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Outpatient antibiotic prescription rate and pattern in the private sector in India: Evidence from medical audit data

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Outpatient antibiotic prescription rate and pattern in the private sector in India: Evidence from medical audit data

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Abstract

The key objective of this research was to generate new evidence on outpatient antibiotic prescription rate and patterns in the private sector in India. We used 12-month period (May 2013 to April 2014) medical audit dataset from IMS Health (now IQVIA). We coded the diagnosis provided in the medical audit data to International Statistical Classification of Diseases and Related Health Problems (ICD-10) and the prescribed antibiotics for the diagnosis to Anatomic Therapeutic Chemical (ATC) classification of World Health Organization (ATC index-2016). We calculated and reported antibiotic prescription rate per 1,000 persons per year, by age groups, antibiotic class and disease conditions. Our main findings are - approximately 519 million antibiotic prescriptions were dispensed in the private sector, which translates into 412 prescriptions per 1,000 persons per year. Majority of the antibiotic prescriptions were dispensed for acute upper respiratory infections (J06) (20.4%); unspecified acute lower respiratory infection (J22) (12.8%); disorders of urinary system (N39) (6.0%); cough (R05) (4.7%); and acute nasopharyngitis (J00) (4.6%) and highest antibiotic prescription rates were observed in the age group 0-4 years. To conclude our study reports first ever country level estimates of antibiotic prescription by antibiotic classes, age groups, and ICD-10 mapped disease conditions. We observed an inappropriate and high antibiotic prescription rates for upper respiratory infections in children age less than 5 years.

Introduction

India is considered to be one of the top users of antibiotics. Previous research had reported that per capita antibiotic consumption in the retail sector in India has increased by around 22%, from 13.1 DID in 2008 to 16.0 DID, in span of five years (2012 to 2016).[1] Current evidence suggests that between 2000 and 2015, antibiotic consumption increased from 3.2 to 6.5 billion DDDs (103%) while the antibiotic consumption rate increased from 8.2 to 13.6 DDDs per 1,000 inhabitants per day (63%) in India.[2]

Literature suggests that high burden of infectious disease is one of the reasons for high antibiotic use in India. Earlier Million Death Study (MDS) had reported that diseases of infectious origin such as pneumonia and diarrhea accounted for around 50% (0·67 million of 1·34 million) of all deaths in children aged less than 5 years in India.[3] However, inappropriate use of antibiotics cannot be ruled out. In spite of the fact that majority of upper respiratory infections like common cold and nasopharyngitis are viral in origin, self limiting in nature and do not require antibiotic therapy,[4-6] literature on antibiotic use and prescription pattern from India indicate high rate of antibiotic prescriptions for respiratory infections in the primary care.[7-9] Previous research had also reported relatively high antibiotic prescription rate in the private health facilities as compared to public health facilities.[8 10] These studies also highlighted frequent use of expensive newer classes of antibiotics as compared to the older ones in the private sector.[8-11] One of the reasons for such a trend is dominance of private sector in funding and provisioning of the health care in India. As per the National Sample Survey

(NSS) nearly 75% of all outpatient visits and about 62% of hospitalization episodes occurred in private health delivery system in the year 2014.[12] Furthermore, households largely buy medicines directly from retail pharmacies as prescribed by the general practitioners in the private sector.[13] Evidence suggests that, of total INR 1338[14] per capita spending on medicines in India, around INR 1208 per capita was spent by households as out of pocket expenditure, which indicates that government's contribution is barely 10 percent.

The health system elements outlined above clearly demonstrate the role and relevance of general practitioners in the private sector in rational medicine use and in particular antibiotic use. Previous research involving micro level surveys revealed several facets of inappropriate medicines use in the Indian context.[8 9 15-17] However, none of them were truly representative of general practitioners because of their limited sample sizes and geographical locations. We conducted this research to generate new evidence on outpatient antibiotic (J01) prescription rate and patterns in the private sector in India. We also performed additional analysis to report age-specific and disease-specific differences by different antibiotic classes.

Material and Methods

Data source and setting

We examined prescription rate and patterns of antibiotics (J01) of general practitioners working in the private sector in India with the help of

Intercontinental Medical Services medical audit data (now IQVIA) for 12 month period (May 2013 to April 2014).[18] IMS Health (now IQVIA) is a for-profit organisation that collects and provides data and information on pharmaceutical market intelligence in over 100 countries around the world. The medical audit data tracks prescription by private practitioners practicing allopathic system of medicine. This data is collected from a panel comprising of 4600 doctors, which include general practitioners (MBBS, Bachelor of Medicine, Bachelor of Surgery), non-MBBS general practitioners, and other medical specialties (such as dentists, pediatrics, gynecology, dermatology, and others) from 23 metropolitan areas (population more than 1 million), 128 class 1 towns (population more than 100,000) and 1A towns (population less than 100,000) of India. The data is then extrapolated to reflect the private sector prescription pattern in the entire country.

