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# Antimicrobial Prescribing in Hospitalized Adults Stratified by Age Data from the ESAC Point-Prevalence Surveys

Peter Zarb,<sup>1</sup> Brice Amadeo,<sup>2</sup> Arno Muller,<sup>3</sup> Nico Drapier,<sup>3</sup> Vanessa Vankerckhoven,<sup>3</sup> Peter Davey<sup>4</sup> and Herman Goossens,<sup>3</sup> on behalf the ESAC-3 Hospital Care Subproject Group

- 1 Infection Control Unit, Mater Dei Hospital, Msida, Malta
- 2 INSERM Unit 897, University of Bordeaux, Bordeaux, France
- 3 Laboratory of Medical Microbiology, Vaccine and Infectious Disease Institute, University of Antwerp, Antwerp, Belgium
- 4 Division of Clinical and Population Sciences and Education, University of Dundee, Dundee, UK

# Abstract

**Background:** Geriatric infectious diseases are a major health care issue. Infections in the elderly occur more frequently than in younger adults, are often associated with higher morbidity and mortality, and may present atypically. Elderly patients are also often taking multiple medications, which increases the likelihood of drug-drug interactions. Dosing decisions should take into consideration the reduced lean body mass and declining renal function in this age group. **Objective:** Antimicrobial prescribing in three age groups (65–74, 75–84 and  $\geq$ 85 years) was compared with a reference age group (18–64 years), with the aim of identifying quality of care indicators specific to the elderly.

**Methodology:** The ESAC (European Surveillance of Antimicrobial Consumption) final phase performed two hospital point-prevalence surveys in 2008 and 2009, respectively, using the defined daily dose (DDD) and Anatomical Therapeutic Chemical (ATC) classification system. The prescribed daily dose (PDD) was compared with the DDD. Differences in prescribing were assessed using multivariate logistic regression analyses.

**Results:** The majority of patients (19 549 [64% of 30 836]) were from Northern Europe and 13 830 (48%) belonged to the reference group. The largest proportion of patients was admitted through the hospital's medical specialty (55% of patients) [range: 49% in the reference group to 72% in the ≥85 years age group]. Penicillins were the most frequently used antimicrobials in all age groups (range: 32% in the reference group to 41% in the ≥85 years age group). Multivariate analyses showed three significant variations between the 65–74 years age group and the reference group (quinolones: odds ratio [OR] 1.17 [95% CI 1.05, 1.29]; tetracyclines: OR 1.58 [95% CI 1.26, 1.98]; aminoglycosides: OR 0.81 [95% CI 0.70, 0.93]). The number of significant variations increased to seven and eight in the 75–84 and ≥85 years age groups, respectively.

A lower likelihood for PDD>DDD was observed in the 65–74 years age group for three parenteral antimicrobials (amoxicillin/clavulanic acid, gentamicin and vancomycin). This was reiterated in the older age groups (75–84 and  $\geq$ 85 years), where piperacillin/tazobactam, meropenem and oral ciprofloxacin also showed a lower likelihood for PDD>DDD.

**Conclusions:** Despite the methodology not being dedicated to elderly patients, the study identified elevated use of antimicrobial agents that are associated with serious adverse effects or a narrow therapeutic index as a target for quality of care improvement in elderly patients.

# Introduction

The average life expectancy in developed countries has increased, making geriatric infectious diseases a major health care issue.<sup>[1]</sup> Infections in the elderly are often associated with higher morbidity and mortality compared with those in younger adults.<sup>[2]</sup> Atypical clinical presentation in the elderly exposes them to more antimicrobials and their side effects, increasing the cost of treatment.<sup>[3]</sup> The frequency of infection in elderly patients, especially those aged  $\geq 85$  years, is higher than that in younger adults.<sup>[4]</sup> Surveillance of antimicrobial use may identify areas of practice that might be improved.

Elderly patients often have 'polypharmacy', increasing the likelihood of drug-drug interactions.<sup>[5,6]</sup> Furthermore, dosing should be based on lean bodyweight in view of reduced lean body mass and decline of renal function in this age group.<sup>[7,8]</sup>

This study aimed to assess differences in antimicrobial prescribing in three age groups of elderly patients (group 1: 65–74 years; group 2: 75–84 years; group 3:  $\geq$ 85 years) compared with the younger adult reference group aged between 18 and 64 years. The study also aimed to identify factors that could be used by institutions or health systems to improve quality of care.

