Clinical Microbiology and Infection 28 (2022) 1272–1277

Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

Original article

Antibiotic use from formal and informal healthcare providers in the Democratic Republic of Congo: a population-based study in two health zones

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A R T I C L E I N F O

Article history:
Received 19 October 2021
Received in revised form
14 March 2022
Accepted 3 April 2022
Available online 18 April 2022

Editor: A. Huttner

Keywords:
Anti-bacterial agents/therapeutic use/
Antibiotic use
Antimicrobial stewardship
Cross-sectional studies
Developing countries
Democratic Republic of the Congo
Antimicrobial resistance
Antibiotic resistance
Healthcare utilization

A B S T R A C T

Objective: In the Democratic Republic of Congo and other low-resource countries, community-acquired pathogens are increasingly resistant to most locally available antibiotics. To guide efforts to optimize antibiotic use to limit antibiotic resistance, we quantified healthcare provider–specific and community-wide antibiotic use.

Methods: From household surveys, we estimated monthly healthcare visit rates by provider. From healthcare visit exit surveys, we estimated prevalence, defined daily doses, and access/watch/reserve distribution of antibiotic use by provider. Combining both, we estimated community-wide antibiotic use rates.

Results: Of 88.7 (95% CI 81.9–95.4) healthcare visits per 1000 person-months (n = 31221), visits to private clinics (31.0, 95% CI 30.0–32.0) and primary health centres (25.5, 95% CI 24.6–26.4) were most frequent. Antibiotics were used during 64.3% (95% CI 55.2–73.5%, 162/224) of visits to private clinics, 51.1% (95% CI 45.1–57.2%, 245/469) to health centres, and 48.8% (95% CI 44.4–53.2%, 344/454) to medicine stores. Antibiotic defined daily doses per 1000 inhabitants per day varied between 1.75 (95% CI 1.02–2.39) in rural Kimpese and 10.2 (95% CI 6.00–15.4) in (peri) urban Kisantu, mostly explained by differences in healthcare utilisation (respectively 27.8 versus 105 visits per 1000 person-months), in particular of private clinics (1.23 versus 38.6 visits) where antibiotic use is more frequent. The fraction of Watch antibiotics was 30.3% (95% CI 24.6–35.9%) in private clinics, 25.6% (95% CI 20.2–31.1%) in medicine stores, and 25.1% (95% CI 19.0–31.2%) in health centres. Treatment durations <3 days were more frequent at private clinics (5.3%, 9/169) and medicine stores (4.1%, 14/338) than at primary health centres (1.8%, 5/277).

Discussion: Private healthcare providers, ubiquitous in peri-urban settings, contributed most to community-wide antibiotic use and more frequently dispensed Watch antibiotics and shortened antibiotic courses. Efforts to optimize antibiotic use should include private providers at community level. **Brecht Ingelbeen, Clin Microbiol Infect 2022;28:1272**

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https://doi.org/10.1016/j.cmi.2022.04.002
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Introduction

In low-and middle-income countries, with a high and persistent burden of infectious diseases, available estimates indicate >80% of bacterial bloodstream infections are resistant against common Access antibiotics, and an increasing proportion is resistant against Watch antibiotics [1–3], threatening effective treatment against bacterial infections and resulting in most deaths attributable to antibiotic resistance [4]. In the Democratic Republic of Congo (DRC), the most frequently isolated pathogens in bloodstream infections, non-typhoidal and Typhi *Salmonella* (respectively 66% and 10% of isolates), are increasingly resistant to fluoroquinolones (7.3% and 24.5%, respectively), third-generation cephalosporins (15.7% and 0.2%), and macrolides (14.9% and 0.4%), on top of widespread multidrug resistance against first-line antibiotics [5,6].

To limit increasing antibiotic resistance, a key objective of the Global Action Plan on Antimicrobial Resistance is to optimize antibiotic use [7]. In low-income countries a significant part of antibiotic use happens outside official healthcare facilities, through informal health seeking or self-medication [8–10], which is overlooked in rare interventions to optimize antibiotic use. Here, sales data or hospital point prevalence surveys do not allow estimating country- and community-wide antibiotic consumption [11–14]. To inform the development and targeted implementation of interventions to optimize antibiotic use in low-resource settings, we estimated antibiotic use from both formal and informal healthcare providers in DRC.

