†	34 M	Pos (167)	Creat = 712, K = 6.7; baseline creat = 69 (11m ago). Kaposi sarcoma, vomiting.	Aciclovir (for 1w, 3w ago)	Possible	No
				Co-amoxiclav (for 1w, 3w ago)	Possible	No
				Indometacin (for 1w, 3w ago)	Possible	No
				Tenofovir (unk)	Possible	No

Case	Age, sex	HIV (CD4)	Presentation	Implicated drugs (duration of exposure)	Causality	Preventable
20†	43 F	Pos (46)	Creat = 1552, K = 8.3; baseline creat = 52 (10w ago). Recurrent *H. influenzae* pneumonia, diarrhoea and vomiting.	Co-trimoxazole (unk)	Possible	No
				Tenofovir (unk)	Possible	No
21†*	33 F	Pos (37)	Hepatorenal failure (mixed LI and AKI). Creat = 608, K = 5.6; baseline creat = 51 (1m ago). Pulmonary TB. Severe hypertension, CVA.	Rifampicin (5d)	Probable	No
22*	50 M	Pos (165)	Hepatorenal failure (cholestatic LI and AKI). Creat = 1133, K = 6.1; baseline creat = 75 (6m ago).	Enalapril (unk) (Could not exclude a potential role played by traditional remedies)	Possible	No
23†*	44 M	Pos (unk)	Hepatorenal failure (hepatocellular LI and AKI). Creat = 259, K = 6.5; baseline creat = 112 (10d ago). Depressed level of consciousness.	Co-trimoxazole (unk)	Possible	Yes
24*	34 M	Pos (208)	Hepatorenal failure (cholestatic LI and AKI). Creat = 907, K = 4.0; baseline creat = 81 (5m ago).	Co-trimoxazole (unk)	Probable	No

* Case also included in Supplementary Table S7
† Patient died (from any cause) during admission or 30-day follow-up period

AKI: acute kidney injury; CD4: CD4-cell count (cells / µL); Creat: serum- creatinine concentration (µmol/L); CVA: cerebrovascular accident; d/w/m/y: duration in days / weeks / months / years; F: female; HCTZ: hydrochlorothiazide; HIVAN: HIV-associated nephropathy; K: serum potassium concentration (mmol/L); LI: liver injury; M: male; neg: HIV-seronegative; pos: HIV-seropositive; TB: tuberculosis; unk: unknown

SDC 8. Summary of presentation of patients admitted for drug-induced hypoglycaemia.

Case	Age, sex	HIV	BG	Renal impairment	Relevant co-morbidities	Implicated drugs (duration of exposure)	Causality	Preventable
25	54 F	Neg	1.4	Yes: Creat=400		Gliclazide (unk) & metformin (unk)	Certain	Yes
26	74 F	Unk	2	Yes: eGFR=32	?Nosocomial sepsis (WCC=10)	Insulin (>10y)	Certain	Yes
27	79 F	Unk	2.1	No		Gliclazide (3d) & metformin (>6m)	Certain	Yes
28	77 F	Unk	1.2	Yes: eGFR=40	Dementia	Gliclazide (unk)	Certain	Yes
29	56 F	Unk	2.2	Yes: Creat=200		Insulin (unk), gliclazide (unk) & metformin (unk)	Certain	Yes
30	52 F	Neg	1.2	Yes: Creat=190	WCC=23	Insulin (unk)	Certain	Yes
31	68 F	Unk	1.9	Yes: Creat=233		Glibenclamide (unk) & metformin (unk)	Certain	Yes
32	60 F	Unk	2.2	No		Glibenclamide (unk) & metformin (unk)	Certain	Yes
33	77 M	Unk	2.8	Yes: Creat=103	?UTI (CRP=37) Dementia	Insulin (unk), gliclazide (unk) & metformin (unk)	Certain	Yes
34†	74 F	Unk	1.7	Yes: Creat=131	Old CVA, repeat CVA, WCC=10, CRP=24	Insulin (unk) & metformin (unk)	Certain	No
35	56 F	Unk	NR	Yes: Creat=88	Gastroenteritis, pneumonia	Gliclazide (unk) & metformin (unk)	Certain	Yes
36	70 F	Unk	NR	Yes: Creat=97		Insulin (>6m)	Certain	Yes
37	55 M	Unk	NR	No	Pneumonia (WCC=13, CRP<5) Skipped a meal but used insulin	Insulin (unk), glibenclamide (unk) & metformin (unk)	Certain	Yes
38†	53 M	Unk	0.7	Yes: eGFR=25		Insulin (1w)	Certain	Yes
39	56 M	Unk	1.8	Yes: eGFR=6	WCC=17	Glibenclamide (1m)	Probable	Yes
40†	73 F	Unk	0.5	Yes: eGFR=31	Sepsis (fever, WCC=14, neutrophilia)	Insulin (>2y)	Probable	No
41	56 F	Unk	0.7	No		Insulin (unk)	Certain	No
42†	61 F	Unk	1.1	Yes: Creat=700	New CVA	Insulin (unk) & unspecified oral hypoglycaemic agents	Certain	No
43	60 M	Unk	2.1	Yes: eGFR=18		Insulin (unk)	Certain	Yes
44	60 F	Unk	2	Yes: eGFR=45	WCC=9, CRP=36	Insulin (>2y)	Certain	Yes
45	78 M	Neg	1.8	Yes: eGFR=53	Bedsores (WCC=10, CRP=63)	Gliclazide (2m) & metformin (2m)	Probable	No
46	63 M	Pos	1.3	Yes: eGFR=48		Insulin (unk)	Certain	Yes

†Patient died (from any cause) during admission or 30-day follow-up period

BG: blood glucose nadir as recorded in file (mmol/L); Creat: creatinine (µmol/L); CRP: C-reactive protein (mg/L); CVA: cerebrovascular accident; d/w/m/y: duration in days/ weeks/ months/ years; eGFR: estimated glomerular filtration rate (as per laboratory report) (mL/min/1.73 m^2); F: female; M: male; neg: HIV-seronegative; NR: not recorded; pos: HIV-seropositive; unk: unknown; UTI: urinary tract infection; WCC: white blood cell count ($x10^9$/L)

SDC 9. Summary of presentation of patients admitted for drug-induced liver injury.