# Methodology

#### Hospitals and Countries

The third and final phase of the ESAC (European Surveillance of Antimicrobial Consumption) Hospital Care subproject carried out two hospital point-prevalence surveys (PPS), one in 2008 and another in 2009. ESAC recruited up to two hospitals per country for the 2008 PPS and as many as possible for the 2009 PPS.<sup>[9,10]</sup> Twelve hospitals from ten countries participated only in PPS 2008 and were added to the 2009 database in order to increase the number of countries, hospitals and patients analysed. Thus 31 countries were represented, namely Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, England, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Israel, Italy, Latvia, Lithuania, Luxembourg, Malta, Northern Ireland, Norway, Portugal, Russian Federation, Scotland, Slovenia, Spain, Switzerland, Turkey and Wales. Three hospitals were very late in validating their data and were not included in previous publications that refer to 172 hospitals.<sup>[10,11]</sup>

#### Data Collection

The data fields were based on a simplified version of the protocol of the first ESAC hospital PPS held in 2006 during the second phase of ESAC.<sup>[12]</sup> Data on antimicrobial use were collected for patients admitted in the hospital for at least 24 hours before the survey and still present at 8am on the day of the survey. The number of patients that satisfied these criteria was used as the hospital denominator. If patients were discharged by the time the survey was conducted, their files were still assessed. All occupied beds in each department (e.g. department of surgery) had to be surveyed in a single day. For each patient treated with systemic antimicrobials, the following data were collected: age; sex; antimicrobial agent(s) [dose per administration, number of doses per day and route of administration]; targeted anatomical site; indication for therapy; and whether the reason why the antimicrobial was prescribed was documented. When the reason for treatment was not documented, the information was sought from the doctor in charge of the patient's care or ward nurses. Classification of the patient's treatment as guideline compliant or non-compliant was based on the clinical expertise of the surveyors or their clinical coordinator. The standard unit used for measuring drug consumption data was the WHO Collaborating Centre for Drug Statistics Methodology defined daily dose (DDD) in association with the Anatomical Therapeutic Chemical (ATC) classification system.<sup>[13]</sup> Since the DDD is defined as "the assumed average maintenance dose per day for a drug used for its main indication in adults",<sup>[13]</sup> often the average prescribed daily dose (PDD) in a particular institution, or across all participating institutions for particular drugs, can deviate from the DDD. The PDD could also possibly vary for different age groups, especially when comparing doses administered in extreme age groups, such as neonates, with those for other age groups.<sup>[9]</sup> It would therefore be reasonable to hypothesize that at least for some antimicrobials this trend would also be observed in older patients.

#### Statistical Analysis

Data were analysed using SAS version 9.2 (SAS Institute, Cary, NC, USA). Variation of antimicrobial prescribing in elderly patients was assessed using multivariate logistic regression analyses by calculating odds ratios (ORs) with 95% confidence intervals. Each arbitrarily assigned elderly age group (group 1: 65–74 years; group 2: 75–84 years; group 3: ≥85 years) was compared with the reference group of younger adults (reference group: 18–64 years). Sex, anatomical site, indication for therapy and specialty were considered as adjustment criteria. Additionally, four European regions (Northern, Southern, Eastern and Western), as defined by the United Nations, [<sup>14]</sup> were used in the statistical analysis.

#### Types of Logistic Regression

Two types of logistic regression were constructed.

In the first regression, variation of antimicrobial prescribing in elderly patients was assessed for each antimicrobial group at ATC level 3 (e.g. penicillins, quinolones, etc.). Separate logistic regressions were built for each ATC group. For each regression, the dependent variable was coded as '1' when the patient received the antimicrobial class in question and '0' when the patient received other antimicrobial agents.

In the second regression, patients receiving PDD > DDD were compared with those receiving PDD  $\leq$  DDD for each elderly age group. Separate logistic regressions were built for each of the ten most utilized antimicrobial agents. For each regression, the dependent variable was coded as '1' when the PDD of the antimicrobial agent was greater than the DDD and '0' when the PDD was less than or equal to the DDD.

