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Antibiotic use in Australian and Swedish primary care: a cross-country comparison

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ABSTRACT

Objective: Antimicrobial resistance is a growing worldwide problem and is considered to be one of the biggest threats to global health by the World Health Organization. Insights into the determinants of antibiotic prescribing may be gained by comparing the antibiotic usage patterns of Australia and Sweden.

Design: Publicly available data on dispensed use of antibiotics in Australia and Sweden between 2006 and 2018. Medicine use was measured using defined daily dose per 1,000 inhabitants per day (DDD/1000/day) and the number of dispensed prescriptions per 1000 inhabitants (prescriptions/1000).

Results: The use of antibiotics increased over the study period in Australia by 1.8% and decreased in Sweden by 26.3%. Use was consistently higher in Australia, double that of Sweden in 2018. Penicillin with extended spectrum was the most used class of antibiotics in Australia followed by penicillin with beta lactamase inhibitors. In Sweden, the most used class was beta lactamase-sensitive penicillin and the least used class was penicillin with beta lactamase inhibitors.

Conclusion: Antibiotic use in Australia is higher than in Sweden, with a higher proportion of broad-spectrum penicillin, including combinations with beta lactamase inhibitors, and cephalosporins. Factors that may contribute to these differences in antibiotic use include differences in guidelines, the duration of national antimicrobial stewardship programs, and differences in funding mechanisms.

KEY POINTS

Australia has had a consistently higher dispensed use of antibiotics compared to Sweden from 2006 to 2018; and up to twice the use in 2018

- A higher proportion of dispensed antibiotics in Australia were broad-spectrum penicillin, including combinations with beta lactamase inhibitors, and cefalosporins.
- The most commonly used class of antibiotics in Australia is penicillin with extended spectrum, compared to beta lactamase sensitive penicillin in Sweden.
- Use of macrolides, sulphonamides and trimethoprim, cephalosporins, penicillin with beta lactamase inhibitors and penicillin with extended spectrum was consistently higher in Australia, whereas in Sweden use of fluoroquinolones, lincosamides, beta lactamase-resistant penicillin and beta lactamase sensitive penicillin was higher.
- The observed differences could be explained by antibiotic choice recommended in guidelines, prevalence of point-of-care testing, models of primary care funding, the presence and duration of national antimicrobial stewardship programmes, and cultural differences.

Introduction

Antimicrobial resistance has important implications for healthcare systems all over the world in terms of increased morbidity, mortality, and healthcare expenditure [1]. Each year in the European Union and the European Economic Area, there are over 670,000 infections due to antibiotic-resistant bacteria and 33,000 people die from these infections. If antimicrobial resistance follows the projected trends, the annual costs for these infections are estimated to have an economic impact of up to €1.1 billion by 2050 in the European Union [2]. The OECD has estimated that

between 2015 and 2050 antimicrobial resistance will lead to a combined economic burden of $75 billion for United States, Canada, and Australia [3]. A 2014 review on antimicrobial resistance estimated that if resistance trends continued there would be a global economic impact in terms of lost productivity of US$100 trillion [4].

There is large variation in prescribing rates among these high-income countries [5]. Antibiotic prescribing practices vary widely within Europe, with higher rates of prescribing and antibiotic resistance in southern and Eastern Europe than in northern Europe [6,7]. Sweden, in particularly has favourable levels of resistance, including methicillin-resistant *Staphylococcus aureus* and resistance to third generation cephalosporins and extended spectrum beta lactamase in *Escherichia coli* compared with other European countries [8,9]. Meanwhile prescribing rates in Australia are higher than any European country [10]. The large variation in antibiotic prescribing among high-income countries is not fully understood but does not seem to be due to differential rates or patterns of bacterial infections [11,12].

Further insights into the determinants of antibiotic prescribing may be gained by comparing the antibiotic usage patterns of Australia and Sweden. Both countries have similar levels of productivity and health outcomes, yet Australia is among the countries with the highest rate of antibiotic use in the Organization for Economic Co-operation and Development (OECD), while Sweden is among the lowest [13]. In both countries, primary care is the largest source of antibiotic prescribing [7,9,14]. Cross-country comparisons of antibiotic use can help determine contributing factors of prescribing behaviour to better understand how to improve prescribing. Therefore, the aim of this study is to compare the dispensed use of antibiotics in Australia and Sweden.