This database provides information on patient characteristics such as age, gender, symptoms, diagnosis and medicines prescribed. The data organizes medicines according to anatomical therapeutic classification (ATC) of the European Pharmaceutical Market Research Association (EphMRA) but not to the World Health Organisation's ATC classification. Also, the diagnosis are not coded to International Statistical Classification of Diseases and Related Health Problems (ICD-10). Furthermore, the data does not capture the public sector prescriptions and therefore our analysis only reflects outpatient antibiotic prescription patterns in the private sector in the country.

Outcome measure

Our primary outcome measure was antibiotic prescription rate per 1,000 persons per year. We also estimated and reported age-specific and disease-specific antibiotic prescription by antibiotic classes.

Statistical analysis

We coded the diagnosis provided in the medical audit data to disease classifications based on the International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10 classification; version: 2016)[19] and antibiotics prescribed for the related diagnosis to 3rd level of Anatomic Therapeutic Chemical (ATC) classification as per the methodology proposed by World Health Organization's Collaborating Centre (WHOCC) of Drug Statistics Methodology's (ATC index-2016).[20]

The utilization of antibiotics (ATC code: J01) was measured in terms of the annual prescription rate, i.e. number of antibiotic prescriptions divided by the 1000 person years. The population estimates were obtained from report of the technical group on population projections constituted by the National Commission on Population.[21] The age-group classification was determined by the medical audit data availability. The prescriptions were divided into the following antibiotic subgroups (ATC codes): tetracyclines (J01A), amphenicols (J01B), penicillins (J01C), other beta-lactams, cephalosporins (J01D), sulfonamides & trimethoprim (J01E), macrolides, lincosamides & streptogramins (J01F), aminoglycosides (J01G), Quinolones (J01M), combinations of

antibacterials (J01R), other antibacterials (J01X). Unclassifiable antibiotics were pooled in the subgroup 'others'.

We used per 1000 person denominator in contrast to individuals because the data was available only for prescription per person and not for an individual for the entire year. Antibiotic prescription rates are more appropriate indicator to describe antibiotic use[22] as compared to defined daily doses (DDD) per person since antibiotic dose depends on a patient's age and body weight. We analyzed and reported antibiotic use by age groups and disease conditions (based on ICD-10 classification) expressed as annual prescription rate per 1,000 persons for each class of antibiotics. We used software STATA 14.0 to perform statistical analysis.

Results

Antibiotic prescribing pattern

We present new evidence on outpatient antibiotic prescription rates and pattern in the private sector in India. Around 519 million antibiotic prescriptions were dispensed in 2014, which translate into 412 prescriptions per 1,000 persons per year. The antibiotic prescription rates were highest for the children age 0-4 years (636 prescriptions per 1,000 persons) and lowest in the age group 10-19 years (280 prescriptions per 1,000 persons) (Fig 1). It may also be noted that across all age groups beta-lactam, cephalosporin (J01D) had the highest

prescription rates (38.3% of all antibiotic prescriptions) followed by beta-lactam, penicillin (J01C) (22.8%) and quinolone (J01M) (16.3%).

Antibiotic prescribing across clinical diagnoses

Of 519 million antibiotic prescriptions, majority were dispensed for the diseases of respiratory system (55%), followed by diseases of genitourinary system (10%), and symptoms, signs and abnormal clinical findings (9%) (Table 1).

Table 1. Distribution of outpatient antibiotic prescriptions in India, by disease conditions, 2013-2014

ICD code	ICD label	Number of prescriptions	Percentage (%)	Prescription rate per 1000 persons per year
1	Certain infectious and parasitic diseases	16,820,293	3.24	13.35
3	Diseases of the blood and blood-forming organs	1,158,125	0.22	0.92
4	Endocrine, nutritional and metabolic diseases	4,566,575	0.88	3.63
5	Mental and behavioral disorders	967,392	0.19	0.77
6	Diseases of the	1,491,169	0.29	1.18

	nervous system			
7	Diseases of the eye and adnexa	3,685,540	0.71	2.93
8	Diseases of the ear and mastoid process	8,653,317	1.67	6.87
9	Diseases of the circulatory system	8,472,213	1.63	6.73
10	Diseases of the respiratory system	286,059,212	55.09	227.10
11	Diseases of the digestive system	28,532,251	5.49	22.65
12	Diseases of the skin and subcutaneous tissue	20,917,567	4.03	16.61
13	Diseases of the musculoskeletal system	5,973,066	1.15	4.74
14	Diseases of the genitourinary system	51,791,862	9.97	41.12
15	Pregnancy, childbirth and the puerperium	977,532	0.19	0.78
17	Congenital malformations, deformations	114,892	0.02	0.09