# Results

#### Demographics and Overview

A total of 30 836 adult patients were categorized into four age groups (table I). The proportion of females was >60% in the  $\geq$ 85 years age group. Within the subdivision by European region, the Northern Europe region included the majority of patients (19 549 [64%]). A similar skew was observed for the reference age group, which also had the widest age range (18-64 years), and included 13 830 patients (48%). However, no significant difference in proportions by age group for the different regions was observed. The Northern European region also had the highest intra-region proportion of patients aged  $\geq 85$  years (13.9%) and the lowest proportion of younger adults (43.3%). Eastern European hospitals had the highest proportion of reference group patients (49.7%) and the lowest proportion of patients in the  $\geq$ 85 years age group (7.2%).

At the specialty level, the highest proportions of patients were admitted through the hospitals' medical specialty (55%), with the proportion increasing from 49% in the reference group to 72% in the  $\geq$ 85 years age group. The relative proportions admitted through intensive care and the surgical specialty decreased with age group,

Characteristics	Age group [n (%)]						
	18–64 y	65–74 y	75–84 y	≥85 y			
Total no. of patients	13830 (44)	6524 (21)	6778 (22)	3704 (12)			
Sex							
Female	6226 (45)	2752 (42)	3313 (49)	2219 (60)			
Region							
Northern Europe	8470 (61)	3979 (61)	4382 (65)	2718 (73)			
Western Europe	2 455 (18)	1131 (17)	1188 (18)	548 (15)			
Southern Europe	1 620 (12)	797 (12)	711 (10)	251 (7)			
Eastern Europe	1 285 (9)	617 (9)	497 (7)	187 (5)			
Specialty							
Medical	6741 (49)	3443 (53)	4382 (65)	2652 (72)			
Surgery	5288 (38)	2246 (34)	1188 (18)	882 (24)			
Intensive care	1 554 (11)	773 (12)	497 (7)	135 (4)			
Other	247 (2)	62 (1)	711 (10)	35 (1)			
Indication							
Community acquired infection	6324 (46)	3046 (47)	3539 (52)	2051 (55)			
Hospital acquired infection	3884 (28)	2180 (32)	2318 (35)	1318 (36)			
Surgical prophylaxis	2212 (16)	877 (13)	651 (9)	211 (6)			
Medical prophylaxis <sup>a</sup>	1 290 (9)	365 (6)	215 (3)	103 (3)			
Undefined	120 (1)	56 (1)	55 (1)	21 (1)			
Diagnosis site							
Respiratory	3 0 6 3 (22)	1841 (28)	2107 (31)	1295 (35)			
Skin, soft tissue, bone and joint	2886 (21)	1290 (20)	1295 (19)	588 (16)			
Gastrointestinal	2633 (19)	1170 (18)	1076 (16)	515 (14)			
Undefined <sup>b</sup>	1 880 (14)	815 (12)	694 (10)	295 (8)			
Urology	1 215 (9)	812 (12)	1126 (17)	869 (23)			
Obstetrics and gynaecology	806 (6)	69 (1)	58 (1)	20 (1)			
Ear, nose and throat	556 (4)	138 (2)	129 (2)	61 (2)			
Central vascular system <sup>c</sup>	391 (3)	306 (5)	239 (4)	44 (1)			
Central nervous system	373 (3)	75 (1)	46 (1)	12 (0)			
Eye	27 (0)	8 (0)	8 (0)	5 (0)			

Table I. Characteristics of patients receiving antimicrobials in four adult age groups in two ESAC (European Surveillance of Antimicrobial Consumption) hospital point-prevalence surveys conducted in 2008 and 2009

a Includes any long-term use of antimicrobial agents for the prevention of infection.

b Completely undefined site with no systemic inflammation.

c Includes treatment and prophylaxis of infectious endocarditis or vascular graft.

especially in the older two groups, as opposed to the younger two groups. The proportions treated for infections (both of community and hospital origin) increased with increasing age group, while they decreased for prophylaxis (both surgical and medical).

The proportions treated for respiratory infections and urinary tract infections (UTIs) increased with increasing age, while skin, soft tissue, bone and joint and gastrointestinal infections decreased in frequency, as did the proportion of infections of non-defined aetiology.

# Antimicrobial Overview

Penicillins (J01C) and other beta-lactams (J01D) were the most used antimicrobials in all age groups (figure 1), but wide variations in antimicrobial use

were observed. Cephalosporins were the major component of the other beta-lactams (J01D) category. Regarding the penicillin class, the proportion ranged from 32% in the younger adults to 41% in the  $\geq$ 85 years age group. Conversely for cephalosporins and other beta-lactams, the proportion ranged from 11% in the  $\geq$ 85 years age group to 20% in the younger adults.

