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► **To cite this version:**

Caroline Emilie, Phebe de Nocker, Nadia Saïdani, Mark Gilchrist, R. Andrew Seaton, et al.. Survey of delivery of parenteral antimicrobials in non-inpatient settings across Europe. *International Journal of Antimicrobial Agents*, 2022, pp.106559. 10.1016/j.ijantimicag.2022.106559 . hal-03622451

**HAL Id: hal-03622451**

**<https://hal.univ-lorraine.fr/hal-03622451>**

Submitted on 22 Jul 2024

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1 **Survey of delivery of parenteral antimicrobials in non-inpatient settings across Europe**

2

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41

42 **Abstract**

43 **Background:** Delivery of parenteral antimicrobials in non-inpatient settings (DPANS) may be  
44 through a dedicated outpatient parenteral antimicrobial therapy (OPAT) service, coordinated  
45 by hospital- or community-based specialized teams, or *via* an infusion service involving  
46 community-based health professionals (nurses, general practitioners) without centralized  
47 hospital oversight, or through *ad hoc* arrangements. DPANS varies among countries.

48 **Objectives:** To describe how DPANS is organized at a national level in European countries.

49 **Methods:** A survey (65-item self-administered questionnaire) was conducted from February  
50 to June 2019 among infection specialists in 34 European countries on behalf of the ESCMID  
51 (European Society of Clinical Microbiology and Infectious Diseases) Study Group for  
52 Antimicrobial Stewardship (ESGAP) and the British Society for Antimicrobial Chemotherapy  
53 (BSAC).

54 **Results:** Most countries (28/34, 82.4%) participated in the survey. DPANS was available in  
55 almost all (n=27/28, 96.4%) responding countries. DPANS was predominantly either  
56 provided *via* specialized OPAT services (n=17/28, 60.7%) or *via* infusion services (n=16/28,  
57 57.1%), with 11 countries providing both services (39.3%). Formal OPAT team structure with  
58 specifically trained staff was reported in only 6 countries (6/17, 35.3%). Some countries (n=4,  
59 14.3%) had no structured services but practiced DPANS *via ad hoc* arrangements. Costs of  
60 all stages of the process were covered for patients managed by specialized OPAT/infusion  
61 services, either completely, partially, or for specific patient groups in the majority (20/28,  
62 71.4%) of countries. The main barriers to implement OPAT/infusion services were lack of  
63 organizational structure or guidelines.

64 **Conclusions:** DPANS with respect to availability and organisation is highly heterogeneous  
65 in Europe. National/European guidelines may help improve and standardize DPANS.

66

67 **Keywords:** OPAT, antimicrobial, antibiotic stewardship, questionnaire, antimicrobial  
68 stewardship, adult and paediatrics

## 69 1. Introduction

70 First developed in the US for paediatric treatment of cystic fibrosis,[1,2] delivery of  
71 parenteral antimicrobials in non-inpatient settings (DPANS)<sup>1</sup> has been practiced for over 40  
72 years. DPANS can be *via* dedicated services, like *via* an “outpatient parenteral antimicrobial  
73 therapy (OPAT)<sup>2</sup> service” or *via* an “infusion service”, or *via ad hoc* arrangements. OPAT  
74 services rely on a structured, multidisciplinary and specialized team (hospital-based or  
75 community-based), that provides input to the choice, dose and duration of therapy, and  
76 usually monitors patient progress and outcomes.[3] An infusion service is a pre-existing  
77 system where all steps to provide DPANS are coordinated by various healthcare agents, but  
78 it does not have such centralized oversight or specialized team. In parallel with these two  
79 structured systems, DPANS is sometimes arranged on an *ad hoc* basis by the general  
80 practitioner (GP)<sup>3</sup>, *via* hospital services outside of OPAT for specific specialist patient groups,  
81 *via* hospital-based ambulatory care (e.g. Acute medical or Emergency department  
82 physicians) or *via* hospital-in-the-home settings outside of an OPAT team, without any  
83 oversight from an infectious diseases (ID)<sup>4</sup> specialist.

84 DPANS *via* an OPAT service is now standard therapy for a large variety of  
85 infections.[3,4] OPAT services are recognised to be cost-effective,[5,6] with associated high  
86 patient satisfaction and improved quality of life.[7,8] Despite these advantages a survey in  
87 2000 suggested OPAT programme’s implementation across Europe has been relatively  
88 slow.[9] Recent publications from European centres can suggest that OPAT implementation  
89 has been increasing but to date this has not been quantified.[10–12] We have not found a  
90 similar body of literature for infusions services' and other *ad hoc* arrangements.

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<sup>1</sup> DPANS: delivery of parenteral antimicrobials in non-inpatient settings

<sup>2</sup> OPAT : outpatient parenteral antimicrobial therapy

<sup>3</sup> GP : general practitioner

<sup>4</sup> ID : infectious diseases

<sup>5</sup> ESCMID : European Society of Clinical Microbiology and Infectious Diseases

<sup>6</sup> ESGAP : ESCMID Study Group for Antimicrobial Stewardship

<sup>7</sup> BSAC : British Society for Antimicrobial Chemotherapy

<sup>8</sup> AMS : antimicrobial stewardship

91 DPANS may vary between countries due to differences in infection management,  
92 health care provision and reimbursement systems, but few published studies have described  
93 how DPANS is organised in different countries. To the best of our knowledge, publications  
94 about DPANS in Europe mostly focused on a single country (in particular the UK,[4][13] Italy  
95 [14] or Spain [11][15]) and rarely include inter-country comparisons. An international  
96 comparison of OPAT services including two European countries (Italy and the UK) was  
97 performed in 2004, but only differences between types of infections treated, antimicrobials  
98 used, patients' characteristics, delivery modalities and clinical outcomes were studied.[16] A  
99 survey in 2017 showed wide discrepancies in DPANS and its organization across 17 Asian  
100 countries.[17] Such inter-country comparisons may however be useful in suggesting areas  
101 for improvement and unmet needs, as well as sharing best practices.