Case	Age, sex	HIV (CD4)	DILI classification at first presentation (t-bili:ALT:ALP)	Hepatic co-morbidity	Implicated drugs (duration of exposure)	Causality	Preventable
47	36 M	Pos (2)	Cholestatic liver injury (71:30:305)		Rifampicin (>4m)	Possible	No
48	57 F	Unk	Cholestatic liver injury (74:13:146)	Alcohol liver disease, portal hypertension and oesophageal varices. Hepatitis C.	Rifampicin (<3w)	Possible	No
49†	58 F	Pos (299)	Cholestatic liver injury (309:71:359)		Rifampicin (4m)	Possible	No
50†	36 F	Pos (unk)	Cholestatic liver injury (146:205:468)		Efavirenz (unk)	Possible	No
51†	34 M	Pos (599)	Cholestatic liver injury (118:93:134)	Abdominal MDR-TB but no bile duct obstruction	Rifampicin (2m)	Probable	No
52	34 M	Pos (54)	Cholestatic liver injury (53:47:169)		Rifampicin (2d)	Possible	No
53	19 F	Pos (44)	Cholestatic liver injury (114:63:153)	Suspected IRIS	Rifampicin (3w)	Possible	No
					Co-trimoxazole (3w)	Possible	No
54†	29 F	Pos (85)	Cholestatic liver injury (157:63:223)		Rifampicin (2w)	Possible	No
55	38 F	Pos (100)	Cholestatic liver injury (16:355:973)		Efavirenz (unk)	Probable	No
56	20 F	Pos (36)	Cholestatic liver injury (87:76:438)		Rifampicin (6w)	Possible	No
57	19 M	Neg	Hepatocellular injury (35:968:88)		Rifampicin (6w)	Possible	No
					Isoniazid (6w)	Possible	No
					Pyrazinamide (6w)	Possible	No
58	47 F	Pos (342)	Hepatocellular injury (16:2237:356)		Erythromycin (course commenced 2w ago)	Possible	No
					Nevirapine (unk)	Possible	No
59†	37 F	Pos (178)	Hepatocellular injury (164:1512:140)	Chronic Hepatitis B	Rifampicin (4m)	Possible	No
					Isoniazid (4m)	Possible	No
					Pyrazinamide (4m)	Possible	Yes

Case	Age, sex	HIV (CD4)	DILI classification at first presentation (t-bili:ALT:ALP)	Hepatic co-morbidity	Implicated drugs (duration of exposure)	Causality	Preventable
60	30 M	Pos (33)	Hepatocellular injury (92:960:448)		Rifampicin (?5m)	Possible	No
					Efavirenz (?1y)	Possible	No
					Isoniazid (?5m)	Possible	No
					Pyrazinamide (?5m)	Possible	No
61	39 F	Pos (130)	Hepatocellular injury (unk:825:218)	Previous DILI. This admission for repeat DILI during rechallenge.	Rifampicin (2w)	Possible	Yes
					Isoniazid (2w)	Possible	Yes
62	22 F	Pos (545)	Mixed liver injury (94:143:146)	Liver biopsy supports DILI	Efavirenz (6m)	Possible	No
21†*	33 F	Pos (37)	Hepatorenal failure (mixed LI and AKI) (58:225:204)		Rifampicin (5d)	Probable	No
22*	50 M	Pos (165)	Hepatorenal failure (cholestatic LI and AKI) (191:13:153)		Enalapril (unk) (Could not exclude a potential role played by traditional remedies)	Possible	No
23†*	44 M	Pos (unk)	Hepatorenal failure (hepatocellular LI and AKI) (73:558:124)	Chronic Hepatitis B	Co-trimoxazole (unk)	Possible	Yes
24*	34 M	Pos (208)	Hepatorenal failure (cholestatic LI and AKI) (174:25:110)		Co-trimoxazole (unk)	Probable	No

* Case also included in Supplementary Table S5
† Patient died (from any cause) during admission or 30-day follow-up period

AKI: acute kidney injury; ALP: alkaline phosphatase (IU/L); ALT: alanine transaminase (IU/L); CD4: CD4-cell count (cells / µL); d/w/m/y: duration in days/ weeks/ months/ years; DILI: drug-induced liver injury; F: female; IRIS: immune reconstitution inflammatory syndrome; LI: liver injury; M: male; MDR-TB: multidrug-resistant tuberculosis; neg: HIV-seronegative; pos: HIV-seropositive; t-bili: total serum-bilirubin (µmol/L); unk: unknown.

SDC 10. Summary of presentation of patients admitted for drug-induced haemorrhage.

Case	Age, sex	HIV	Haemorrhage	Implicated drugs	Indication for warfarin	Causality	Preventable
63	70 F	Unk	Gingival bleeding	Warfarin (INR > 10)	DVT	Certain	Yes
64	56 F	Unk	Gastric haemorrhage	Warfarin (INR = 4.8)	Valve replacement	Certain	Yes
65	61 F	Unk	Gastric haemorrhage	Diclofenac		Probable	No
66	90 F	Unk	Gastrointestinal haemorrhage	Acetylsalicylic acid		Possible	No
67	79 F	Unk	Gastrointestinal haemorrhage	NSAIDs, unspecified		Possible	No
68	83 M	Unk	Gastritis haemorrhagic	Acetylsalicylic acid		Possible	No
69	62 F	Unk	Lower gastrointestinal haemorrhage	Warfarin (INR = 4.7)	Valvular disease	Probable	No
70	58 F	Unk	Haemoptysis	Warfarin (INR = 4.9)	Valve replacement	Probable	Yes
71	18 F	Pos	Haemoptysis	Warfarin (INR > 10)	Right ventricular thrombosis secondary to dilated cardiomyopathy	Certain	Yes
72	72 F	Unk	Haemoptysis	Warfarin (INR = 2.0)	Valvular disease	Possible	No
73	53 F	Neg	Epistaxis	NSAIDs, unspecified		Possible	No
74	77 F	Unk	Haemarthrosis	Warfarin (INR = 4.3)	DVT	Certain	Yes
75	87 F	Unk	Haematuria	Warfarin (INR > 10)	Atrial fibrillation	Certain	Yes
76	48 F	Unk	Retroperitoneal haemorrhage	Warfarin (INR = 1.5)	Valve replacement	Probable	Yes
77	40 F	Unk	Menorrhagia	Warfarin (INR > 10)	DVT	Certain	Yes
78	30 F	Pos	Menorrhagia	Warfarin (INR = 6.9)	DVT	Certain	Yes
79†	79 F	Unk	Cerebral haemorrhage	Warfarin (INR = 4.6)	DVT	Certain	Yes
80†	79 F	Unk	Haemorrhage intracranial	Warfarin (INR = 9.2)	Atrial fibrillation	Probable	Yes
81†	67 F	Pos	Subarachnoid haemorrhage	Acetylsalicylic acid		Possible	No

† Patient died (from any cause) during admission or 30-day follow-up period

F: female; M: male; neg: HIV-seronegative; pos: HIV-seropositive; unk: unknown; INR: international normalised ratio; NSAIDs: non-steroidal antiinflammatories; DVT: deep venous thrombosis

SDC 11. Summary of presentation of patients admitted for drug-induced blood dyscrasias.