Methods

Population

The study was conducted in the Kisantu and Kimpese health zones in Kongo-Central province, 120 and 210 km Southwest of Kinshasa. In each health zone, we selected two health areas, corresponding to neighbourhood(s) or village(s) with at least one primary health centre. Health centres are supervised by the health zone. Patients presenting with severe illness can be referred from health centres to the general referral hospital of the health zone. In Kisantu health zone, health areas Nkandu (urban, more densely populated; 2019 estimated population 26 876) and Kavuaya (peri-urban, less densely populated; 2019 estimated population 7617) were selected (Supplementary Figure S1). In Kimpese health zone, health areas Malanga (rural, nonetheless on the national road N1 to Kinshasa; 2019 estimated population 5431) and Viaza (rural, more remote; 2020 estimated population 3788) were selected, both part of an existing health demographic surveillance system, in which demographic and health-related indicators are collected during regular household visits.

Study design

We conducted a household survey to estimate the population's rate of healthcare visits by type of provider and a healthcare visit exit survey to estimate the prevalence of antibiotic use per healthcare visit. We then combined both measures to estimate community-wide antibiotic use.

Healthcare utilisation household survey

In Kisantu, we used a prior healthcare utilisation household survey from March 2019, part of a study measuring the incidence of typhoid fever [15]. Stratified spatial sampling was used to randomly select households, nearest to the randomly generated geographic coordinates within the selected health areas, as primary sampling unit. Where several households were identified within a selected structure, the first household located on the right side in the structure was approached. Six hundred forty-five households per health area were randomly selected. Healthcare visits and self-treatment, not involving a healthcare visit, during the past 3 months were recorded of all household members, using a paper-based structured questionnaire. In Kimpese, an electronic questionnaire was added to the health demographic surveillance system round during February to June 2020, recording every community member's healthcare visits in the past 3 months. By conducting the surveys in the same months of the year, seasonal differences in healthcare utilisation between both sites were accounted for.

Healthcare visit exit surveys

In a preceding qualitative study, we identified all healthcare providers and provider types in the four selected health areas through semi-structured, in-depth interviews with a convenience sample of formal and informal healthcare providers and patients (Heyerdahl, in preparation). We selected three providers of each of the following healthcare provider types per health area: primary health centres, medicine stores (including private community pharmacies with qualified dispensers and informal stores, as most were in the grey zone in between both), private clinics, traditional healers, and religious leaders that could sometimes be consulted for medical advice or care. Consecutively presenting patients of any age (or caretakers if aged below 18 years of age) were requested to participate in a healthcare visit exit survey after completing their healthcare visit. When a patient survey was completed, the next patient finishing a visit was selected for the survey. This continued until all visits that day were done. We aimed to interview at least 50 patients who used an antibiotic per provider type per health area, to obtain 95% confidence interval limits of 10% of the proportions of antibiotic groups. If in a selected health area, less than three providers of a provider type existed or agreed to participate, the number of healthcare visit exit surveys to be conducted was equally distributed between available providers. In addition, in the general referral hospital in Kisantu, all patients admitted in the hospital were interviewed twice, and antibiotic use in the previous 24 hours and treatment duration were recorded, with 1 week in between both rounds. Because certain providers had few patient visits per day, the number of exit surveys could remain under the sample size target.

Using an electronic questionnaire, all patients, or caretakers of paediatric patients, were asked about antibiotics for systemic use that were dispensed or purchased (generic name), number of units (tablet, capsule, vial, bottle) per treatment course, dose, route of administration, intake frequency, duration of treatment, the patient's age, and date of symptom onset. Surveys were conducted in Kisantu in October 2019 and in Kimpese in January 2020.

Data analysis

We estimated the monthly rate of healthcare utilisation by provider type by area, allowing a finite population correction to account for the fraction of residents sampled from the total population within each area and a potential cluster effect within households, using the "survey" package in R. We inferred the rate by health zone and for both health zones combined using population weights (npopulation_of_area/nstudy_opulation_of_area). The overall rate is the sum of provider type–specific rates.

We estimated the prevalence of antibiotic use, the distribution of antibiotics used by AWaRe (Access/Watch/Reserve) group [16] and by antibiotic class, the distribution of routes of administration, the mean number of defined daily doses (DDD), and median duration of treatment, by healthcare provider type and area. We used population weights to extrapolate to the health zone and to both health zones combined.