18	Symptoms, signs and abnormal clinical and laboratory	44,506,708	8.57	35.33
19	Injury, poisoning and external causes	33,398,837	6.43	26.52
20	External causes of morbidity and mortality	37,318	0.01	0.03
21	Factors influencing health status	1,118,282	0.22	0.89
	Total	519,242,151	100.00	412.23

As per the ICD-10 classification, following top ten disease conditions contributed approximately 63% of the antibiotic prescriptions - acute upper respiratory infections (J06) (20.4%), unspecified acute lower respiratory infection (J22) (12.8%), disorders of urinary system (N39) (6.0%), cough (R05) (4.7%), acute nasopharyngitis (J00) (4.6%), acute pharyngitis (J02) (3.9%), acute bronchitis (J20) (3.4%), injury, poisoning and others (T14) (2.5%), cutaneous abscess and furuncle (L02) (2.3%), and asthma (J45) (2.2%) (Fig 2). It may be further noted that cephalosporins (J01D) were the most commonly prescribed antibiotic across all diagnoses with the exception of disorders of urinary system where quinolones (J01M) were more commonly prescribed. (For full information on antibiotic prescription rates across disease conditions and antibiotic classes see supplementary file (S1 and S2 Table).

Figure legends:

Fig1: Outpatient antibiotic prescription rate per 1000 persons per year, by age groups and antibiotic classes, India (2013-2014)

Fig 2: Number of antibiotic prescriptions, by disease conditions and antibiotic classes, India (2013-2014)

Discussion

To the best of our knowledge, this study provides first ever country level estimates of outpatient antibiotic prescription rates and patterns in the private sector. Our findings illustrate significant variations in antibiotic prescription rates across age groups, by disease conditions (ICD-10 classification) and by antibiotic classes (ATC classification). Earlier Von Bockel et al. and Klein et al. had reported estimates of antibiotic consumption in India through use of pharmaceutical sales data[2 23]. However, their study did not provided information on antibiotic use by disease conditions and age groups. While other prescription analysis based studies from India had reported antibiotic utilization in public and private sector health facilities[8-11 15 24], they were not nationally representative because of limited sample sizes and geographical locations.

Our estimates suggest high proportion of antibiotic prescription for upper respiratory tract infections (acute upper respiratory infections (J06) (20.4%), cough (R05) (4.7%), acute nasopharyngitis (J00) (4.6%), and acute pharyngitis (J02) (3.9%)). These infections are viral in origin and are generally self-limiting in nature; hence this high rate of antibiotic prescription is inappropriate in the

light of evidence based medicine and standard treatment guidelines. Previous research on prescription practices had also highlighted the problem of inappropriate use of broad-spectrum antibiotics in India. For example, Kotwani et al had reported that in the private sector, not only the antibiotic prescription rates were higher but also the choice of antibiotics for the treatment of uncomplicated respiratory infections was inappropriate.[9] Chandy et al had reported widespread use of fluoroquinolone, especially by general practitioners[10] in the private sector. Other studies have reported high cephalosporin use in urban hospitals and pharmacy shops.[10 25]

Previous research shows that that inappropriate antibiotic use is linked to supply-side incentives, which lead to over prescription of antibiotics in private sector.[15 24 26] This problem of inappropriate use of antibiotics get accentuated multifold because of limited access to care and medicines in the public health system[27] which forces patients to seek care in private sector. Limited access to medicines in public sector also results in over the counter purchase of antibiotics, which is a major driver of inappropriate use in India. Laxminarayanan et al had reported that non-prescription sales of carbapenems in India are among the highest in the world and contribute to growing carbapenem resistance.[28] Although, over the counter access of antibiotics is a complex problem in India on account of the fact that insufficient access and delays in access to antibiotics cause more deaths than antibiotic resistance,[29] numerous have reported increasing level of antimicrobial resistance for last resort antibiotics like carbapenem. Using a private laboratory network data on patient blood cultures collected over a 7-year period from January 2008 to