Material and methods

Study design

We analysed publicly available data on dispensed use of antibiotics in Australia and Sweden between 2006 and 2018. We developed a list of antibiotics regularly used in primary care in each country through consensus of two Australian and one Swedish general practitioners. We selected antibiotics from the Anatomical Therapeutic Chemical (ATC) classification J01-systemic antibiotics [15].

We measured antibiotic use using two metrics: (i) 'DDD' – the daily defined dose per 1000 inhabitants per day (DDD/1000/day) and (ii) 'counts' – the number of dispensed prescriptions per 1000 inhabitants (prescriptions/1000). The DDD is the average daily dose of a specific medicine used for its main indication in adults [16]. We obtained the DDD values from WHO Collaborating Centre for Drug Statistics Methodology [17]. The DDD use was available from the Australian Statistics on Medicine (ASM) until 2015 and after that we calculated the DDD use from the Date of Supply reports [18].

Descriptive statistics and graphical presentation was used to explore trends. Linear regression was used to assess change in dispensed use of antibiotics over time. Independent samples *t*-test was used to determine the difference in mean total antibiotic dispensed (DDD/1000/day) between Australia and Sweden.

Australian data sources

We obtained data on antibiotic use in Australia from the Pharmaceutical Benefits Scheme (PBS) and the Repatriation PBS (RPBS, both schemes termed PBS from now on). These are schemes funded by the Australian government to provide access to medicines in the community for the general population (PBS) and for veterans specifically (RPBS). Medicines funded by the national government in Australia are known as PBS/RPBS-subsidised medicines. There were two sources for the Australian data for dispensed use of antibiotics: (1) ASM (pre 2016) [19]; and (2) Date of Supply Reports (Section 85, 2016–2018) [20]. The ASM contains data on dispensed use from three sources: PBS subsidised; PBS non-subsidised; and private (non-subsidised). From 2006 to 2011, ASM data for non-subsidised PBS and private dispensed use were collated from a survey of representative community pharmacies in Australia. Date of Supply reports became available in 2012 and contain data on both PBS subsidised and non-subsidised dispensed use but not for private use. To estimate private use after 2012 we used data on private use that were available for only 2010 and 2011 and calculated the proportion of private to total use for each antibiotic. We used this proportion to extrapolate private use in subsequent years and added the estimated private use to the empirical data of PBS subsidised and non-subsidised use from Date of Supply reports.

DDD/1000/day data for trimethoprim with sulphamethoxazole was not available on the ASM before 2016 and had to be calculated based on PBS prescribing rates and population data from the Australian Bureau of Statistics [21].

Swedish data sources

The Swedish data were retrieved from the National Swedish Drug Registry [22], as prescriptions/1000 and the Public Health Agency as DDD/1000/day for antibiotic classes. The National Swedish Drug Registry provides statistics for all drugs dispensed at all pharmacies in Sweden.

Ethical considerations

This was a retrospective analysis of routinely collected data available in the public domain for which ethics approval was not necessary.

Results

Overall antibiotic use

Antibiotic use in Australia was consistently higher than Sweden over the study period (Figure 1). Antibiotic use in Australia ranged from 21.8 DDD/1000/day in 2006 to 22.2 DDD/1000/day in 2018 with a peak use of 25.9 DDD/1000/day in 2008. The antibiotic use in Sweden ranged from 14.5 DDD/1000/day in 2006 to 10.7 DDD/1000/day in 2018 with a steady decrease during the whole period. Antibiotic use increased by 1.8% in Australia and decreased by 26.3% in Sweden between 2006 and 2018. However, in Australia antibiotic use declined with 14.3% between the peak in 2008 and the end of the period where most of that decline took place between 2015 and 2018.

Regression analysis found a significant reduction in antibiotic prescribing over time for Sweden (R^2 0.956; $p < 0.001$), but not Australia (R^2 0.361; $p = 0.226$). Over the study period, the mean antibiotic use was significantly greater in Australia compared with Sweden (mean difference 12.2 DDD/1000/day, 95% CI 11.3, 13.1).