We multiplied the provider type and health zone–specific antibiotic use indicators (prevalence, prevalence of Watch antibiotics, DDD) with the monthly healthcare utilisation rate of that provider type in that health zone, to estimate the monthly community-wide rate of antibiotic use and the DDD used per 1000 inhabitants per day (DID), of any antibiotic and of Watch group antibiotics. Because we could not conduct patient surveys in the Kimpese hospital, we used the antibiotic use indicators from the Kisantu hospital instead when estimating the community-wide rate of antibiotic use in Kimpese. We also estimated the median number of days between symptom onset and healthcare visit and the age distribution of patients from the visit exit surveys.

Ethical considerations

The study protocol was approved by the Institute of Tropical Medicine institutional review board (ref. 1333/19) and the Université Protestante du Congo ethics committee (ref. CEUPC0060). Study participants provided written informed consent: patient or caretaker for healthcare exit survey and household head for healthcare utilisation.

Results

Frequency and timing of healthcare visits

During 2447 household visits (552 in Kisantu, 1850 in Kimpese), healthcare utilisation of 10 407 individuals was recorded (3185 in Kisantu, 7222 in Kimpese). The mean age of participants who sought health care was 23.6 years in Kisantu and 22.5 years in Kimpese. In Kisantu, 14.5% were under 5 years old (in Kimpese, 29.9%).

Combined, 88.7 healthcare visits and 58.0 episodes of self-treatment were reported per 1000 person-months. Private clinics and health centres were the most frequently visited providers (Table 1). The overall healthcare utilisation rate in Kisantu was fourfold the rate in Kimpese. For the age-specific distribution of healthcare utilisation, see web-only Supplementary Figure S2.

Patients visited health centres and private clinics a median of 3 days after symptom onset (interquartile range [IQR] 2–6 days) and medicine stores a median of 2 days after onset (IQR 1–4). Hospital admissions (median 9 days, IQR 6–14) and visits to traditional healers (median 9 days IQR 5–15) occurred later (Supplementary Figure S3).

Table 1
Rate of healthcare utilisation by type of provider and health zone

Type of provider	Monthly healthcare visits per 1000 person-months (95% confidence) intervals)		
	Kisantu	Kimpese	Combined
Hospital	1.26 (0.256–2.24)	1.15 (0.55–1.75)	1.20 (1.02–1.38)
Health centre	27.8 (21.5–34.1)	18.8 (16.4–21.2)	25.5 (24.6–26.4)
Private clinic	38.6 (31.4–45.7)	1.23 (0.61–1.85)	31.0 (30.0–32.0)
Medicine store	20.9 (15.1–26.8)	5.09 (3.82–6.35)	17.6 (16.9–18.3)
Traditional healer	16.5 (12.1–21.1)	1.39 (0.73–2.06)	13.4 (12.8–14.0)
Religious leader[a]	NA	0.16 (0.00–0.39)	0.07 (0.03–0.16)
OVERALL	105 (94.2–116)	27.8 (24.8–30.8)	88.7 (81.9–95.4)
Self-treatment[b]	58.0 (49.4–66.6)	NA	58.0 (49.4–66.6)

[a] Visits to religious leaders were not recorded in Kisantu; NA, not applicable.
[b] Self-treatment: use of medicines for an episode of illness not involving a healthcare visit. Not recorded in Kimpese.

Antibiotic use during healthcare visits

From 2022 healthcare visit exit surveys (1375 in Kisantu and 647 in Kimpese), the population-weighted prevalence of antibiotic use was 74.7% (95% confidence interval [CI] 70.5–78.9%, $n = 412$) among hospital-admitted patients, 64.3% (95% CI 55.2–73.5%, $n = 224$) at private clinics, 51.1% (95% CI 45.1–57.2%, $n = 469$) at health centres, and 48.8% (95% CI 44.4–53.2%, $n = 850$) at medicine stores. The prevalence of antibiotic use differed importantly between health zones: at health centres 54.8% (95% CI 47.3–62.3%, $n = 255$) in Kisantu versus 37.4% (95% CI 30.7–44.0%, $n = 214$) in Kimpese; at medicine stores 56.0% (95% CI 50.5–61.4%, $n = 454$) in Kisantu versus 21.9% (95% CI 17.9–26.0%, $n = 396$) in Kimpese (Fig. 1). The fraction of Watch antibiotics was higher in private clinics (30.3%, 95% CI 24.6–35.9%) than health centres (25.1%, 95% CI 19.0–31.2%) or medicine stores (25.6%, 95% CI 20.2–31.1%). No Reserve antibiotics or antibiotics that were not on the 2021 WHO Essential Medicines List were reported.