The multivariate analyses taking into account adjustment criteria identified significant variations in antimicrobial use between the three age groups of elderly patients and the reference group. Table II shows three significant variations in antimicrobial use between the 65–74 years age group and the reference group, whereas there were seven and eight significant variations in the 75–84 and ≥85 years age groups, respectively. For example, there was a significant higher likelihood of quinolone (J01M) and tetracycline (J01A) use when the 65–74 years age group was compared with the reference group (quinolones: OR 1.17 [95% CI 1.05, 1.29]; tetracyclines: OR 1.58 [95% CI 1.26, 1.98]). Conversely, there was a significantly lower likelihood of aminoglycoside (J01G) use (OR 0.81 [95% CI 0.70, 0.93]).

### Prescribed Daily Dose Overview for the Top 10 Antimicrobials

Figure 2 shows the PDD: DDD ratio for the ten most utilized drugs, taking into account the route of administration. It shows a wide range of PDD: DDD ratios for all drugs, especially oral amoxicillin/clavulanic acid. From this graph, a trend in dose reduction with each increasing age group is observed only for gentamicin. Piperacillin/ tazobactam and oral metronidazole have a median PDD: DDD ratio of <1 across all age groups. These PDD: DDD data were further analysed by multivariate analysis models.

Only nine models were performed, because there were no instances of PDD > DDD for oral metronidazole (table III). For six of the remaining nine most commonly used antimicrobials, the



Fig. 1. Proportions of antimicrobials prescribed in four adult age groups based on data from two ESAC (European Surveillance of Antimicrobial Consumption) hospital point-prevalence surveys conducted in 2008 and 2009. The antibacterial codes used are those of the Anatomical Therapeutic Chemical (ATC) classification system.<sup>[13]</sup>

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Models <sup>b</sup>	PENs (J01C)	CEPHs & other B-Ls (J01D)	Other AntiBs (J01X)	QUINs (J01M)	MLs (J01F)	AntiMs for SU (J02A)	AMINs (J01G)	SMs & TM (J01E)	NM deriv. (P01AB)	TCs (J01A)
18–64 y	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
65–74 y	0.99 (0.93, 1.06)	0.94 (0.87, 1.02)	1.02 (0.93, 1.11)	1.17 (1.05, 1.29)	0.90 (0.78, 1.02)	0.89 (0.77, 1.03)	0.81 (0.70, 0.93)	0.88 (0.75, 1.04)	1.13 (1.05, 1.29)	1.58 (1.26, 1.98)
75–84 y	1.18 (1.11, 1.26)	0.90 (0.83, 0.98)	0.93 (0.85, 1.03)	1.13 (1.02, 1.25)	0.80 (0.71, 0.91)	0.57 (0.48, 0.68)	0.64 (0.55, 0.76)	0.94 (0.81, 1.10)	1.42 (1.18, 1.71)	1.18 (0.93, 1.50)
≥85 y	1.31 (1.21, 1.41)	0.75 (0.67, 0.85)	0.82 (0.73, 0.93)	0.97 (0.85, 1.10)	0.81 (0.70, 0.95)	0.39 (0.30, 0.51)	0.48 (0.38, 0.61)	1.23 (1.04, 1.45)	2.02 (1.64, 2.49)	1.20 (0.91, 1.58)
Variation	l <sub>c</sub>									
18–64 y	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
65–74 y	=	=	=	+	=	=	-	=	=	+
75–84 y	+	-	=	+	-	-	-	=	+	=
≥85 y	+	-	-	=	-	-	-	+	+	=

**Table II.** The odds ratio (95% CI) of receiving one antimicrobial at the third level<sup>a</sup> of the Anatomical Therapeutic Chemical (ATC) classification system among the three elderly age groups compared with younger adults (reference [ref.] age group 18–64 y)

a The third level of the ATC code indicates the therapeutic/pharmacological subgroup and consists of one letter (e.g. J01C).

b Separate logistic regressions were constructed for each ATC group. For each regression, a dependent variable was coded as '1' when the patient received the antimicrobial in question and '0' when the patient received the other antimicrobial agents. All models were adjusted for sex, anatomical site, indication for therapy, specialty and European region.

c The direction of the variation is given for each elderly age group compared with ref.