Use by antibiotic class

In Australia, penicillin with extended spectrum was the most frequently used class of antibiotics, followed by penicillin with beta lactamase inhibitors (Figure 2). The use of penicillinwith extended spectrum decreased from 5.3 DDD/1000/day in 2006 to 4.9 DDD/1000/day in 2018, with a peak use of 6.8 DDD/1000/day in 2008. The use of penicillin with beta lactamase inhibitors increased during the period from 3.2 DDD/1000/day in 2006 to 4.1 in 2018 with a peak of 4.9 in 2014 and 2015. The least frequently used class of antibiotics in Australia during the period was lincosamides. The use of fluoroquinolones, macrolides, penicillin with extended spectrum and beta lactamase-resistant penicillin decreased in Australia from the beginning to the end of the period while the use of penicillin with beta lactamase inhibitors and cephalosporins increased and the use of lincosamides, sulphonamides and trimethoprim, beta lactamase-sensitive penicillin, and tetracyclines did not substantially change.

In Sweden (Figure 3), the most frequently used class of antibiotics was beta lactamase-sensitive penicillin with a prescribing rate of 4.1 DDD/1000/day in 2006 and 2.9 DDD/1000/day in 2018 followed by tetracyclines at 3.2 DDD/1000/day in 2006 and 2.2 DDD/1000/day in 2018. The least used class was penicillin with betalactamase inhibitors. The prescribing of fluoroquinolones, macrolides, sulphonamides and trimethoprim, cephalosporins, beta lactamase sensitive penicillin, penicillin with extended spectrum and tetracyclines decreased consistently during the period while the use of beta lactamase resistant penicillin increased and the use of lincosamides and penicillin with beta lactamase inhibitors remained the same.

Australia consistently had a higher use of macrolides, sulphonamides and trimethoprim, cephalosporins, penicillin with beta lactamase inhibitors and penicillinwith extended spectrum than Sweden, whereas in Sweden the use of fluoroquinolones,
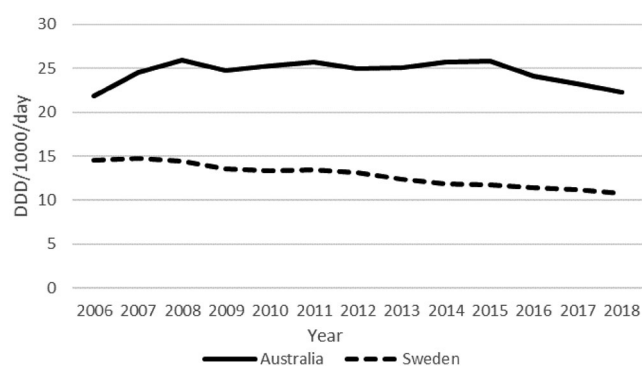