Parental use of antibiotics was more frequent in private clinics (46.3%, 95% CI 38.1–54.4%) than health centres (15.4% 95% CI 10.3–20.4%). The mean defined daily doses of antibiotic use per visit were comparable among health centres (2.9 DDD, 95% CI 2.4–3.4), private clinics (2.8 DDD, 95% CI 2.3–3.3), and medicine stores (2.7 DDD, 95% CI 2.2–3.1).

The median duration of treatment was 7 days (IQR 5–7) at health centres and 5 days (IQR 5–7) at private clinics ($p < 0.01$). It was 7 days (IQR 5–7) at traditional healers and 5 days (IQR 5–7) at medicine stores. Duration of treatment <3 days was more frequent at private clinics (5.3%, 9/169) and medicine stores (4.1%, 14/338) than at primary health centres (1.8%, 5/277, $p = 0.05$ and $p = 0.04$, respectively).

Community-wide antibiotic use

Antibiotics were used during the previous month by 6.2% (95% CI 4.4–8.9%) of the population in Kisantu and 0.81% (95% CI 0.46–1.2%) in Kimpese. The overall antibiotic use was 10.2 DID (95% CI 6.00–15.4 DID) in Kisantu and 1.75 DID (95% CI 1.02–2.39 DID) in Kimpese (Supplementary Figure S4). Most of this gap is explained by differences in healthcare utilisation: in Kisantu overall fourfold higher and more frequent visits to private clinics, where antibiotic use was higher (Fig. 1). Visits to private healthcare providers accounted for 70.8% of DID in Kisantu and 13.0% of DID in Kimpese. The overall Watch group antibiotic use was 3.25 DID (95% CI 1.48–5.60 DID) in Kisantu and 0.37 DID (95% CI 0.15–0.64 DID) in Kimpese.

Choice of antibiotics

Community wide, the most frequently used antibiotic classes were penicillins (49.5%, 95% CI 46.7–52.3%), cephalosporins (14.2%, 95% CI 12.3–16.2%), nitroheterocyclics (12.1%, 95% CI 10.3–14.0%, mainly metronidazole), fluoroquinolones (7.1%, 95% CI 5.7–8.5%), and macrolides (6.4%, 95% CI 5.1–7.8%) (Fig. 2). Cephalosporins were more frequently used in private clinics (25.3%, 95% CI 18.8–31.7%) than medicine stores (11.8%, 95% CI 8.5–15.1%) or health centres (9.3%, 95% CI 5.9–12.7%). Fluoroquinolones were more frequently used in medicine stores (9.0%, 95% CI 6.1–12.0%) and health centres (7.0%, 95% CI 4.0–10.0%) than private clinics (5.1%, 95% CI 1.8–8.3%). Supplementary Tables provide the distribution of antibiotic classes among <5 year olds and of individual antibiotics.