102 We present the results of a large survey, aiming to describe the national organization  
103 of systems available to deliver parenteral antimicrobials in non-inpatient settings in various  
104 European countries.

## 105 **2. Methods**

### 106 *2.1. Study design*

107 Members of the European Society of Clinical Microbiology and Infectious Diseases  
108 (ESCMID)<sup>5</sup> Study Group for Antimicrobial Stewardship (ESGAP)<sup>6</sup> and the British Society for  
109 Antimicrobial Chemotherapy (BSAC)<sup>7</sup>, OPAT initiative, conducted a survey using an Internet-  
110 based, self-administered, questionnaire on DPANS in European countries.

111

### 112 *2.2. Questionnaire*

113 The 65-item questionnaire (Table 1 and Supplementary material) was developed by  
114 the multidisciplinary (infectious diseases specialists, microbiologists, public health specialists,  
115 hospital pharmacists) scientific committee. It was based on the literature and expert  
116 opinion.[3,17]

117 The definitions of « OPAT », « Infusion service », « Prescription », « Dispensing », «  
118 Administration », « Parenteral », « Outpatients » were specified at the beginning of the  
119 questionnaire and at the beginning of each section.

120

### 121 *2.3. Survey*

122 The questionnaire was formatted using SurveyMonkey® online survey software. It  
123 was pilot tested among 15 practitioners (scientific committee members and close  
124 collaborators) for feasibility and clarity.

125 The questionnaire was distributed to 34 contacts from different European countries,  
126 from the professional network of the authors. They were selected because of their  
127 participation to national and/or European scientific societies and were particularly involved in  
128 antimicrobial management in their respective countries. Contacts were asked to recruit  
129 another expert on the topic from the same country, to fill in the questionnaire together and  
130 provide a single concerted common reply. Contacts were also encouraged to consult other  
131 national colleagues in case of doubt, to ensure that their responses would be representative  
132 of the national picture.

133 National contacts were recruited from February 2019 to June 2019 by the scientific  
134 committee through a personalised invitation mail containing a PDF version of the  
135 questionnaire (to help them prepare their answers) and a hyperlink to the electronic  
136 questionnaire.

137 Reminder emails were sent to non-responders at least once. If no response was  
138 received, alternative participants from the same country were contacted. Participation was  
139 not anonymous, not remunerated nor compensated.

140 A list of 15 specified parenteral antimicrobials (all antibiotics) was drawn, based on a  
141 voting consensus procedure among the scientific committee, to explore availability and  
142 organization of DPANS for specific molecules at a national level.

143

#### 144 *2.4. Analysis*

145 The data were extracted from SurveyMonkey® and analysed using Microsoft Excel®.  
146 Questionnaires were included in the analysis when the following criteria were met: first  
147 section of the questionnaire fully completed and at least one question from sections 2 or 3  
148 answered. Results are presented as numbers and percentages.

149

#### 150 *2.5. Ethical statement*

151 According to French legislation (the country where the study was coordinated), as no  
152 intervention was conducted and no information on health of participants was collected,  
153 ethical approval was not required.



154 **3. Results**

155 Responses were received from 28/34 (82.4%) countries (Figure 1), and two  
156 participants completed the questionnaire in a joint national reply in 26 countries (26/28,  
157 92.9%). Participants were predominantly ID physicians (n=29) and pharmacists (n=15), along  
158 with three specialized ID nurses, two microbiologists, two general practitioners, one  
159 emergency physician, one palliative care physician and one internal medicine physician.

160

161 3.1. National organization of DPANS in Europe (n=28 countries)

162 Parenteral antibiotics, antifungals and antivirals were available in the outpatient  
163 setting in respectively 27 (96.4%), 18 (64.3%) and 12 (42.9%) of the 28 participating  
164 European countries (Table S1, available as Supplementary material). From a list of 15  
165 specified parenteral antimicrobials, ceftriaxone was the drug most widely available (Table 2).

166 Most European countries organized the DPANS either through OPAT services  
167 (17/28, 60.7%), or infusion services (16/28, 57.1%). Both services were available in 11  
168 countries (11/28, 39.3%). Four countries (14.3%) had no structured OPAT team or infusion  
169 services, but DPANS was available through *ad hoc* arrangements. These *ad hoc*  
170 arrangements were also available in many countries, in addition to OPAT/infusion services  
171 (n=22, 78.6%) (Figure 1, Table 3).

172 Reimbursement was available in most countries for DPANS through OPAT or infusion  
173 services (n=20/28, 71.4%), either partially or completely (Table 3). As a comparison, oral  
174 antibiotics were refunded by national health insurance or a similar system and did not need  
175 funding from a complementary insurance or from the patient him/herself for hospitalized  
176 patients in 23 countries (82.1%) and for outpatients in eight countries (28.6%).