Case	Age, sex	HIV (CD4)	Adverse drug reaction	Implicated drugs	Causality	Preventable
82	48 M	Pos (unk)	Anaemia	Zidovudine	Probable	Yes
83	58 F	Pos (338)	Anaemia	Zidovudine	Possible	No
84	55 M	Pos (206)	Anaemia macrocytic	Zidovudine and lamivudine	Probable	Yes
85	33 F	Pos (11)	Anaemia normochromic normocytic	Zidovudine	Possible	No
86†	29 F	Pos (16)	Aplastic anaemia	Co-trimoxazole	Certain	Yes
87†	32 M	Pos (78)	Pancytopenia	Co-trimoxazole	Possible	No
88	33 F	Pos (24)	Thrombocytopenia	Co-trimoxazole	Possible	No
89	65 M	Pos (54)	Thrombocytopenia	Co-trimoxazole	Possible	No
90	23 M	Neg	Thrombocytopenia	Rifampicin	Probable	No
				Amoxicillin	Possible	No
91	31 M	Pos (207)	Thrombocytopenia	Rifampicin	Possible	No
				Isoniazid	Possible	No
92	26 M	Pos (622)	Thrombocytopenia	Valproic acid	Possible	No
93†	60 M	Pos (331)	Neutropenia	Stavudine	Possible	No
94	63 F	Unk	Neutropenia	Allopurinol	Possible	No
				Colchicine	Possible	No
95	70 F	Unk	Leukopenia	Methotrexate and chloroquine	Certain	No

† Patient died (from any cause) during admission or 30-day follow-up period

CD4: CD4-cell count (cells / µL); F: female; M: male; neg: HIV-seronegative; pos: HIV-seropositive; unk: unknown;

SDC 12. Summary of presentation of patients admitted for other* Type A adverse drug reactions.

Case	Age, sex	HIV	Adverse drug reaction	Implicated drugs	Causality	Preventable
96	22 F	Neg	Cardiac failure	Carvedilol	Possible	No
97	67 F	Unk	Cardiac failure	Carvedilol	Possible	Yes
98	79 M	Unk	Cardiac failure	Atenolol	Probable	Yes
99	52 F	Neg	Cardiac failure	Propranolol	Probable	No
100	72 F	Unk	Cardiac failure	Amlodipine and atenolol	Possible	Yes
101	55 F	Unk	Cardiac failure	Nifedipine	Possible	No
102	84 F	Unk	Cardiac failure	Atenolol	Possible	No
103	51 F	Neg	Cardiac failure	Atenolol and diltiazem	Possible	Yes
104	75 F	Unk	Cardiac failure	Atenolol	Possible	No
105	83 F	Unk	Hypotension	Enalapril and furosemide	Possible	No
106	55 M	Unk	Hypotension	Carvedilol, enalapril, and furosemide	Probable	Yes
107	53 M	Unk	Hypotension	Enalapril and furosemide	Possible	No
108	88 F	Unk	Orthostatic hypotension	Amlodipine, enalapril, and hydrochlorothiazide	Possible	Yes
109	75 F	Unk	Syncope	Tramadol, clonazepam, furosemide, propranolol, phenytoin, and levodopa with decarboxylase inhibitor	Possible	Yes
110	75 F	Unk	Cerebrovascular accident	Amlodipine, atenolol, enalapril, and hydrochlorothiazide	Possible	Yes
111	55 F	Unk	Acute myocardial infarction	Tranexamic acid	Possible	No
112	36 F	Pos	Gastritis	Acetylsalicylic acid and paracetamol (combination formulation)	Probable	Yes
113	52 F	Pos	Vomiting	Tenofovir-lamivudine-efavirenz (fixed drug combination)	Possible	No
114	45 F	Neg	Vomiting	Metformin	Certain	No
115†	65 F	Pos	Diarrhoea	Lopinavir-ritonavir	Possible	No
116	65 F	Unk	Pneumonia	Prednisone	Possible	No
117†	19 M	Unk	Pneumonia	Tacrolimus and prednisone	Possible	No

Case	Age, sex	HIV	Adverse drug reaction	Implicated drugs	Causality	Preventable
118	56 F	Unk	Pneumonia	Imatinib	Possible	No
119	57 F	Neg	Pneumonia	Azathioprine and prednisone	Possible	No
120	18 M	Unk	Gastroenteritis	Ciclosporin	Probable	No
121†	76 F	Unk	Pyelonephritis acute	Chlorambucil and prednisone	Possible	No
122†	27 F	Pos	*Pneumocystis jirovecii* pneumonia	Prednisone	Possible	No
123	50 M	Unk	Diabetes mellitus	Prednisone	Possible	No
124	64 F	Unk	Diabetes mellitus	Hydrochlorothiazide and prednisone	Probable	Yes
125	69 F	Unk	Hypokalaemia	Furosemide	Certain	Yes
126†	56 F	Neg	Hypokalaemia	Hydrochlorothiazide	Possible	Yes
127	69 F	Unk	Hypokalaemia	Furosemide and prednisone	Certain	Yes
128	58 F	Unk	Hyperkalaemia	Enalapril	Probable	Yes
129	69 F	Pos	Hyponatraemia	Co-trimoxazole and hydrochlorothiazide	Probable	No
130	66 F	Unk	Hyponatraemia	Hydrochlorothiazide	Possible	No
131	47 F	Unk	Hyponatraemia	Hydrochlorothiazide	Possible	No
132†	53 M	Pos	Lactic acidosis	Stavudine	Possible	Yes
133†	61 F	Pos	Lactic acidosis	Stavudine	Probable	Yes
134	82 M	Unk	Asthenia	Digoxin	Certain	Yes
135	23 M	Unk	Confusional state	Phenytoin	Certain	Yes
136†	82 F	Unk	Confusional state	Tramadol	Possible	No
137†	89 F	Unk	Confusional state	Digoxin	Certain	Yes
138	43 F	Pos	Confusional state	Efavirenz	Possible	No
139	34 M	Pos	Confusional state	Efavirenz	Probable	No
140	62 F	Unk	Confusional state	Phenytoin	Certain	Yes
141	91 F	Unk	Confusional state	Tramadol, risperidone, and zopiclone	Probable	Yes
142	40 M	Unk	Confusional state	Phenobarbital and phenytoin	Probable	Yes

Case	Age, sex	HIV	Adverse drug reaction	Implicated drugs	Causality	Preventable
143†	39 F	Pos	Ataxia	Efavirenz	Possible	No
144	33 M	Unk	Ataxia	Phenytoin	Certain	Yes
145	36 M	Unk	Ataxia	Phenytoin	Certain	Yes
146	53 M	Unk	Loss of consciousness	Phenytoin	Probable	Yes
147	58 F	Unk	Generalised tonic-clonic seizure	Theophylline, chlorpromazine, and zuclopenthixol	Possible	No
148	65 M	Neg	Generalised tonic-clonic seizure	Theophylline	Possible	No
149	34 F	Pos	Optic neuritis	Ethambutol	Certain	Yes
150	34 F	Neg	Headache	Levonorgesterel and estrogen (combined oral contraceptive)	Possible	No
151	21 M	Unk	Hallucination	Phenytoin	Probable	Yes
152	29 M	Neg	Aggression	Phenytoin	Certain	Yes
153	40 F	Pos	Acute psychosis	Efavirenz	Possible	No
154†	44 F	Pos	Renal tubular disorder	Tenofovir	Possible	No
155	35 F	Pos	Renal tubular disorder	Kanamycin and tenofovir	Certain	Yes

* Excludes patients admitted for drug-induced hypoglycaemia, drug-induced blood dyscrasias, drug-related haemorrhage, and drug-induced renal failure / impairment
† Patient died (from any cause) during admission or 30-day follow-up period

F: female; M: male; neg: HIV-seronegative; pos: HIV-seropositive; unk: unknown

SDC 13. Summary of presentation of patients admitted for other* Type B adverse reactions.