 $\begin{array}{l} \textbf{AMINs} = aminoglycosides; \ \textbf{AntiMs for SU} = antimycotics \ for \ systemic \ use; \ \textbf{CEPHs} \ \& \ \textbf{other B-Ls} = cephalosporins \ and \ other \ beta-lactams; \\ \textbf{MLs} = macrolides; \ \textbf{NM \ deriv.} = nitroimidazole \ derivatives; \ \textbf{Other AntiBs} = other \ antibacterials; \ \textbf{PENs} = penicillins; \ \textbf{QUINs} = quinolones; \\ \textbf{SMs} \ \& \ \textbf{TM} = sulfonamides \ and \ trimethoprim; \ \textbf{TCs} = tetracyclines; \ + \ indicates \ a \ positive \ difference \ (increased \ likelihood \ that \ the \ drug \ class \ is \ prescribed \ in \ the \ age \ group); \ - \ indicates \ a \ negative \ difference \ (increased \ likelihood \ that \ the \ drug \ class \ is \ prescribed \ in \ the \ age \ group); \ = \ indicates \ no \ difference. \end{array}$ 

two older age groups (75–84 years and  $\geq$ 85 years) were associated with a lower likelihood of receiving a PDD > DDD compared with the reference group after adjustment for patient characteristics. With respect to the 65–74 years age group, a lower likelihood of receiving a PDD > DDD compared with the reference group was observed for three parenteral antimicrobials (amoxicillin/clavulanic acid, gentamicin and vancomycin). No significant difference was identified for oral amoxicillin/clavulanic clavulanic acid, parenteral cefuroxime and parenteral metronidazole.

# Discussion

This study evaluated the use of antimicrobials in three different elderly age groups compared with younger adults. The main findings of our study were that respiratory tract infections and UTIs were more prevalent with increasing age group. In addition the beta-lactam antibacterials (penicillins and cephalosporins) were the most commonly prescribed antimicrobial agents across the board. However, the proportion of penicillins increased whereas that of cephalosporins decreased with age. The penicillins, despite being the most used in all categories, represented 32% of prescriptions in the two younger age groups (18-64 and 65-74 years), increasing to around 40% in the older groups (75–84 and  $\geq$ 85 years). An opposing trend was observed for the cephalosporins, for which use was the lowest (11%) in the  $\geq$ 85 years age group. This latter finding could be deemed as surprising given the excellent safety profile of cephalosporins.<sup>[15]</sup> On the other hand, it has been reported that hospitals that had problems with Clostridium difficile-associated diarrhoea and reduced the use of cephalosporins managed to reduce the prevalence of C. difficile-associated diarrhoea.<sup>[16,17]</sup> Therefore, this could mean that clinicians are more wary of C. difficile-associated diarrhoea in older patients.

Antibacterial use in the younger 'elderly' age group (65–74 years) was not significantly different from that in the reference group (18–64 years), with some exceptions (e.g. aminoglycosides). This finding indicates that the younger 'elderly' age group (65–74 years) is more comparable with 'younger adults' than 'elderly' as exemplified by the proportion of patients admitted to surgery and intensive care.

The major differences in antimicrobial use were identified between the two older 'elderly' groups (75–84 and  $\geq$ 85 years) and the reference group (18–64 years). Regarding the younger 'elderly' group (65–74 years), antimicrobial use was very similar to the reference group except with respect to a few antimicrobials. For instance, the significantly lower use of aminoglycosides amongst all the elderly groups is reassuring, as their use in the elderly should be reserved for limited indications where no safer alternatives are available.<sup>[15]</sup>

Although this study provides additional information about prescribing in the elderly, it has a number of limitations. The ESAC hospital PPS methodology was intended for whole hospital data collection, and this was a *post hoc* analysis. Therefore, specific factors related to age might have not been included in the data collection. Furthermore, European hospitals participated exclusively on a voluntary basis, with the consequence of overrepresentation of the Northern European region. However, in the multivariate models, hospitals were adjusted for European region, minimizing the potential bias of the geographic effect on the analysis. A limitation of any PPS is that these studies take a 'snapshot' of the data and therefore contain no information about duration of therapy and whether duration is appropriate or not. Excessively prolonged duration of treatment increases the likelihood of complications and/or adverse reactions. However, the ESAC hospital PPS collected data on duration of surgical prophylaxis, which could be classified as appropriate (from 1 dose up to 1 day of cover) or prolonged (>1 day).<sup>[10,11]</sup> Similarly to duration of treatment, no information on outcome of treatment is collected in PPS. Data on the use of invasive devices could be collected and this was a limitation of our methodology. This is especially relevant in view



Fig. 2. Distribution of prescribed daily dose/defined daily dose ratio (PDD : DDD) for the ten most frequently prescribed antimicrobials in the four adult age groups. For some antimicrobials the range of PDD : DDD was too wide for the interquartile ranges to be displayed in the respective plot. Error bars represent standard deviations; horizontal lines are median values. O = oral; P = parenteral.