177 Elastomeric pumps were used for continuous infusions of certain parenteral  
178 antimicrobials in 16 countries (57.1%). Subcutaneous administration of ceftriaxone and  
179 ertapenem occurred respectively in nine (32.1%) and three (10.7%) countries.

180

181 3.2. Evaluation of the structure of parenteral antimicrobial therapy for outpatients (Table 4)

182 3.2.1 *OPAT services (n=17 countries)*

183 3.2.1.1 *Framework*

184 No country had a specific legal framework to organize an OPAT service. Five  
185 countries (Denmark, Ireland, the Netherlands, Spain and the UK; 29.4%) had national  
186 guidelines or good practices recommendations for OPAT services.

187 OPAT services provided care to both adults and children in 12 countries (70.6%), and  
188 only to adults in three countries (17.6%).

189 3.2.1.2 *Composition of the team, staffing costs and antimicrobial stewardship*

190 OPAT services were coordinated by specialized clinical teams, which were all  
191 hospital-based in the responding countries. Only six countries (Iceland, Ireland, Malta, Spain,  
192 Sweden and the UK; 35.3%) had a formal OPAT team structure with dedicated, specifically  
193 trained staff. In all cases, these OPAT teams included ID physicians, hospital pharmacists  
194 and specialized OPAT nurses. OPAT teams staffing costs were fully funded in Sweden, the  
195 UK and Malta to compensate time spent on OPAT activities.

196 In nine countries (52.9%), OPAT teams' members were part of antimicrobial  
197 stewardship (AMS)<sup>8</sup> teams. OPAT services were part of the AMS programme in four  
198 countries (23.5%). In three countries (17.6%), OPAT services were not a formal part of the  
199 AMS programme but could be responsible to the AMS programme. There was no link  
200 between OPAT teams and AMS activities in five countries (29.4%).

201 3.2.1.3 *Referring practitioners and prescription*

202 In all countries offering OPAT services, outpatient therapy could be a continuation of  
203 a previous antimicrobial treatment initiated as an inpatient (Table S2). It could also be  
204 planned as a newly initiated treatment for outpatients taken care of in the hospital (clinics or  
205 emergency department) who are discharged (n=13, 76.5%) or for outpatients in the  
206 ambulatory setting (e.g. by the GP) (n=10, 58.8%).

207 ID specialists (n=16, 94.1%) and treating physicians in the hospital (other than  
208 infection specialists) (n=15, 88.2%) were the main clinicians to refer patients for an OPAT  
209 service (Table S3).

210 Several healthcare professionals prescribed (initiated) the parenteral antimicrobials  
211 used for OPAT services, in particular ID specialists (n=16, 94.1%), treating physicians in the  
212 hospital (n=13, 76.5%) or GPs (n=6, 35.3%). Non-medical professionals such as nurses and  
213 pharmacists who belong to the OPAT team could also prescribe in the UK (Table S4).

#### 214 3.2.1.4 *Preparation*

215 The preparation of the parenteral antimicrobials (e.g. infusion solution, filling of  
216 elastomeric pump) was mainly performed by hospital pharmacists (n=10, 58.8%) or by  
217 nurses (n=14, 82.4%). Nurses could either be community nurses (n=11, 64.7%), nurses  
218 belonging to the OPAT team (n=10, 58.8%) or hospital nurses (n=9, 52.9%).  
219 Caregivers/relatives or patients themselves were allowed to prepare the treatment  
220 respectively in six (35.3%) and five (29.4%) countries (Table S5).

#### 221 3.2.1.5 *Medical devices delivery*

222 Delivery of the associated medical devices (e.g. needles, syringes) was mainly  
223 performed by hospital pharmacists (n=14, 82.4%) (Table S6).

#### 224 3.2.1.6 *Administration*

225 Administration of the parental antimicrobial treatment mainly took place at home (15  
226 countries, 88.2%), except in Greece and Slovenia, where it took place only in hospital day  
227 clinics or at medical doctor primary care practices. Administration of antimicrobials was  
228 mainly performed by community (n=13, 76.5%) or hospital nurses (n=11, 64.7%) (Table S7).  
229 In six countries (35.3%), these were specialized nurses with a specific training. Self-  
230 administration by patients or caregivers (n=10, 58.8%) was frequent and could even be the  
231 standard practice, like in Switzerland and in the UK.

#### 232 3.2.1.7 *Monitoring*

233 Professionals responsible for the monitoring of a patient receiving parenteral  
234 antimicrobials in an OPAT service (e.g. clinical monitoring, laboratory tests) were usually ID

235 specialists (n=15, 88.2%), treating physicians in the hospital (n=15, 88.2%) or members of  
236 the specialized OPAT team (n=11, 64.7%) (Table S8).

#### 237 3.2.1.8 *Reimbursement*

238 A financial system covered the costs of the whole process for the benefiting patients  
239 (costs of antimicrobials, infusion fluids, medical devices, laboratory tests and remuneration of  
240 the professionals involved in the follow-up, the preparation and the administration of  
241 treatments) in almost all countries, either completely (n=10, 58.8%), or partially or free only  
242 for some patients (n=6, 35.3%) (Figure S1).