Case	Age, sex	HIV	Adverse Drug Reaction	Implicated Drugs	Causality	Preventable
156	69 F	Unk	Pancreatitis acute	Simvastatin	Possible	No
157	51 M	Pos	DRESS	Hydrochlorothiazide	Probable	No
158	22 F	Neg	DRESS	Phenytoin	Certain	No
159	72 M	Unk	DRESS	Phenytoin	Certain	No
160	38 F	Pos	DRESS	Rifampicin	Certain	No
161	58 M	Neg	Dermatitis exfoliative	Allopurinol	Possible	No
				Imatinib	Possible	No
162	36 F	Pos	Stevens-Johnson syndrome	Co-trimoxazole	Possible	No
				Unspecified ART	Possible	No
				Unspecified TBT	Possible	No
163	57 F	Unk	Angioedema	Perindopril	Certain	No
164	50 F	Unk	Interstitial lung disease	Methotrexate	Possible	No

* Excludes admissions for drug-induced liver injury, drug-induced renal impairment, and drug-induced blood dyscrasias
† No known deaths (from any cause) during admission or 30-day follow-up period

ART: antiretroviral treatment; DRESS: drug reaction with eosinophilia and systemic symptoms; F: female; neg: HIV-seronegative; pos: HIV-seropositive; M: male; TBT: tuberculosis treatment; unk: unknown

SDC 14. All ADRs causing admission (n=164), mapped to higher-level terms, higher-level groups, and system-organ classes, according to the MedDRA® taxonomy. Asterisks indicate preferred terms mapping to more than one heading.

Adverse Drug Reaction	Frequency	Proportion
Blood and lymphatic system disorders	**14**	**8.5%**
Anaemias, nonhaemolytic and marrow depression	6	3.6%
Anaemias	4	2.4%
Anaemia	2	1.2%
Anaemia, macrocytic (*)	1	<1%
Anaemia, normochromic normocytic	1	<1%
Marrow depression and hypoplastic anaemias	2	1.2%
Aplastic anaemia	1	<1%
Pancytopaenia	1	<1%
Platelet disorders	5	3.1%
Thrombocytopaenias	5	3.1%
Thrombocytopaenia	5	3.1%
White blood cell disorders	3	1.8%
Leukopaenias	1	<1%
Leukopaenia	1	<1%
Neutropaenias	2	1.2%
Neutropaenia	2	1.2%
Cardiac disorders	**14**	**8.5%**
Heart failures	9	5.5%
Heart failures	9	5.5%
Cardiac failure	9	5.5%
Cardiac disorder signs and symptoms	4	2.4%
Cardiac signs and symptoms	4	2.4%
Haemoptysis (*)	3	1.8%
Syncope (*)	1	<1%
Coronary artery disorders	1	<1%
Ischaemic coronary artery disorders	1	<1%
Acute myocardial infarction (*)	1	<1%
Endocrine disorders	**24**	**15%**
Glucose metabolism disorders	24	15%
Hypoglycaemic conditions	22	13%
Hypoglycaemia (*)	22	13%
Diabetes mellitus	2	1.2%
Diabetes mellitus (*)	2	1.2%
Eye disorders	**1**	**<1%**
Ocular infections, irritations and inflammations	1	<1%
Optic nerve infections and inflammation	1	<1%
Optic neuritis (*)	1	<1%
Gastrointestinal disorders	**14**	**8.5%**
Gastrointestinal haemorrhages	5	3.1%
Non-site specific GI haemorrhage	3	1.8%
Gastrointestinal haemorrhage (*)	2	1.2%
Lower gastrointestinal haemorrhage (*)	1	<1%
Gastric and oesophageal haemorrhages	2	1.2%
Gastric haemorrhage (*)	2	1.2%
Gastrointestinal inflammatory conditions	2	1.2%
Gastritis (excl infective)	2	1.2%
Gastritis	1	<1%
Gastritis haemorrhagic (*)	1	<1%

Gastrointestinal signs and symptoms	2	1.2%
Nausea and vomiting symptoms	2	1.2%
Vomiting	2	1.2%
Dental and gingival conditions	1	<1%
Gingival haemorrhages	1	<1%
Gingival bleeding (*)	1	<1%
Exocrine pancreas conditions	1	<1%
Acute and chronic pancreatitis	1	<1%
Acute pancreatitis	1	<1%
Gastrointestinal infections	1	<1%
Gastric and gastroenteric infections	1	<1%
Gastroenteritis (*)	1	<1%
Gastrointestinal motility and defaecation disorders	1	<1%
Diarrhoea (excl infective)	1	<1%
Diarrhoea	1	<1%
Peritoneal and retroperitoneal conditions	1	<1%
Peritoneal and retroperitoneal haemorrhage	1	<1%
Retroperitoneal haemorrhage (*)	1	<1%
General disorders and administration site conditions	**4**	**2.4%**
General system disorders	4	2.4%
Gait disorders	3	1.8%
Ataxia (*)	3	1.8%
Asthenic conditions	1	<1%
Asthenia	1	<1%
Hepatobiliary disorders	**20**	**12%**
Hepatic and hepatobiliary disorders	20	12%
Hepatocellular damage and hepatitis	16	9.8%
Cholestatic liver injury	10	6.1%
Hepatocellular injury	5	3.1%
Mixed liver injury	1	<1%
Hepatic failure and associated disorders	4	2.4%
Hepatorenal failure (*)	4	2.4%
Immune system disorders	**8**	**4.9%**
Allergic conditions	7	4.3%
Allergies to foods, food additives, drugs and other chemicals	5	3.0%
Drug reaction with eosinophilia and systemic symptoms (*)	4	2.4%
Dermatitis exfoliative (*)	1	<1%
Allergic conditions	1	<1%
Stevens-Johnson syndrome (*)	1	<1%
Angioedemas	1	<1%
Angioedema (*)	1	<1%
Autoimmune disorders	1	<1%
Nervous system autoimmune disorders	1	<1%
Optic neuritis (*)	1	<1%
Infections and infestations	**8**	**4.9%**
Infections - pathogen unspecified	6	3.7%
Lower respiratory tract and lung infections	4	2.4%
Pneumonia (*)	4	2.4%
Abdominal and gastrointestinal infections	1	<1%
Gastroenteritis (*)	1	<1%
Urinary tract infections	1	<1%
Pyelonephritis acute	1	<1%
Ancillary infectious topics	1	<1%
Inflammatory disorders following infection	1	<1%
Stevens-Johnson syndrome (*)	1	<1%
Fungal infectious disorders	1	<1%