December, 2014, Gandra et al reported increased carbapenem resistance in *Escherichia coli* and *Klebsiella pneumonia.*[30] Other hospital based retrospective studies have also reported rise in carbapenem resistant isolates of *E. coli* from 10% to 13% during 2008 to 2013[28] and increase in carbapenem resistance among *K. pneumoniae* from 2% to 52% during 2002 to 2009[31]. Evidence also suggest that inappropriate antibiotic use not only has profound impact on antimicrobial resistance[32] but also on treatment cost because of drug resistant organism.[33]

Our analyses suggest that antibiotic prescription rates (412 prescriptions per 1000 persons in 2014) in India are significantly lower than various European nations. For example, antibiotic prescription rates in Italy (957 prescriptions per 1000 persons), Germany (561 prescriptions per 1000 persons), UK (555 prescriptions per 1000 persons), Denmark (481 prescriptions per 1000 persons)[34] and Greece (1100 antibiotics per 1000 person)[25] are much higher than India. Our findings for antibiotic prescription are consistent with antibiotic sales in India. Our previous analysis on pharmaceutical sales data had also suggested that the antibiotic consumption (16.0 DID) in India was significantly below the mean antibiotic consumption (21.5 DID) of the European countries.[1] However, antibiotic prescription rates for certain antibiotic classes are on higher side in India as compared to developed nations. For example, the percentage of prescriptions with cephalosporins and quinolones (38.2% and 16.3%) in India were significantly higher than USA (14.0% and 12.7%)[35], and also Greece (32.9% and 0.5%).[25] Such unusually high prescription rate of beta-lactams-penicillins and cephalosporins in uncomplicated upper respiratory infections in children is

in stark contrast to the prescription rates and pattern reported from European countries.[34] The potential reasons for high prescription rates of broad spectrum antibiotics like cephalosporins and quinolones are not only high burden of infectious diseases, but also lack of diagnostic support services and inadequate training of the physicians[10]. Literature also suggests that perceived demand and expectation from the patients, influence from medical representatives and inadequate knowledge influences doctors decisions to prescribe antibiotics.[36] Given the fee-for-service payment mechanisms followed by private practitioners, prescriptions and dispensing of medicines are often subject to influence by medical representatives. Previous research has highlighted that inappropriate use of medicines is rampant in less regulated health markets[37] and can take several forms: overuse, underuse, misuse, and unnecessary expensive use. This inappropriate use of antibiotics not only poses health risk on individuals and community in form of antimicrobial resistance but also leads to inefficient use of limited financial resources at household level.

To address the problems related to inappropriate use of antibiotics government of India has deployed multipronged strategy. This includes setting up treatment guidelines for antimicrobial use[38] and multi-centric surveillance for tracking antimicrobial resistance[39]. In addition, over-the-counter (OTC) sales of 3rd and 4th generation antibiotics are now regulated through Schedule H1 of Drugs & Cosmetics Rules.[40] Furthermore, to reduce burden of pneumonia and diarrhea and the demand for antibiotics, new vaccines have been introduced in the universal immunization program[41]. However, success of these strategic measures in terms of achieving intended objectives is yet to be demonstrated.

Considering that more than 519 million antibiotic prescriptions were dispensed in India during one year period (2013-2014), an antibiotic stewardship program or an intervention with a potential to reduce antibiotic prescription rates by just 10 % would result in 52 million less antibiotic prescriptions and a commensurate reduction in healthcare costs and potentially antimicrobial resistance rates. Our analysis suggest around 100 million prescriptions were dispensed for acute upper respiratory tract infections (ARTI) alone, antibiotic stewardship programs directed towards diagnosis and treatment of ARTI could result into significant reduction in antibiotic use.

Our study has certain limitations. The scope of our study was limited to analysis of antibiotic prescription pattern in the private sector, as we had no access to public sector prescription data. Therefore, the study is not representative of the prescriptions generated in public sector facilities. This may have resulted in an underestimation of antibiotic prescription rates albeit only marginally, since more than 80% of the population seeks care in private sector and approximately 90% of medicine expenditure occurs in private sector. In addition, a small proportion (<1%) of antibiotic prescriptions sometimes got mapped to completely unrelated diagnosis because IMS medical audit data is coded in such a way that antibiotics on prescriptions gets mapped to every differential diagnosis (related or completely unrelated) on the prescription.

Conclusions

This research work provided the first ever country level estimates on antibiotic prescription rate and pattern in the outpatient general practice in the private sector. Overall antibiotic prescription rates in India are still much lower than Europe. However, prescription rates for broad-spectrum beta-lactam antibiotics are much higher as compared to European nations, especially in children. Approximately one-fifth antibiotic prescriptions were dispensed for upper respiratory infections, which rarely require an antibiotic therapy. Our findings highlight that primary care physicians in the private sector can play a key role in reducing antibiotic misuse and overuse. Our research findings also provide critical information to target antimicrobial stewardship programs to specific constituencies and stakeholders. This baseline information can also be used as a benchmark for measuring the impact of current and future interventions directed towards reducing inappropriate antibiotic use.