#### 243 3.2.1.9 *Barriers and perspective*

244 Availability of OPAT services on the whole national territory varied between countries;  
245 9 (52.9%) had OPAT services implemented in a limited number of hospitals. The main  
246 barriers preventing access to an OPAT service for all eligible patients were a lack of an  
247 organizational infrastructure (n=9, 52.9%), a lack of experience or expertise (n=9, 52.9%)  
248 and a lack of guidelines or good practices recommendations (n=7, 41.2%). Fifteen countries  
249 (88.2%) reported ongoing initiatives to increase the implementation of OPAT services.

250

### 251 3.2.2. *Infusion services (n=16 countries)*

#### 252 3.2.2.1 *Framework*

253 Legal frameworks (except in Denmark, Luxembourg and France) and guidelines  
254 (except in France) were not available in the 16 countries reporting having infusion services.

255 In most of the countries (n=14, 87.5%), infusion services were available to both adult  
256 and paediatric populations, except in Greece (restricted to the adult population).

#### 257 3.2.2.2 *Prescription*

258 Infusion services could be used in many different clinical situations: as a newly  
259 initiated treatment in an outpatient seen in the hospital (clinics, emergency department...)  
260 who is not admitted to the hospital or as a continuation of a previous antimicrobial treatment

261 for the same clinical indication initiated as an inpatient (n=14 for both situations, 87.5%), as  
262 a newly initiated treatment in a hospitalized patient who is discharged (n=13, 81.3%) or as a  
263 newly initiated treatment in an outpatient coming from the ambulatory setting (e.g. seen by  
264 GP) (n=12, 75%) (Table S9).

265 GPs or primary care physicians could initiate the parenteral antimicrobials used for  
266 infusion services respectively in 13 (81.3%) and 11 (68.8%) countries (Table S10); treating  
267 physicians in the hospital (non-ID physicians) could do so in 15 countries (93.8%). The  
268 prescription remained strictly hospital-based in Slovak Republic, Ireland and the Netherlands.

#### 269 3.2.2.3 *Preparation*

270 Professionals who might prepare the parenteral antimicrobials were mostly  
271 community nurses (n=11, 68.8%), followed by private compounding services and hospital  
272 pharmacies (n=9 for both, 56.3%) and specialized nurses (n=8, 50%) (Table S11).  
273 Caregivers and patients' relative or patients could do it respectively in 7 (43.8%) and 6  
274 (37.5%) countries, despite a lack of legal support in some countries (in France for example).

#### 275 3.2.2.4 *Medical devices delivery*

276 Associated medical devices were delivered either by community pharmacists in 12  
277 countries (75%) or by hospital pharmacists in 10 countries (62.5%) (Table S12). Delivery by  
278 private specialized services (n=8, 50%) or directly by community nurses (n=11, 68.8%) were  
279 also frequent.

#### 280 3.2.2.5 *Administration*

281 Parenteral antimicrobials could be administered by community nurses in all countries  
282 but Czech Republic (n= 15, 93.8%), by caregivers or relatives (n=10, 62.5%, most frequent  
283 way in Israel), by physicians (n=9, 56.3%, most frequent way in Germany) or by patients  
284 themselves (n=8, 50%) (Table S13). Less frequently, it could be administered by hospital  
285 nurses in six countries (37.5%). Nurses allowed to administer antimicrobials were only  
286 specialized nurses or nurses with a specific training in three countries (Denmark, Ireland and  
287 The Netherlands, 18.8%).

288 Antimicrobials were mostly administered at home (n=16, 100%) or in nursing homes  
289 (n=15, 93.8%). They could also be administered in hospital clinics (n=10, 62.5%), at medical  
290 primary care practices (n=9, 56.3%), or less frequently in hospital emergency departments  
291 (n=6, 37.5%).

#### 292 3.2.2.6 *Monitoring*

293 In almost all countries, treating physicians in the hospital (n=14, 87.5%) or GPs  
294 (n=14, 87.5%) were responsible for the monitoring of patients receiving parenteral  
295 antimicrobials in infusion services (Table S14). Other community doctors or ID specialists  
296 could be involved in respectively 12 (75%) and nine (56.3%) countries. Nurses were involved  
297 in only six countries (37.5%) and pharmacists in none.

#### 298 3.2.2.7 *Reimbursement*

299 Infusion services' costs (costs of antimicrobials, infusion fluids, medical devices,  
300 laboratory tests and remuneration of the professionals involved in the follow-up, the  
301 preparation and the administration of treatments) were totally covered in seven countries  
302 (43.8%), partially or free only for some patients in six (37.5%) and not covered at all in one  
303 country (Bulgaria, 6.3%) (Figure S2).

#### 304 3.2.2.8 *Barriers and perspective*

305 Infusion services were considered to be not easily available to all eligible patients in  
306 nine countries (56.3%). Lack of organizational infrastructure (7 countries, 43.8%), lack of  
307 good practices recommendations (6 countries, 37.5%) and geographical constraints (5  
308 countries, 31.3%) were the most commonly reported barriers. Lack of a legal framework, not  
309 enough expertise and absence of interest in infusion services were also pointed out as  
310 possible barriers in four countries (25%). Currently ongoing initiatives to improve  
311 implementation of infusion services were mentioned in five countries (31.3%).