	Pneumocystis infections	1	<1%
	Pneumocystis jirovecii pneumonia (*)	1	<1%
Injury, poisoning and procedural complications		**3**	**1.8%**
Bone and joint injuries		1	<1%
Bone and joint injuries		1	<1%
	Haemarthrosis (*)	1	<1%
Exposures, chemical injuries and poisoning		1	<1%
Poisoning and toxicity		1	<1%
	Stevens-Johnson syndrome (*)	1	<1%
Injuries		1	<1%
Cerebral injuries		1	<1%
	Subarachnoid haemorrhage (*)	1	<1%
Metabolism and nutrition disorders		**34**	**21%**
Glucose metabolism disorders		24	15%
Hypoglycaemic conditions		22	13%
	Hypoglycaemia (*)	22	13%
Diabetes mellitus		2	1.2%
	Diabetes mellitus (*)	2	1.2%
Electrolyte and fluid balance conditions		7	4.3%
Potassium imbalance		4	2.4%
	Hypokalaemia	3	1.8%
	Hyperkalaemia	1	<1%
Sodium imbalance		3	1.8%
	Hyponatraemia	3	1.8%
Acid-base disorders		2	1.2%
Metabolic acidosis		2	1.2%
	Lactic acidosis	2	1.2%
Vitamin-related disorders		1	<1%
Vitamin deficiencies		1	<1%
	Anaemia macrocytic (*)	1	<1%
Musculoskeletal and connective tissue disorders		**1**	**<1%**
Joint disorders		1	<1%
Arthropathies		1	<1%
	Haemarthrosis (*)	1	<1%
Nervous system disorders		**22**	**13%**
Neurological disorder		13	7.9%
Cortical dysfunction		8	4.9%
	Confusional state (*)	8	4.9%
Coordination and balance disturbance		3	1.8%
	Ataxia (*)	3	1.8%
Disturbances in consciousness		2	1.2%
	Loss of consciousness	1	<1%
	Syncope (*)	1	<1%
CNS vascular disorder		4	2.4%
CNS haemorrhages and cerebrovascular accidents		4	2.4%
	Cerebral haemorrhage (*)	1	<1%
	Cerebrovascular accident (*)	1	<1%
	Haemorrhage intracranial (*)	1	<1%
	Subarachnoid haemorrhage (*)	1	<1%
Seizures		2	1.2%
Generalised tonic-clonic seizures		2	1.2%
	Generalised tonic-clonic seizure	2	1.2%
Cranial nerve disorders		1	<1%
Optic nerve disorders		1	<1%
	Optic neuritis (*)	1	<1%
Headaches		1	<1%

		Headaches	1	<1%
		Headache	1	<1%
	Neuromuscular disorders		1	<1%
		Autonomic nervous system disorders	1	<1%
		Orthostatic hypotension (*)	1	<1%
Psychiatric disorders			**11**	**6.7%**
	Deliria		8	4.9%
		Confusion and disorientation	8	4.9%
		Confusional state (*)	8	4.9%
	Disturbances in thinking and perception		1	<1%
		Perception disturbances	1	<1%
		Hallucination	1	<1%
	Personality disorders and disturbances		1	<1%
		Behaviour and socialisation disturbances	1	<1%
		Aggression	1	<1%
	Schizophrenia and other psychotic disorders		1	<1%
		Psychotic disorder	1	<1%
		Acute psychosis	1	<1%
Renal and urinary disorders			**28**	**17%**
	Renal disorders (excl nephropathies)		25	15%
		Renal failure and impairments	24	15%
		Renal failure acute	13	7.9%
		Renal failure	7	4.3%
		Hepatorenal failure (*)	4	2.4%
		Renal infections and inflammations	1	<1%
		Acute pyelonephritis	1	<1%
	Nephropathies		2	1.2%
		Nephropathies and tubular disorders	2	1.2%
		Renal tubular disorder	2	1.2%
	Urinary tract symptoms and signs		1	<1%
		Urinary abnormalities	1	<1%
		Haematuria (*)	1	<1%
Reproductive system and breast disorders			**2**	**1.2%**
	Menstrual cycle and uterine bleeding disorders		2	1.2%
		Menstruation with increased bleeding	2	1.2%
		Menorrhagia	2	1.2%
Respiratory, thoracic and mediastinal disorders			**10**	**6.1%**
	Respiratory tract infections		5	3.0%
		Lower respiratory tract infections	4	2.4%
		Pneumonia (*)	4	244%
		Fungal lower respiratory tract infections	1	<1%
		Pneumocystis jirovecii pneumonia (*)	1	<1%
	Respiratory disorders		3	1.8%
		Coughing and associated symptoms	3	1.8%
		Haemoptysis (*)	3	1.8%
	Lower respiratory tract disorders (excl obstruction and infection)		1	<1%
		Parenchymal lung disorders	1	<1%
		Interstitial lung disease	1	<1%
	Upper respiratory tract disorders (excl infections)		1	<1%
		Nasal disorders	1	<1%
		Epistaxis (*)	1	<1%
Skin and subcutaneous tissue disorders			**7**	**4.3%**
	Epidermal and dermal conditions		6	3.7%
		Dermatitis ascribed to specific agent	4	2.4%

		Drug reaction with eosinophilia and systemic symptoms (*)	4	2.4%
	Bullous conditions		1	<1%
		Stevens-Johnson syndrome (*)	1	<1%
	Exfoliative conditions		1	<1%
		Dermatitis exfoliative (*)	1	<1%
Angioedema and urticaria			1	<1%
	Angioedemas		1	<1%
		Angioedema (*)	1	<1%
Vascular disorders			**24**	**15%**
Vascular haemorrhagic disorders			17	10%
	Gastrointestinal haemorrhages		7	4.3%
		Gastric haemorrhage (*)	2	1.2%
		Gastrointestinal haemorrhage (*)	2	1.2%
		Gastritis haemorrhagic (*)	1	<1%
		Gingival bleeding (*)	1	<1%
		Lower gastrointestinal haemorrhage (*)	1	<1%
	Haemorrhages		7	4.3%
		Haemoptysis (*)	3	1.8%
		Epistaxis (*)	1	<1%
		Haemarthrosis (*)	1	<1%
		Haematuria (*)	1	<1%
		Retroperitoneal haemorrhage (*)	1	<1%
	Nervous system haemorrhagic disorders		3	1.8%
		Cerebral haemorrhage (*)	1	<1%
		Haemorrhage intracranial (*)	1	<1%
		Subarachnoid haemorrhage (*)	1	<1%
Decreased and nonspecific blood pressure disorders and shock			5	3.0%
	Vascular hypotensive disorders		4	2.4%
		Hypotension	3	1.8%
		Orthostatic hypotension (*)	1	<1%
	Circulatory collapse and shock		1	<1%
		Syncope (*)	1	<1%
Arteriosclerosis, stenosis, vascular insufficiency and necrosis			1	<1%
	Coronary necrosis and vascular insufficiency		1	<1%
		Acute myocardial infarction (*)	1	<1%
Vascular disorders			1	<1%
	Cerebrovascular and spinal vascular disorders		1	<1%
		Cerebrovascular accident (*)	1	<1%

SDC 15. Drugs implicated in ADR-related admissions, by ATC-classification.