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Supporting information

S1 Table. Antibiotic prescription rate per 1000 person per year, by age group, India (2013-2014)

S2 Table. Distribution of outpatient antibiotic prescriptions by disease conditions and antibiotic classes, India (2013-2014)

Fig 1

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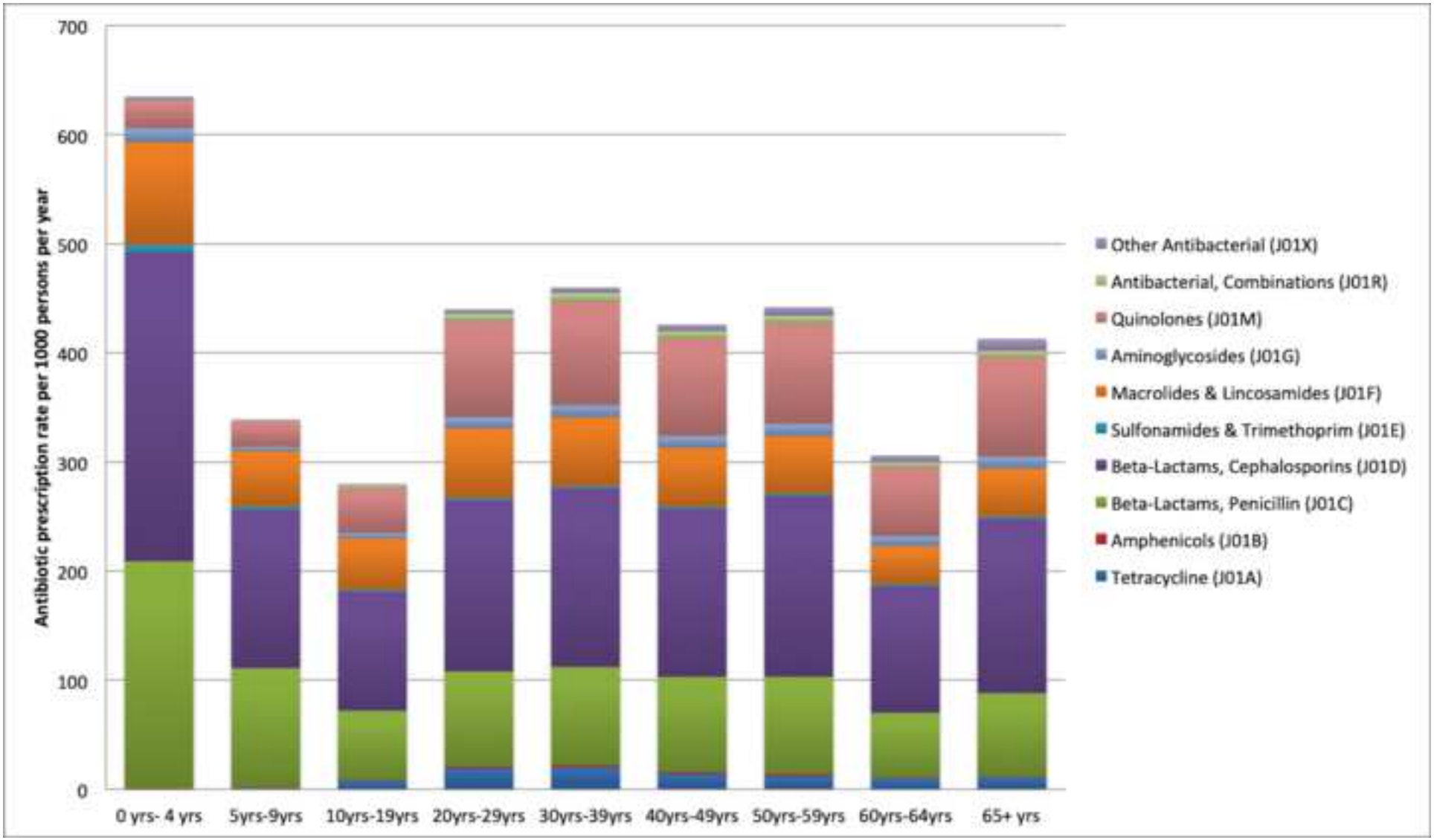

Fig 2

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