#### 312 **4. Discussion**

313 Parenteral antimicrobials were available for outpatients in almost all 28 participating  
314 European countries, through OPAT services in 17 countries and through infusion services in  
315 16. Four countries (4/28, 14.3%) did not have any of those structured systems available.  
316 Legal frameworks and guidelines were frequently lacking at the national level and the level of  
317 organization of DPANS was highly variable between countries. Several barriers to optimal  
318 implementation were reported, such as a lack of organizational infrastructure or a lack of  
319 guidelines and good practices recommendations.

320 Regarding OPAT services, OPAT teams were all hospital-based, with a close  
321 collaboration with hospital AMS programmes in half of the cases. Unfortunately, dedicated  
322 and specifically trained staff, with related funding to compensate the time spent on OPAT  
323 activities, were in place in only about one third of the countries. This is concerning as well  
324 structured OPAT services are likely to be of increasing importance because of the growing  
325 prevalence of multi-resistant bacterial infections requiring parenteral treatment,[18] the  
326 necessity to improve comfort, patients' autonomy [7,13,19] and the need to reduce health  
327 services costs while ensuring patient safety.[20–23]

328 Evidence for inequity of access to OPAT services was seen within countries: in nine  
329 countries (52.9%), OPAT services were reported to be restricted to a limited number of  
330 hospitals and in seven countries costs were not fully reimbursed (41.2%).[24] Availability of  
331 telemedicine potentially might improve access to OPAT when geographic barriers are  
332 evident and additional support can be provided within the community.[25] It is encouraging  
333 that in 15 countries (88.2%) ongoing initiatives to improve uptake were reported.

334 For both OPAT and infusion services, antimicrobials were mostly administered at  
335 home and self-administration was frequent but not universal in either OPAT or infusion  
336 services. Wider use of this modality should be explored since it appears to be safe,  
337 convenient and economical.[6,15,26,27]

338 A large panel of antimicrobials were available to outpatients, consistent with  
339 pharmaceutical data (molecule stability, pharmacokinetics, pharmacodynamics...), safety

340 and specific modalities to administer parenteral antimicrobials to outpatients.[28] However,  
341 adequate conditions for infusion at point of care may not be guaranteed given the lack of  
342 formal guidance in most of the countries. Specific training and recommendations are for  
343 example needed to use elastomeric pumps for continuous injection in an optimal manner, to  
344 reduce the risk of complications.[29,30] Further studies about antimicrobials' stability and  
345 appropriate infusion fluids in a continuous "in-use" utilization are necessary.[31] Recent  
346 pharmaceutical testing has demonstrated that a continuous infusion with selected beta-  
347 lactams using body-worn devices up to 32 degrees centigrade is possible, on the condition of  
348 strict assessment of each molecule's stability.[32–34]

349 Infusion services mostly relied on community-based professionals (pharmacies,  
350 nurses) and gave a prominent place to GPs and hospital physicians (other than ID  
351 specialists). In our opinion, this might lead to less appropriate antimicrobial treatment and  
352 less adherence to stewardship principles (for example excessive treatment duration, missed  
353 opportunities to switch to oral therapy prior to or during outpatient therapy and overuse of  
354 unnecessarily broader spectrum agents) than management *via* a specialized OPAT team  
355 (medical infection specialists, specialized nurses and pharmacists) working within an AMS  
356 framework, ideally with monitoring of quality indicators.[35,36] Moreover, given the fact that  
357 no centralized oversight exists on infusion services' activities, we can anticipate that wide  
358 disparities exist in the actual treatment modalities and that international guidelines and good  
359 practices recommendations may not be always followed, which might result in less  
360 favourable outcomes and more adverse events than with a formal OPAT service or oversight  
361 by an AMS team. Studies comparing quality of care and access to DPANS between OPAT  
362 and infusion services are however lacking and further investigation is needed.

363 The main limitations for the implementation for both OPAT and infusion services were  
364 the lack of organizational structure, guidelines or recommendations, with the lack of  
365 experience also frequently cited for OPAT services. Coordinating DPANS at national level,  
366 within a national framework, would address these barriers and would promote good practice  
367 within the same country and between countries. The use of identified core elements of an



368 OPAT programme and regular assessments with recognized quality indicators could for  
369 example help structure OPAT services.[35,37] Several national OPAT guidelines/good  
370 practice recommendations have been published recently and may be suitable for adaptation  
371 to other settings.[27,38] Formal national coordination, or even European cooperation, may be  
372 a clue to overcome these limitations and benefit to countries where no OPAT programme is  
373 existing. The BSAC OPAT initiative has been in existence for 13 years and has developed a  
374 comprehensive national OPAT programme incorporating antimicrobial stewardship and  
375 including regular national educational events, a drug stability programme, Good Practice  
376 Recommendations, a national outcomes registry and an OPAT service directory to enable  
377 peer support and networking.[39]

378 Paediatric DPANS was observed to be widely practiced (in 70.6% and 87.5% of the  
379 countries where OPAT services or infusion services were available respectively). It is of  
380 fundamental importance that international guidelines apply to all-age patients (which is the  
381 case for American and British guidelines),[27,38] and, as established in recent specific  
382 guidelines on paediatric DPANS,[40] that this route of administration, rely on strongly  
383 structured systems to ensure safety and efficiency for younger patients.