Drug class / Drug	Number of ADR-related admissions in which the drug / drug class was implicated				
	Type A ADRs (alone)[a]	**Type A ADRs (comb)[b]**	**Type B ADRs (alone)[c]**	**Type B ADRs (comb)[d]**	**Total[e]**
A ALIMENTARY TRACT AND METABOLISM	**12**	**11**			**23**
A10 Drugs used in diabetes	12	11			23
A10A Insulins and analogues	9	5			14
A10B Oral blood glucose lowering drugs	3	11			14
A10BA Biguanides	1	10			11
A10BA02 Metformin	1	10			11
A10BB Sulfonamides, urea derivatives	1	9			11
A10BB01 Glibenclamide	1	3			4
A10BB09 Gliclazide	1	6			7
Unspecified oral blood glucose lowering drugs		1			1
B BLOOD AND BLOOD FORMING ORGANS	**17**	**1**			**18**
B01 Antithrombotic agents	16	1			17
B01A Antithrombotic agents	16	1			17
B01AA Vitamin K antagonists	13				13
B01AA03 Warfarin	13				13
B01AC Platelet aggregation inhibitors, excl. heparins	3	1			4
B01AC06 Acetylsalicylic acid	3	1			4
B02 Antihaemorrhagics	1				1
B02A Antifibrinolytics	1				1
B02AA Amino acids	1				1
B02AA02 Tranexamic acid	1				1
C CARDIOVASCULAR SYSTEM	**16**	**16**	**4**	**1**	**37**
C01 Cardiac therapy	2				2
C01A Cardiac glycosides	2				2
C01AA Digitalis glycosides	2				2
C01AA05 Digoxin	2				2
C02 Antihypertensives		1			1
C02D Arteriolar smooth muscle, agents acting on		1			1
C02DB Hydrazinophthalazine derivatives		1			1
C02DB02 Hydralazine		1			1
C03 Diuretics	4	14	1		19
C03A Low-ceiling diuretics, thiazides	3	6	1		10
C03AA Thiazides, plain	3	6	1		10
C03AA03 Hydrochlorothiazide	3	6	1		10
C03C High-ceiling diuretics	1	10			11
C03CA Sulfonamides, plain	1	10			11
C03CA01 Furosemide	1	10			11
C03D Potassium-sparing agents		2			2
C03DA Aldosterone antagonists		2			2
C03DA01 Spironolactone		2			2
C07 Beta-blocking agents	6	6			12
C07A Beta-blocking agents	6	6			12
C07AA Beta-blocking agents, non-selective	1	1			2
C07AA05 Propranolol	1	1			2
C07AB Beta-blocking agents, selective	3	4			7
C07AB03 Atenolol	3	4			7
C07AG Alpha- and beta-blocking agents	2	1			3
C07AG02 Carvedilol	2	1			3
C08 Calcium channel blockers	1	5			6
C08C Selective calcium channel blockers with mainly vascular effects	1	4			5

Drug class / Drug	Number of ADR-related admissions in which the drug / drug class was implicated: Type A ADRs (alone)[a]	Type A ADRs (comb)[b]	Type B ADRs (alone)[c]	Type B ADRs (comb)[d]	Total[e]
C08CA Dihydropyridine derivatives	1	4			5
C08CA01 Amlodipine		4			4
C08CA05 Nifedipine	1				1
C08D Selective calcium channel blockers with direct cardiac effects		1			1
C08DB Benzothiazepine derivatives		1			1
C08DB01 Diltiazem		1			1
C09 Agents acting on the renin-angiotensin system	3	10	2	1	16
C09A ACE-inhibitors, plain	3	9	2	1	15
C09AA ACE-inhibitors, plain	3	9	2	1	15
C09AA01 Captopril		1			1
C09AA02 Enalapril	3	8	1	1	13
C09AA04 Perindopril			1		1
C09B ACE-inhibitors, combinations		1			1
C09BA ACE-inhibitors and diuretics		1			1
C09BA04 Perindopril and diuretics		1			1
C09C Angiotensin II antagonists, plain		1			1
C09CA Angiotensin II antagonists, plain		1			1
C09CA03 Valsartan		1			1
C10 Serum lipid reducing agents			1		1
C10A Cholesterol and triglyceride reducers			1		1
C10AA HMG-coA reductase inhibitors			1		1
C10AA01 Simvastatin			1		1
G GENITO-URINARY SYSTEM AND SEX HORMONES	**1**				**1**
G03 Sex hormones and modulators of the genital system	1				1
G03A Hormonal contraceptives for systemic use	1				1
G03AA Progestogens and oestrogens, fixed combinations	1				1
G03AA07 Levonorgestrel and oestrogen	1				1
H SYSTEMIC HORMONAL PREPARATIONS, EXCL. SEX HORMONES AND INSULINS	**3**	**5**			**8**
H02 Corticosteroids for systemic use	3	5			8
H02A Corticosteroids for systemic use, plain	3	5			8
H02AB Glucocorticoids	3	5			8
H02AB07 Prednisone	3	5			8
J ANTI-INFECTIVES FOR SYSTEMIC USE	**25**	**4**	**14**	**14**	**57**
J01 Antibacterials for systemic use	4	2	2	8	16
J01C Beta-lactam antibacterials, penicillins				3	3
J01CA Penicillins with extended spectrum				1	1
J01CA04 Amoxicillin				1	1
J01CR Combinations of penicillins, incl. beta-lactamase inhibitors				2	2
J01CR02 Co-amoxiclav				2	2
J01E Sulfonamides and trimethoprim	4	1	2	4	11
J01EE Combinations of sulfonamides and trimethoprim, incl. derivatives	4	1	2	4	11
J01EE01 Sulfamethoxazole and trimethoprim	4	1	2	4	11
J01F Macrolides, lincosamides and streptogramins				1	1
J01FA Macrolides				1	1
J01FA01 Erythromycin				1	1
J01G Aminoglycoside antibacterials		1			1
J01GB Other aminoglycosides		1			1
J01GB04 Kanamycin		1			1
J04 Antimycobacterials	1		9	9	19
J04A Drugs for treatment of tuberculosis	1		9	9	19
J04AB Antibiotics			9	8	17