Figure 1. Dispensed use of antibiotics in Australia and Sweden (DDD/1000/day).
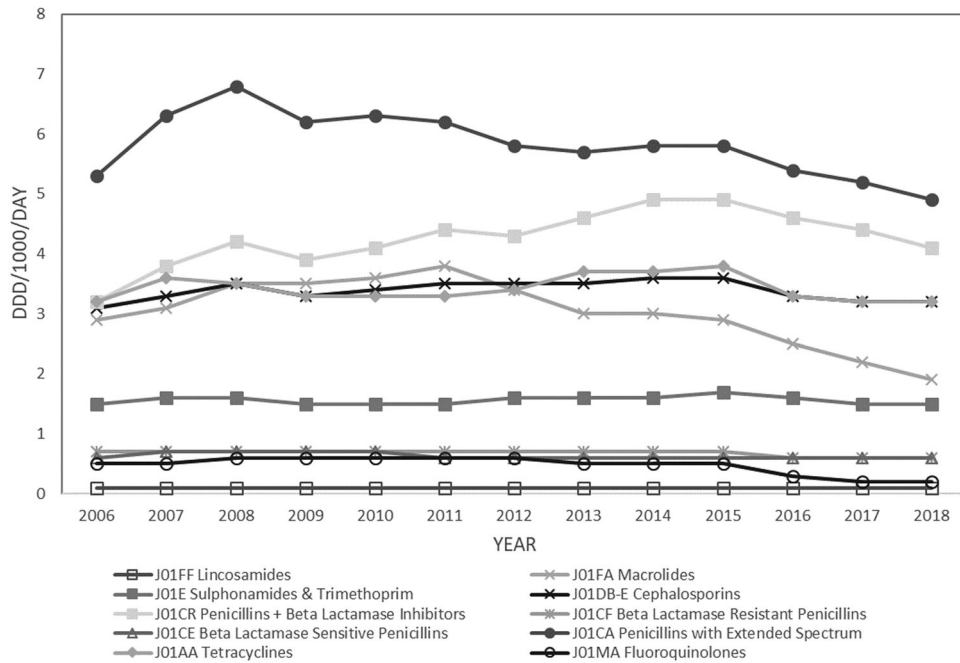
Figure 2. Dispensed use of antibiotics by class in Australia (DDD/1000/day).
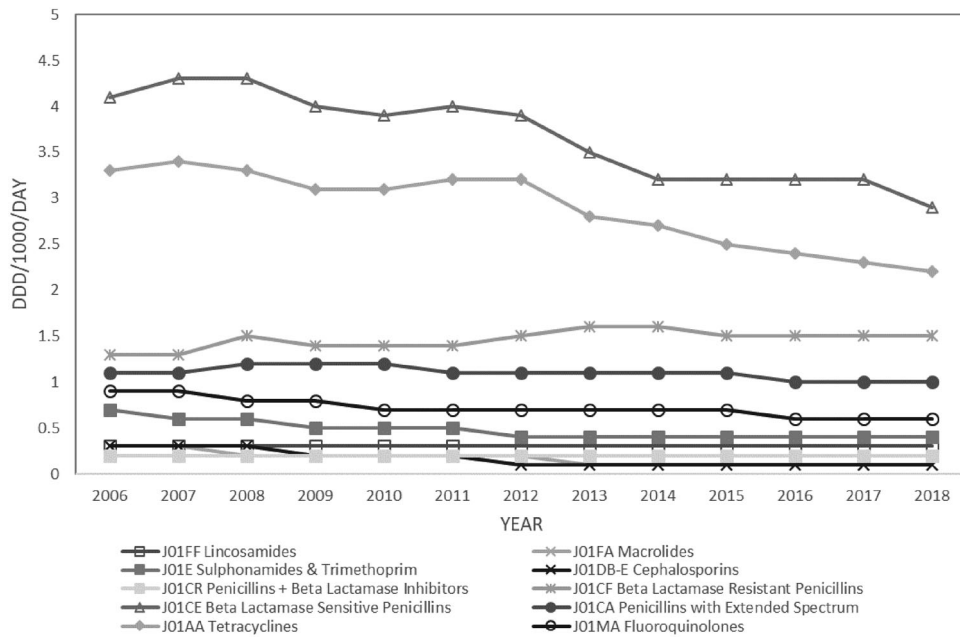

Figure 3. Dispensed use of antibiotics by class in Sweden (DDD/1000/day).

lincosamides, beta lactamase-resistant penicillin and beta lactamase sensitive penicillin was higher than Australia. The use of tetracyclines was higher in Sweden in 2006 but then higher in Australia in the subsequent years.

Most commonly dispensed antibiotics

The five most commonly dispensed antibiotics in Australia during the study period were amoxycillin,

cefalexin, amoxycillin with clavulanic acid, roxithromycin and doxycycline but the order of the most used within that five changed during the study period (Table 1). Amoxycillin was the most used antibiotic from 2006 until 2017, with a peak of 307.7 prescriptions/1000 in 2008. Cefalexin was the most commonly used antibiotic in Australia in 2018, with 220.6 prescriptions/1000. In Sweden, the five most used antibiotics in 2006 were phenoxymethylpenicillin, doxycycline, flucloxacillin, amoxycillin and

Table 1. Top five antibiotics with highest dispensed use in Australia and Sweden (prescriptions/1000 population).