384 To the best of our knowledge, this is the first study attempting to depict how DPANS is  
385 organized at a national level in a large number of European countries, which healthcare  
386 professionals or other stakeholders are involved, what legal framework exists for this practice  
387 and what financial support is existing at the national level. We provided data from DPANS  
388 leading experts for 28 countries, with a high response rate (82%). Our work has however  
389 some limitations: although our questionnaire was mostly completed by two respondents per  
390 country with expertise on both DPANS and AMS, we cannot be certain responses were fully  
391 representative of the national DPANS landscape, and it is possible that respondents may not  
392 have fully captured the diversity of practice in their respective countries, particularly in federal  
393 states. However, we tried to frame and minimise as much as possible these biases by  
394 allowing respondents to consult other national colleagues in case of doubt and to provide

395 semi-quantitative answers to most of the questionnaire's questions with the item "It varies a  
396 lot" and/or to provide free text answers in the answer "Other" or "free text for details".

397 **5. Conclusion**

398 DPANS is organized very differently from one country to another in Europe and we  
399 identified several barriers to optimal implementation of DPANS. Sharing good practices  
400 within the same country and between countries appears to be needed. European guidelines  
401 and a practical toolkit addressing different organizations providing DPANS might be useful,  
402 as well as further studies assessing DPANS different systems' efficiency.

## 403 **Acknowledgements**

404 The authors are grateful to all the survey participants, who were part of the ESGAP-BSAC  
405 OPAT survey working group†: Austria (F. Thalhammer, M. Alt), Belgium (D. Huis in 't Veld,  
406 S. Deryckere), Bulgaria (H. Lebanova, I. Uzunova), Croatia (N. Radošević Quadranti), Czech  
407 Republic (M. Stefan, A. Chrdle), Denmark (T. Vestergaard, U.W. Sönksen), Estonia (P. Mitt,  
408 M. Altmets), France (S. Kernéis, R. Batista), Germany (W.V. Kern, M. Stegemann), Greece  
409 (D.P. Kofteridis, P. Ioannou), Iceland (M. Kristjánsson, A. Tómasdóttir), Ireland (E. Feeney,  
410 K. Schaffer), Israel (D. Yahav, B. Calvarysky), Italy (A. Pan, D. Di Benedetto), Latvia (U.  
411 Dumpis, A. Vilde), Luxembourg (T. Staub, V. Knepper), Malta (P. Zarb, C. Mallia Azzopardi),  
412 Netherlands (M. Berrevoets), Norway (H. Fjeld, M. Neteland), Poland (A. Deptula, L.  
413 Honoto), Portugal (N. Rocha-Pereira, A.C. Carvalho), Slovenia (B. Beovic, J. Perme), Slovak  
414 Republic (V. Krcmery, G. Mikolasova), Spain (L.E. López Cortés, M.V. Gil Navarro), Sweden  
415 (S. Stenmark, H. Angström), Switzerland (S. De Vallière, C. Pluess-Suard), Turkey (C.  
416 Cimen, B. Madran), United Kingdom (R A. Seaton, M. Gilchrist).

417

## 418 **Declarations**

419 **Funding:** This study was conducted as part of our routine work. This research did not  
420 receive any specific grant from funding agencies in the public, commercial, or not-for-profit  
421 sectors.

422 **Competing Interests:** M.G. has received consulting fees from Pfizer. All other authors: none  
423 to declare.

424 **Ethical Approval:** Not required

425

## 426 **Authors' contribution**

427 C.P. conceived the study, wrote the first draft of the protocol and coordinated data collection.  
428 All authors reviewed the survey protocol and questionnaire. C.E., P.D.N. and N.S. analysed  
429 the data and wrote the first draft of the manuscript. All authors reviewed the manuscript.

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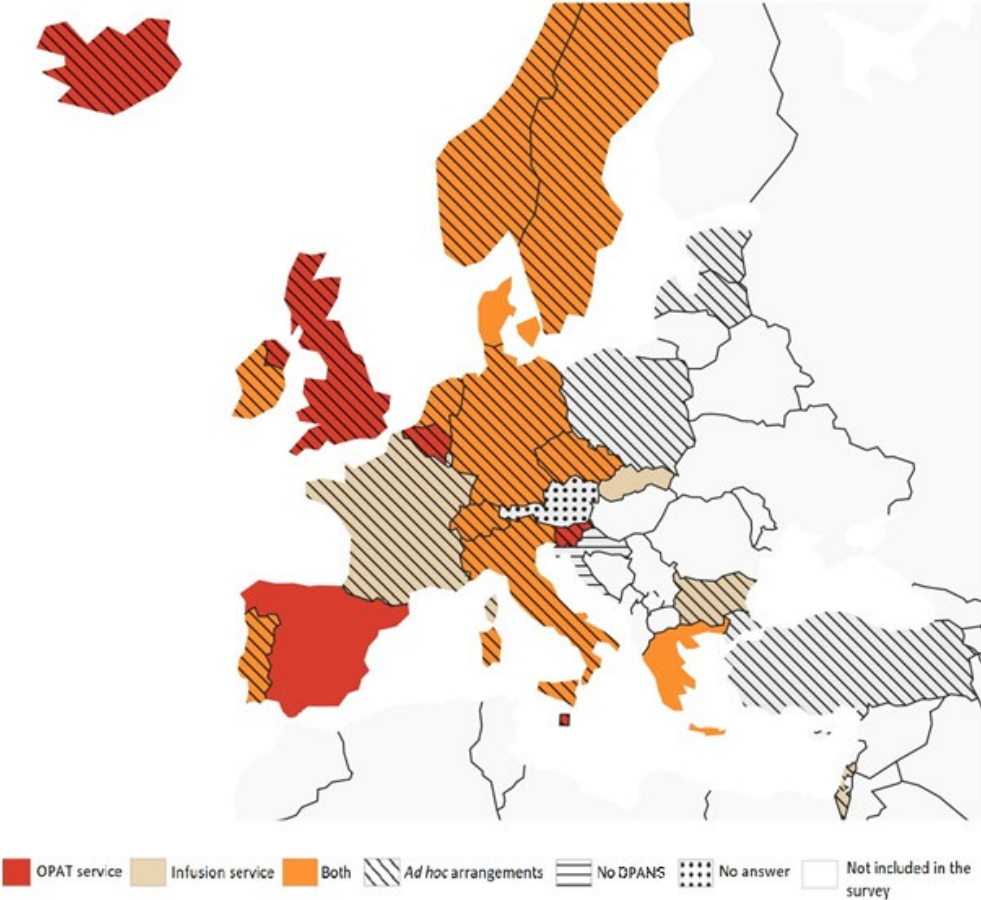
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**Figure 1: Geographical distribution of delivery of parenteral antimicrobials in non-inpatient settings (DPANS) in Europe.**