Drug class / Drug	Number of ADR-related admissions in which the drug / drug class was implicated				
	Type A ADRs (alone)[a]	Type A ADRs (comb)[b]	Type B ADRs (alone)[c]	Type B ADRs (comb)[d]	Total[e]
J04AB02 Rifampicin			9	8	17
J04AC Hydrazides				5	5
J04AC01 Isoniazid				5	5
J04AK Other drugs for treatment of tuberculosis	1			3	4
J04AK01 Pyrazinamide				3	3
J04AK02 Ethambutol	1				1
Unspecified treatment for tuberculosis				1	1
J05 Antivirals for systemic use	20	3	3	6	32
J05A Direct-acting antivirals	20	3	3	6	32
J05AB Nucleosides and nucleotides, excl. reverse transcriptase inhibitors				1	1
J05AB01 Aciclovir				1	1
J05AE Protease inhibitors	1				1
J05AE30 Lopinavir-ritonavir	1				1
J05AF Nucleoside and nucleotide reverse transcriptase inhibitors	15	3		3	21
J05AF01 Zidovudine	3	1			4
J05AF04 Stavudine	3				3
J05AF05 Lamivudine		1			1
J05AF07 Tenofovir disoproxil	9	2		3	14
J05AF09 Emtricitabine		1			1
J05AG Non-nucleoside reverse transcriptase inhibitors	4	1	3	2	10
J05AG01 Nevirapine				1	1
J05AG03 Efavirenz	4	1	3	1	9
Unspecified antiretroviral therapy				1	1
L ANTINEOPLASTIC AND IMMUNOMODULATING AGENTS	**2**	**4**	**1**	**1**	**8**
L01 Antineoplastic agents	1	1		1	3
L01A Alkylating agents		1			1
L01AA Nitrogen mustard analogues		1			1
L01AA02 Chlorambucil		1			1
L01X Other antineoplastic agents	1			1	2
L01XE Protein kinase inhibitors	1			1	2
L01XE01 Imatinib	1			1	2
L04 Immunosuppressive agents	1	3	1		5
L04A Immunosuppressive agents	1	3			5
L04AD Calcineurin inhibitors	1	1			2
L04AD01 Ciclosporin	1				1
L04AD02 Tacrolimus		1			1
L04AX Other immunosuppressive agents		2	1		3
L04AX01 Azathioprine		1			1
L04AX03 Methotrexate		1	1		2
M MUSCULO-SKELETAL SYSTEM	**3**			**4**	**7**
M01 Anti-inflammatory and antirheumatic products	3			2	5
M01A Anti-inflammatory and antirheumatic products, non-steroids	3			2	5
M01AB Acetic acid derivatives and related substances	1			1	2
M01AB01 Indometacin				1	1
M01AB05 Diclofenac	1				1
M01AE Propionic acid derivatives				1	1
M01AE01 Ibuprofen				1	1
Unspecified non-steroidal anti-inflammatories	2				2
M04 Antigout preparations				2	2
M04A Antigout preparations				2	2
M04AA Preparations inhibiting uric acid production				2	2
M04AA01 Allopurinol				2	2
M04AC Preparations with no effect on uric acid metabolism				1	1
M04AC01 Colchicine				1	1

Drug class / Drug	Number of ADR-related admissions in which the drug / drug class was implicated				
	Type A ADRs (alone)[a]	**Type A ADRs (comb)[b]**	**Type B ADRs (alone)[c]**	**Type B ADRs (comb)[d]**	**Total[e]**
N NERVOUS SYSTEM	**9**	**4**	**3**		**16**
N02 Analgesics	2	2			4
N02A Opioids	1	2			3
N02AX Other opioids	1	2			3
N02AX02 Tramadol	1	2			3
N02B Other analgesics and antipyretics	1				1
N02BE Anilides	1				1
N02BE51 Paracetamol, combinations excl. psycholeptics	1				1
N03 Anti-epileptics	7	2	3		12
N03A Anti-epileptics	7	2	3		12
N03AA Barbiturates and derivatives		1			1
N03AA02 Phenobarbital		1			1
N03AB Hydantoin derivatives	7	2	2		11
N03AB02 Phenytoin	7	2	2		11
N03AE Benzodiazepine derivatives		1			1
N03AE01 Clonazepam		1			1
N03AG Fatty acid derivatives			1		1
N03AG01 Valproic acid			1		1
N04 Anti-Parkinson drugs		1			1
N04B Dopaminergic agents		1			1
N04BA Dopa and dopa derivatives		1			1
N04BA02 Levodopa and decarboxylase inhibitor		1			1
N05 Psycholeptics		2			2
N05A Antipsychotics		2			2
N05AA Phenothiazines with aliphatic side-chain		1			1
N05AA01 Chlorpromazine		1			1
N05AF Thioxanthene derivatives		1			1
N05AF05 Zuclopenthixol		1			1
N05AX Other antipsychotics		1			1
N05AX08 Risperidone		1			1
N05C Hypnotics and sedatives		1			1
N05CF Benzodiazepine-related drugs		1			1
N05CF01 Zopiclone		1			1
P ANTIPARASITIC PRODUCTS, INSECTICIDES AND REPELLENTS		**1**			**1**
P01 Antiprotozoals		1			1
P01B Antimalarials		1			1
P01BA Aminoquinolines		1			1
P01BA01 Chloroquine		1			1
R RESPIRATORY SYSTEM	**1**	**1**			**2**
R03 Drugs for obstructive airway	1	1			2
R03D Other systemic drugs for obstructive airway diseases	1	1			2
R03DA Xanthines	1	1			2
R03DA04 Theophylline	1	1			2

(a) Number of type A ADR-related admissions in which the drug / drug class was the sole implicated drug.
(b) Number of type A ADR-related admissions in which the drug / drug class was an implicated drug in combination with other drugs.
(c) Number of type B ADR-related admissions in which the drug / drug class was the sole implicated drug.
(d) Number of type B ADR-related admissions in which the drug / drug class was an implicated drug together with other implicated drugs.
(e) Total number of ADR-related admissions in which the drug / drug class was implicated.

SDC 16. Alternative generalized estimation equation model of associations with adverse drug reaction-related admission, including all admissions (n=1951 admissions in 1904 patients).

		Crude			Adjusted[d]		
	n	**OR**	**(95% CI)**	**Wald *P* value**	**OR**	**(95% CI)**	**Wald *P* value**
Sex							
Male (referent)	864	1.00			1.00		
Female	1087	1.67	(1.19 to 2.35)	.003	1.57	(1.10 to 2.23)	.01
Age[a]	1951	1.06	(0.98 to 1.15)	.17	1.03	(0.92 to 1.15)	.65
HIV and ART							
HIV-negative/unknown (referent)	1378	1.00			1.00		
HIV-infected, not on ART	259	0.69	(0.38 to 1.25)	.22	1.04	(0.54 to 2.00)	.91
HIV-infected, on ART	314	2.43	(1.69 to 3.51)	<.001	2.02	(1.22 to 3.33)	.006
Anti-tuberculosis therapy							
Not on ATT (referent)	1764	1.00			1.00		
On ATT	187	2.41	(1.57 to 3.72)	<.001	1.24	(0.72 to 2.12)	.44
Drug count[b]	1951	1.23	(1.18 to 1.28)	<.001	1.17	(1.11 to 1.23)	<.001
Comorbidity score[c]	1951	1.34	(1.20 to 1.51)	<.001	1.24	(1.07 to 1.42)	.003

(a) Included in the model as a continuous variable. The reported odds ratio is for each 10-year increment.
(b) Included in the model as a continuous variable. The reported odds ratio is for each additional drug.
(c) Included in the model as a continuous variable. The reported odds ratio is for each additional point on the modified Charlson comorbidity score.
(d) Adjusted for other factors in the model.