Models <sup>a</sup>	AMOX & EI (O)	AMOX & EI (P)	PIP & EI (O)	CEF (P)	MERO (P)	GENT (P)	CIP (O)	VAN (P)	MET (P)
18–64 y	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
65–74 у	NS	0.45 (0.28, 0.72)	0.81 (0.55, 1.19)	NS	0.97 (0.66, 1.41)	0.51 (0.33, 0.81)	0.81 (0.50, 1.30)	0.45 (0.27, 0.78)	NS
75–84 у	NS	0.59 (0.38, 0.91)	0.37 (0.25, 0.61)	NS	0.59 (0.40, 0.87)	0.55 (0.34, 0.88)	0.55 (0.33, 0.92)	0.12 (0.04, 0.32)	NS
≥85 y	NS	0.51 (0.30, 0.88)	0.29 (0.15, 0.54)	NS	0.51 (0.29, 0.92)	0.44 (0.22, 0.79)	0.32 (0.13, 0.78)	0.14 (0.03, 0.58)	NS
Variation <sup>i</sup>	D,C								
18–64 y	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
65–74 y	=	-	=	=	=	-	=	-	=
75–84 y	=	-	-	=	-	-	-	-	=
≥85 y	=	_	_	=	_	_	_	_	=

Table III. The odds ratio (95% CI) of receiving a prescribed daily dose (PDD) > the defined daily dose (DDD) for the nine most frequently used agents among the three elderly age groups compared with younger adults (reference [ref.] age group 18–64 y)

a Separate logistic regressions were constructed for the nine most frequently used agents. For each regression, a dependent variable was coded as '1' when the PDD of the antimicrobial agent was > the DDD and '0' when the PDD was ≤ the DDD. All models were adjusted for sex, anatomical site, indication for therapy, specialty and European region.

b The direction of the variation is given for each elderly age group compared with ref.

c No '+' symbol was recorded as there was no drug with a positive difference, i.e. increased likelihood that PDD > DDD in any of the test age groups compared with ref.

$$\label{eq:MOX} \begin{split} & \text{AMOX} = \text{amoxicillin; } \textbf{CEF} = \text{cefuroxime; } \textbf{CIP} = \text{ciprofloxacin; } \textbf{EI} = \text{enzyme inhibitor; } \textbf{GENT} = \text{gentamicin; } \textbf{MERO} = \text{meropenem; } \textbf{MET} = \text{metronidazole; } \textbf{NS} = \text{not statistically significant; } \textbf{O} = \text{oral; } \textbf{P} = \text{parenteral; } \textbf{PIP} = \text{piperacillin; } \textbf{VAN} = \text{vancomycin; } - \text{indicates a negative difference} \\ (\text{decreased likelihood that PDD} > \text{DDD in the age group); = indicates no difference.} \end{split}$$

of the fact that such devices put the patient at greater risk of infections and consequently treatment with antimicrobials.

Our data have shown that with increasing age group the proportion of community and hospital infections increases. This corroborates with a decrease in medical and surgical prophylaxis, possibly due to the fact that conservative treatment might be preferred in older and frailer patients. This finding is similar to that reported in an observational study of early-stage prostate cancer patients.<sup>[18]</sup> Medical prophylaxis was another indication more common in the reference group. This category includes immunocompromised patients who are on long-term antimicrobial prophylaxis.

UTIs were more common in the older age groups, who are more likely to have indwelling urinary catheters.<sup>[19]</sup> Furthermore, in persons aged  $\geq$ 85 years, a history of UTI is associated with both recurrence and incontinence.<sup>[20]</sup> Our data showed a higher proportion of women in the  $\geq$ 85 years age group, in whom UTI is considered

a major public health problem.<sup>[21]</sup> The higher proportion of females in the  $\ge 85$  years age group (table I) can be partially explained by a higher mean life expectancy of about 4 years in females compared with males.<sup>[22,23]</sup>

The proportion of aminoglycosides used decreased with increasing age. Aminoglycosides were the only drug class that showed a consistent decrease in likelihood to be prescribed across all three age groups tested versus the reference age group. This was to be expected since the most important side effects of aminoglycosides are ototoxicity and nephrotoxicity and these occur more commonly in the elderly. All hospitals should aim to minimize aminoglycoside use in patients aged >75 years, restricting their use to patients in whom no valid alternative is available.