Rank	Australia 2006		2012		2018		Sweden 2006		2012		2018	
1	Amoxycillin	238.2	Amoxycillin	254.2	Cefalexin	220.6	Phenoxymethyl-penicillin	126.3	Phenoxymethyl-penicillin	114.1	Phenoxymethyl-penicillin	83.4
2	Cefalexin	188.6	Cefalexin	226.5	Amoxycillin	203.9	Doxycycline	49.2	Doxycycline	39.3	Flucloxacillin	36.2
3	Amoxycillin + clavulanic acid	147.8	Amoxycillin + clavulanic acid	192.7	Amoxycillin + clavulanic acid	184.7	Flucloxacillin	42.4	Flucloxacillin	39.1	Pivmecillinam	32.8
4	Roxithromycin	96.5	Roxithromycin	89.1	Doxycycline	90.0	Amoxycillin	28.3	Pivmecillinam	32.4	Nitrofurantoin	25.8
5	Doxycycline	70.8	Doxycycline	74.7	Roxithromycin	47.8	Trimethoprim	26.2	Nitrofurantoin	23.3	Doxycycline	22.0

trimethoprim. By 2012, pivmecillinam and nitrofurantoin use overtook that of amoxicillin and trimethoprim. The most used antibiotic was phenoxymethylpenicillin throughout the whole period, declining steadily from 126.3 prescriptions/1000 in 2006 to 83.4 in 2018 and was constantly being used more than twice as much as the second most prescribed antibiotic.

Discussion

Summary of findings

This retrospective time series shows that Australia had a greater dispensed use of antibiotics compared to Sweden. A higher proportion of dispensed antibiotics in Australia were broad-spectrum penicillin, including combinations with beta lactamase inhibitors, and cefalosporins. Although antibiotic use in Australia has declined since the peak in 2008, it has increased overall between 2006 and 2018. Use of antibiotics in Sweden has consistently decreased over time. The most commonly used class of antibiotics in Australia is penicillin with extended spectrum, compared to beta lactamase sensitive penicillin in Sweden. Use of macrolides, sulphonamides and trimethoprim, cephalosporins, penicillin with beta lactamase inhibitors and penicillin with extended spectrum was consistently higher in Australia, whereas in Sweden use of fluoroquinolones, lincosamides, beta lactamase-resistant penicillin and beta lactamase sensitive penicillin was higher. The five most commonly used antibiotics in Australia remained the same from 2006 to 2018 but changed in order. In Sweden, two of the five most commonly used antibiotics changed during the period.

Interpretation of findings in literature context

Differences in prescribing patterns between countries can be understood in terms of medical, contextual and policy evidence [23]. In our antibiotic dispensing analysis, this can be applied to a number of areas, including differences in: (1) guidelines, (2) costs, (3) availability of point-of-care testing, (4) timing of approval for the antibiotics, (5) primary care funding mechanisms, (5) national antimicrobial stewardship programs, and (6) culture.

Our findings suggest that antibiotic guidelines had an impact on which antibiotics became the most used in Australia and Sweden. Although guidance on when to prescribe antibiotics was similar, there were differences in the choice of antibiotics recommended in

guidelines. For respiratory tract infections, amoxycillin is the most recommended as first-line therapy in the Australian guidelines while phenoxymethylpenicillin is recommended as first-line therapy in the Swedish guidelines. The high use of amoxycillin, doxycycline and amoxycillin with clavulanic acid in Australia is consistent with Australian guidelines; however, there is also high use of cephalexin and roxithromycin in Australia despite those antibiotics not being recommended. The top five most commonly used antibiotics in Sweden from 2012 to 2018 are all consistent with Swedish guideline recommendations for most respiratory tract infections, urinary tract infections and skin and soft tissue infections. In both countries, the two most prescribed antibiotics are those recommended for respiratory tract infections [24,25]. These findings accord with the cross-sectional survey by Gunnarsson et al. [26], which was conducted across five countries, including Sweden and Australia, and that differences in national antibiotic prescribing guidelines were associated with differences in the attitudes of medical practitioners. For example, physicians in countries such as Sweden that had guidelines that recommended throat swabs were more likely to perceive throat swabs as an important 'objective' test, compared to countries such as Australia that did not have throat swabs recommended in guidelines.

There are differences in the funding mechanisms for primary care between the two countries, which may contribute to differences in antibiotic use. Funding for Australian primary care is on a fee-for-service basis [27,28]. In contrast, the funding model for Swedish primary care is a combination of fixed capitation for registered individuals and fee-for-service [28]. Therefore, funding for primary care in Sweden is less dependent on patient fees, which could make it easier to limit the prescribing of antibiotics.