ART: antiretroviral therapy, ATT: antituberculosis therapy, CI: confidence interval, OR: odds ratio.

SDC 17. Alternative generalized estimation equation model of associations with adverse drug reaction-related admission, excluding patients in whom no drug history was recorded in the medical records, as well as patients documented to have had zero drug exposure (n=1469 admissions in 1432 patients).

		Crude			Adjusted[d]		
	n	**OR**	**(95% CI)**	**Wald *P* value**	**OR**	**(95% CI)**	**Wald *P* value**
Sex							
Male (referent)	603	1.00			1.00		
Female	866	1.47	(1.04 to 2.08)	.03	1.47	(1.04 to 2.09)	.03
Age[a]	1469	1.00	(0.92 to 1.09)	.94	1.00	(0.90 to 1.12)	.96
HIV and ART							
HIV-negative/unknown (referent)	1029	1.00			1.00		
HIV-infected, not on ART	126	1.10	(0.59 to 2.02)	.77	1.28	(0.65 to 2.52)	.48
HIV-infected, on ART	314	1.76	(1.22 to 2.55)	.002	1.77	(1.09 to 2.85)	.02
Anti-tuberculosis therapy							
Not on ATT (referent)	1282	1.00			1.00		
On ATT	187	1.69	(1.10 to 2.61)	.02	1.21	(0.73 to 2.00)	.46
Drug count[b]	1469	1.15	(1.10 to 1.20)	<.001	1.11	(1.05 to 1.17)	<.001
Comorbidity score[c]	1469	1.23	(1.09 to 1.39)	.001	1.22	(1.07 to 1.41)	.004

(a) Included in the model as a continuous variable. The reported odds ratio is for each 10-year increment.
(b) Included in the model as a continuous variable. The reported odds ratio is for each additional drug.
(c) Included in the model as a continuous variable. The reported odds ratio is for each additional point on the modified Charlson comorbidity score.
(d) Adjusted for other factors in the model.

ART: antiretroviral therapy, ATT: antituberculosis therapy, CI: confidence interval, OR: odds ratio.

SDC 18. Summary of systematic reviews of studies determining the proportion of adult hospital admissions attributable to ADRs.

Review	Restrictions applied at search stage						No of studies identified	No of patients/ admissions	Heterogeneity	Subgroup analyses?	Main outcome	Selected other outcomes
	Databases	Publication Date	Language	Settings	ADR definition	Design						
Einarson, 1993[1]	Medline, Index Medicus, IPA	1966 to 1989	English only	No restriction	Cluff definition[2] and non-compliance. Excluded overdose, intentional poisoning, abuse, intoxication.	No restriction reported.	37	69187 admissions	Not measured, but discussed range of study size and study duration.	Yes, for paediatric studies; and for non-compliance studies.	Median ADRad proportion of 37 studies is 4.9%, IQR 2.9% to 6.7%	Proportion of patients who die subsequent to ADRad (11 studies): 5.0% of ADRad patients; 0.3% of all admissions.
Muehlberger, 1997[3]	Medline, EMBASE, Toxline, SoMed, Geriatrics, Deutsche Bibliographie, Chemical Abstracts	1970 to 1996	English or German	No restriction	Authors' definition had to be largely consistent with WHO definition[4].	No restriction.	25	160354 admissions / consultations/ patients	Not measured, but implied in design of the analysis.	Yes, by setting, and by study design.	Median ADRad proportion of 25 studies is 4.1%, IQR 2.5% to 5.9%	Selective study setting, and comprehensive detection design, resulted in higher ADRad proportions. For studies of medical inpatients, with comprehensive monitoring (n=12 studies, n=20037 admissions) median ADRad proportion is 5.8%, IQR 4.2% to 6.0%
Lazarou, 1998[5]	Medline, EMBASE, IPA, SCI, hand search	1966 to 1996	English (or English translation available)	Only US studies	WHO definition[4] only; excluded 'possible' ADRs.	Only prospective studies included.	21 (in ADRad analysis)	28017 patients (in ADRad analysis)	Not measured, but discussed.	Yes, for fatal ADRs.	Meta-analytic estimate 4.7% (95% CI 3.1% to 6.2%) admissions are ADRad.	Proportion of fatal ADRs (ADRad and ADR during inpatient stay): 0.32% of 46625 patients studied.
Wiffen, 2001[6]	Medline, EMBASE, IPA	1966 to 1999	No restriction	No restriction	No restriction, but excluded administration errors, non-compliance, overdose, abuse or therapeutic failure.	No restriction.	37 (in ADRad analysis)	133741 patients (in ADRad analysis)	Not measured, but implied.	Yes, by study design, geographical setting, clinical setting, and date.	Weighted mean ADRad proportion is 3.1% (CI not reported).	Subgroup analyses combine ADRad and ADRs in inpatients.

Review	Restrictions applied at search stage						No of studies identified	No of patients/ admissions	Heterogeneity	Subgroup analyses?	Main outcome	Selected other outcomes
	Databases	Publication Date	Language	Settings	ADR definition	Design						
Beijer, 2002[7]	Medline, Cochrane Library, hand search	1966 to 2000	Not reported	No restriction	WHO definition[4]. Excluded illicit drug use, abuse, therapeutic failure, overdose.	No restriction reported.	68	123794 admissions	Confirmed heterogeneity: smaller studies show higher proportions.	Yes, by age group, date of publication, geographical region, and by clinical setting.	Weighted mean ADRad proportion is 4.9% (95% CI 4.8% to 5.0%).	For studies of non-elderly (n=51 studies, n=116241admissions): weighted mean ADRad proportion is 4.1% (95% CI 4.0% to 4.2%).
Kongkaew, 2008[8]	CINAHL, EMBASE, Medline	To Aug 2007	No restriction	No restriction	WHO definition[4] or another ADR definition that mapped to it.	Only prospective studies included.	25	106586 admissions	Confirmed heterogeneity: I^2= 98.5%.	Yes, by age group, and by ADR detection method.	Median ADRad proportion is 5.3%, IQR 2.7% to 9.0%.	For studies of adults (n=10 studies, n=11477 patients): median ADRad proportion is 6.3%, IQR 3.9% to 9.0%.

ADR: adverse drug reaction; ADRad: admissions due to an adverse drug reaction; CI: confidence interval; CINAHL: Cumulative Index to Nursing and Allied Health Literature; EMBASE: Excerpta Medica Database; IPA: International Pharmaceutical Abstracts; IQR: interquartile range; SCI: Science Citation Index; WHO: World Health Organization

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