**Table 1: Structure and content of the 65-item questionnaire**

<b>Section</b>	<b>Content</b>	<b>Number of questions</b>
<b>1</b>	Information about participants: countries, names, contacts	5
<b>2</b>	Organization of general DPANS at a national level: DPANS availability, availability of 15 parenteral antimicrobials, available systems to provide DPANS in each country (several systems could be available in the country), reimbursement, route, mode of administration	15
<b>3</b>	OPAT service (if existing): framework, structure (composition of the team, staffing costs and antimicrobial stewardship), organization (referring practitioners, prescription, delivery, administration, monitoring), reimbursement, barriers, prospects	25
<b>4</b>	Infusion service (if existing): framework, organization (prescription, delivery, administration, monitoring), reimbursement, barriers, prospects	20

**Table 2: Compared availability to hospitalized patients and outpatients (either via an OPAT service, infusion service or other process) of 15 parenteral antimicrobials in European countries where parenteral antimicrobials are available in the outpatient setting (n=27).**

	Hospitalized patients (n=27)	Outpatients (n=27)		
		OPAT service (n=17)	Infusion service (n=16)	Other process (n=22)
<b>Amikacin, n (%)</b>	27 (100)	13 (76.5)	10 (62.5)	3 (13.6)
<b>Amoxicillin, n (%)</b>	18 (66.7)	6 (35.3)	8 (50)	0
<b>Cefazolin, n (%)</b>	24 (88.9)	8 (47.1)	7 (43.8)	3 (13.6)
<b>Ceftazidime, n (%)</b>	25 (92.6)	12 (70.6)	10 (62.5)	3 (13.6)
<b>Ceftazidime/avibactam, n (%)</b>	24 (88.9)	5 (29.4)	4 (25)	1 (4.5)
<b>Ceftriaxone, n (%)</b>	24 (88.9)	14 (82.4)	12 (75)	7 (31.8)
<b>Colistin, n (%)</b>	26 (96.3)	7 (41.2)	5 (31.3)	2 (9.1)
<b>Daptomycin, n (%)</b>	22 (81.5)	12 (70.6)	7 (43.8)	2 (9.1)
<b>Ertapenem, n (%)</b>	25 (92.6)	13 (76.5)	7 (43.8)	4 (18.2)
<b>Flucloxacillin, n (%)</b>	23 (85.2)	10 (58.8)	9 (56.3)	1 (4.5)
<b>Meropenem, n (%)</b>	26 (96.3)	10 (58.8)	10 (62.5)	2 (9.1)
<b>Piperacillin/tazobactam, n (%)</b>	26 (96.3)	9 (53)	9 (56.3)	3 (13.6)
<b>Teicoplanin, n (%)</b>	23 (85.2)	13 (76.5)	6 (37.5)	2 (9.1)
<b>Temocillin, n (%)</b>	8 (29.6)	2 (11.8)	2 (12.5)	0
<b>Vancomycin, n (%)</b>	27 (100)	12 (70.6)	9 (56.3)	3 (13.6)