The differences in the countries may also be due to differences in availability point-of-care testing between countries. Point-of-care tests, such as the C-reactive protein test, enables clinicians to discern bacterial infections from other causes of inflammation [29]. While point-of-care testing is rare in Australian general practice, it is commonplace in Sweden [30–32]. Point-of-care testing may reduce the diagnostic uncertainty for the Swedish doctors compared with the Australian doctors [33].

A key factor in antibiotic use may be the nature and timing of national antimicrobial stewardship programs in each country. The main objectives of these programmes have been to increase general awareness of antibiotic resistance and treatment recommendations for common infections, to implement antibiotic stewardship practices in healthcare settings, and to monitor antibiotic resistance [8]. The Swedish national strategic program (STRAMA) has been in place since 1995, possibly contributing to their lower antibiotic use in 2006 and the continuously decreasing trend over time [34]. In contrast, Australia's National Antimicrobial Resistance Strategy was not launched until 2015. Since the implementation of this strategy, Australia's antibiotic prescribing has declined for the first time since the late 1990s [35,36]. This suggests a relationship between antibiotic use and national strategic programs and the associated high-level government commitment in both countries.

Finally, the differences in prescribing may reflect differences in culture. These cultural differences can be either patient-related, practitioner-related, or both [37]. There are a number of cultural factors that determine antibiotic prescribing, including attitudes towards authority, and tolerance for uncertainty and ambiguity [38]. Some of these differences may be reflected in adherence to guidelines. Previous studies have shown that adherence to antibiotic guidelines among general practitioners in Australia is poor and there are reports of antibiotics being overprescribed [36,39–42]. In 2015, 45% of the Australian population was prescribed an antimicrobial [42] and an estimated third of these prescriptions were considered inappropriate [39–41]. In 2017, 92% of Australian patients with acute bronchitis and 52% with influenza who consulted a general practitioner were prescribed a systemic antibiotic even though the therapeutic guidelines do not recommend using antibiotics for these conditions [36]. Studies on antibiotic prescribing in Swedish primary care have shown that adherence to guidelines is increasing over time with a decreasing trend of prescribing antibiotics for respiratory tract infections since 2000 and a change from broader to more narrow spectrum antibiotics for treatment of urinary tract infections [43,44].

Limitations

The major weakness of this study is the absence of indications for the antibiotics and the lack of information about population demographics. Although we know which antibiotics the guidelines recommend for each type of infection, we cannot be certain that general practitioners prescribe the antibiotics recommended by the guidelines, which leaves the impact of guidelines on prescribing uncertain in this study. The comparison may also be affected by differences in the

data captured in each of the national databases (i.e. the component of general practice and outpatient care). The antibiotics on our list of those used in Australian and Swedish primary care are not solely used in primary care and therefore a proportion of the antibiotics could come from prescribing to hospital outpatients. We are not able to estimate the size of this proportion, but the non-primary care prescribing component is unlikely to represent a large proportion of total antibiotic use. Unfortunately, we could not compare use of individual antibiotics using the DDD/1000/day metric as data for several individual antibiotics were not accessible in this format from the Swedish database.

Implications for practice

Australia having such higher rates of antibiotic prescribing and such greater use of broad-spectrum antibiotics compared with Sweden makes it important to understand how medical, contextual and policy evidence differs between the two countries. Understanding these causal factors is crucial so that Australia can learn from Swedish practices and improve antimicrobial stewardship.

Conclusion

Australia has had a consistently higher dispensed use of antibiotics compared to Sweden from 2006 to 2018; and up to twice the use in 2018. The countries differed in use of individual antibiotics and antibiotic classes. The observed differences could be explained by antibiotic choice recommended in guidelines, models of primary care funding, and the presence and duration of national antimicrobial stewardship programmes. Our findings point to the importance of national guidelines on antibiotic treatment and of implementing and sustaining nationally supported antimicrobial stewardship programs. The success of such programmes is context sensitive and may require adaptation or alternative implementation strategies to succeed in different healthcare settings.

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Disclosure statement

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Data availability statement

The data that support the findings of this study are openly available from the PBS and the National Swedish Drug Registry.

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