Despite the fact that fluoroquinolones have favourable characteristics and are relatively safe for use in the elderly, this class of drugs was used less frequently in the  $\geq 85$  years age group. This decrease in use could be partially attributed to warnings similar to that of the Committee on

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Safety of Medicines (CSM) advice in the *British National Formulary* about tendinitis, especially in the elderly.<sup>[24]</sup>

Interestingly, multivariate analysis of the PDD: DDD ratios for the different age groups highlighted the fact that different drugs were used with different degrees of caution in elderly patients. In the 65-74 years age group, two of the three antimicrobials that showed a significantly lower likelihood of PDD > DDD were drugs with a narrow therapeutic index and were associated with toxicity, namely, gentamicin and vancomycin. These drugs were also less likely to have a PDD>DDD in the two older age groups, and their use, especially at higher doses, should also be targeted by hospital administrations, as these drugs can be a source of iatrogenesis, possibly increasing length of stay, cost, morbidity and even mortality.

An elevated use of antimicrobial agents with a narrow therapeutic index has been identified in this study as a target for quality of care improvement. Future research specifically targeting elderly hospitalized patients should gather data about whether therapeutic drug monitoring is implemented. In addition, monitoring of whether interventions to correct suboptimal or toxic doses are used would also be relevant as a quality indicator. Other factors that are more 'elderly specific,' such as appropriateness of dosing based on the patient's renal function, would also be indicated. The use of urinary catheterization could also help in categorizing by case mix. Furthermore, the need for such catheters should be evaluated and monitored. Hospitals where patients might be catheterized just for convenience should then aim at ensuring that patients are catheterized only if they really need to be, as invasive devices increase the risk of infections. Another important quality indicator applicable to all age groups is that of documentation of indication and expected duration of therapy in patients' medical notes. The fact that a considerable proportion of patients were receiving antimicrobials with an 'undefined' diagnosis (i.e. a completely undefined site with no systemic inflammation [table I]) is a sign of antimicrobial prescribing without an obvious reason.

#### Conclusions

The ESAC hospital PPS methodology, despite not being developed specifically for elderly patients, allowed for the analysis of antimicrobial use by age group and the identification of targets for quality improvement in geriatric patients. It is possible that surveys dedicated exclusively to hospitalized elderly patients might be able to identify more specific indicators but these would not allow comparisons with younger patients. The current study enabled the identification of the use of antibacterials associated with serious adverse drug reactions (e.g. vancomycin and aminoglycosides) as a target for improvement of quality of care in elderly hospitalized patients with infectious diseases.

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The ESAC-3 Hospital Care Subproject Group: Sigrid Metz-Gercek (Austria), Hilde Jansens (Belgium), Boyka Markova (Bulgaria), Christiana Kontemeniotou (Cyprus), Arjana Andrasevic (Croatia), Jiri Vlcek (Czech Republic), Niels Frimodt-Møller (Denmark), Piret Mitt (Estonia), Outi Lyytikainen (Finland), Xavier Bertrand (France), Katja de With (Germany), Anastasia Antoniadou (Greece), Gabor Ternak (Hungary), Robert Cunney (Ireland), Raul Raz (Israel), Silvio Brusaferro (Italy), Elina Dimina (Latvia), Vitalija Butkyte (Lithuania), Bruch Marcel (Luxembourg), Peter Zarb (Malta), Jon Birger Haug (Norway), Janina Pawlowksa (Poland), Ines Teixeira (Portugal), Svetlana Ratchina (Russian Federation), Milan Cižman (Slovenia), Mercedes Sora (Spain), Gunilla Skoog (Sweden), Giorgio Zanetti (Switzerland), Margreet Filius (the Netherlands), Yesim Cetinkaya Sardan (Turkey), Jonathan Cooke (UK - England), Hugh Webb (UK - Northern Ireland), Peter Davey (UK – Scotland), Margaret Heginbothom (UK – Wales).

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Correspondence: Mr *Peter Zarb*, Infection Control Unit, Mater Dei Hospital, Tal-Qroqq, Msida, MSD 2090, Malta. E-mail: peter.zarb@gov.mt Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.