**Table 3: Overview of the availability and reimbursement of parenteral antimicrobials to outpatients.**

	Availability	Reimbursement <sup>5</sup>	
		Completely	Partially
<b>Austria</b>	NA	NA	NA
<b>Belgium</b>	OPAT service Other <sup>1</sup>	No	Yes
<b>Bulgaria</b>	Infusion service Other <sup>2</sup>	No	No
<b>Croatia</b>	No		
<b>Czech Republic</b>	OPAT service Infusion service Other <sup>1,3</sup>	Yes <sup>6</sup>	No
<b>Denmark</b>	OPAT service Infusion service	Yes	No
<b>Estonia</b>	Other <sup>1,2</sup>		
<b>France</b>	Infusion service Other <sup>2,4</sup>	No	Yes
<b>Germany</b>	OPAT service Infusion service Other <sup>1,2,3</sup>	Yes	No
<b>Greece</b>	OPAT service Infusion service	Yes <sup>7</sup>	Yes <sup>8</sup>
<b>Iceland</b>	OPAT service Other <sup>1,3</sup>	Yes	No
<b>Ireland</b>	OPAT service Infusion service Other <sup>1,3</sup>	Yes	No
<b>Israel</b>	Infusion service Other <sup>1,3</sup>	Yes	No
<b>Italy</b>	OPAT service Infusion service Other <sup>1,2,3</sup>	Yes	No
<b>Latvia</b>	Other <sup>2</sup>		
<b>Luxembourg</b>	Infusion service Other <sup>3,4</sup>	No	Yes
<b>Malta</b>	OPAT service Other <sup>2</sup>	Yes	No
<b>Netherlands</b>	OPAT service Infusion service Other <sup>1</sup>	Yes	No
<b>Norway</b>	OPAT service Infusion service Other <sup>1,2,4</sup>	No	Yes <sup>9</sup>
<b>Poland</b>	Other <sup>2,3</sup>		
<b>Portugal</b>	OPAT service Infusion service Other <sup>1,2,4</sup>	No	Yes
<b>Slovak Republic</b>	Infusion service	Yes	No
<b>Slovenia</b>	OPAT service Other <sup>1</sup>	No	No <sup>+</sup>
<b>Spain</b>	OPAT service	Yes	No

<b>Sweden</b>	OPAT service Infusion service Other <sup>1,2,4</sup>	Yes	No
<b>Switzerland</b>	OPAT service Infusion service Other <sup>1,2,3</sup>	No	Yes
<b>Turkey</b>	Other <sup>1,2</sup>		
<b>UK</b>	OPAT service Other <sup>1,3,4</sup>	Yes	No

NA: No answer, <sup>1</sup> Other: via hospital-based ambulatory care (e.g. Acute medical or Emergency department physicians), <sup>2</sup> Other: via hospital services outside of OPAT for specific patient groups (e.g. Oncology, Cystic fibrosis), <sup>3</sup> Other: via general practitioners/primary care practitioners, <sup>4</sup> Other: via hospital-in-the-home setting outside of OPAT, <sup>5</sup> with an OPAT service or an infusion service, <sup>6</sup> "I don't know" answer with infusion service, <sup>7</sup> With an OPAT service, <sup>8</sup> With an infusion service, <sup>9</sup> With an OPAT service, "Other" answer with an infusion service, <sup>+</sup> Other : for hospital based OPAT

**Table 4: Comparison of the main characteristics of OPAT and infusion services.**

		<b>Countries offering OPAT services</b>	<b>Countries offering infusion services</b>
		(n=17)	(n=16)
<b>Legal framework, n (%)</b>		0 (0)	3 (18.8)
<b>Guidelines available, n (%)</b>		5 (29.4)	1 (6.3)
<b>Reimbursement, n (%)</b>	All costs	10 (58.8)	7 (43.8)
	Part of the costs	6 (35.3) <sup>1</sup>	6 (37.5) <sup>3,4</sup>
<b>Patients who benefit, n (%)</b>	Both adults and children	12 (70.6)	14 (87.5)
	Only adults	3 (17.6) <sup>1,2</sup>	1 (6.3) <sup>5</sup>
<b>Clinical situations, n (%)</b>	Continuation of a previous treatment (whether it is the same antimicrobial or not) for the same clinical indication in a hospitalized patient who is discharged	17 (100)	14 (87.5)
	Newly initiated treatment in a patient seen in the hospital (clinics, emergency department...) who is discharged	13 (76.5)	14 (87.5)
	As a newly initiated treatment in a hospitalized patient who is discharged	12 (70.6)	13 (81.3)
<b>Professionals who refer to the service (%)</b>		Infectious diseases specialist (94.1), treating physician in the hospital (88.2)	
<b>Prescription (%)</b>		Infectious diseases specialist (94.1), treating physician in the hospital (76.5)	Treating physician in the hospital (93.8), general practitioner (81.3), infectious diseases specialist (75)
<b>Preparation (%)</b>		Community nurse (64.7), OPAT nurse (58.8), hospital pharmacy (58.8), hospital nurse (52.9)	Community nurse (68.8), private compounding service (56.3), hospital pharmacy (56.3), specialized nurse (50)



<b>Medical devices delivery (%)</b>	Hospital pharmacy (82.4), community pharmacy (52.9), private specialized service (52.9)	Community pharmacy (75), community nurse (68.8)
<b>Administration (%)</b>	Community nurse (76.5), hospital nurse (64.7), caregiver/relative (58.8), patient (58.8)	Community nurse (93.8), caregiver/relative (62.5)
<b>Location of administration (%)</b>	Any hospital day clinics (94.1), home (88.2), nursing homes (88.2)	Home (100), nursing homes (93.8), any hospital day clinics (62.5)
<b>Monitoring (%)</b>	Infectious disease specialist (88.2), treating physician in the hospital (88.2), OPAT team member (64.7)	Treating physician in the hospital (87.5), general practitioner (87.5), other primary care doctor (75)

<sup>1</sup> "Other" proposition: n=1 (5.9%), <sup>2</sup> "It varies a lot" proposition: n=1 (5.9%), <sup>3</sup> No answer: n=2 (12.5%), <sup>4</sup> No reimbursement: n=1 (6.3%), <sup>5</sup> "It varies a lot" proposition: n=1 (6.3%)