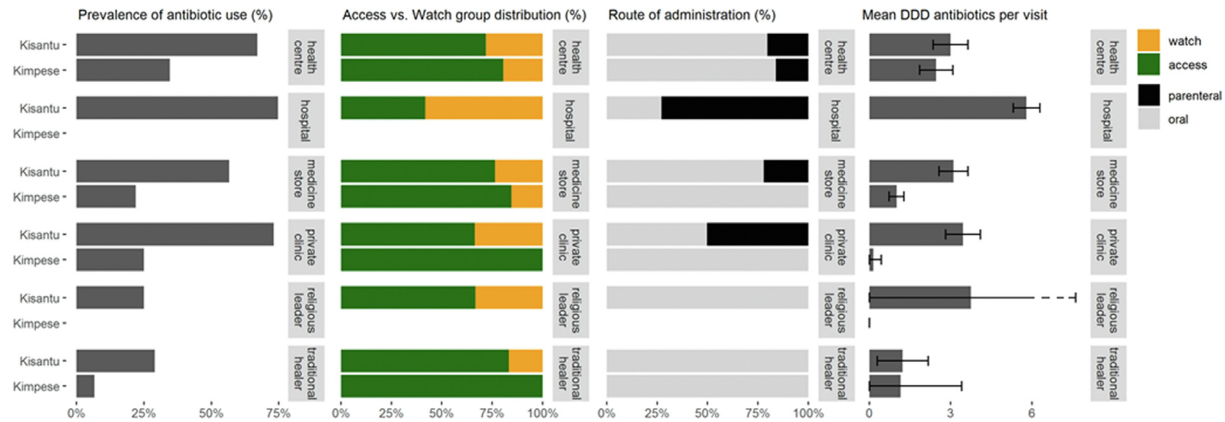

Fig. 1. The prevalence of antibiotic use (among all visits), the distribution of AWaRe groups among antibiotics used, the distribution of routes of administration, and the mean number of defined daily doses of antibiotic used during/following one healthcare visit, by health zone. The 95% confidence interval of mean DDD during visits to religious leaders in Kisantu was −3.6 to 11.1.

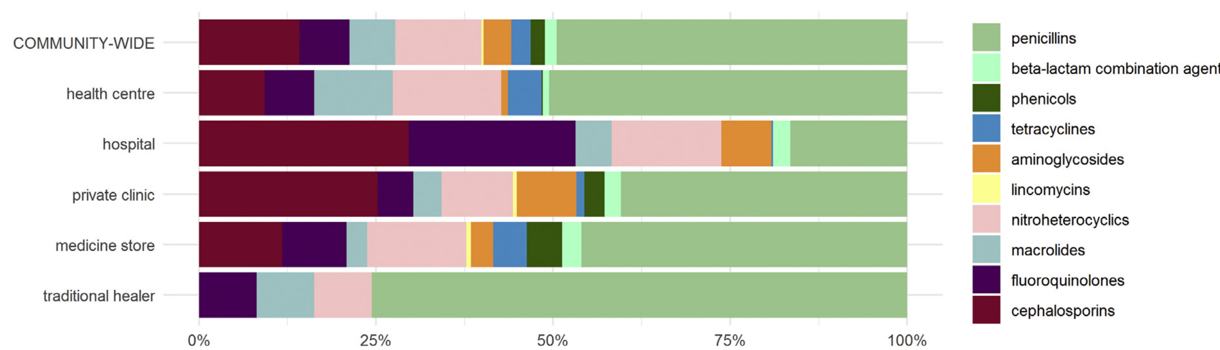

Fig. 2. Antibiotic class distribution of antibiotic courses used, by type of healthcare provider and community wide, combining Kimpese and Kisantu health zones by weighting for population size and for the provider-specific healthcare utilisation rate.

Discussion

Over 50% of community-wide antibiotic use resulted from visits to private healthcare providers, although their share was higher in urban Kisantu than in rural Kimpese. Private providers not only dispensed antibiotics more frequently, but their treatment courses also consisted of Watch antibiotics more frequently and were more frequently shortened. Only 3% of community-wide antibiotic use resulted from the hospital, owing to infrequent hospital admissions.

Antibiotic use in Kisantu (10.2 DID) was comparable to lower-middle–income countries (median 10.8 DID), and that of Kimpese (1.75 DID) was lower than that in any country in a 2015 study of 76 high- and middle-income countries [14]. In both sites, antibiotic use was two- to elevenfold lower than in most European countries (mean 20.0 DID, range 8.9–34.1 DID), emphasizing the lack of access to appropriate antibiotic treatment or to health care in general [17,18]. The prevalence of antibiotic use during health centre visits (51.1%) was similar, and that during private clinic visits (64.3%) was higher than the pooled prevalence during primary care centre visits (52%) estimated in a systematic review in 27 low- and middle-income countries [19]. Hence, low community-wide antibiotic use can be explained by infrequent healthcare seeking owing to poor access to healthcare. That could also explain the difference between both study health zones despite their geographical proximity. Socioeconomic and health system differences determine health care frequency (in peri-urban Kisantu fourfold that in rural Kimpese) and to a lesser extent to the prevalence of antibiotic use per visit (in Kisantu nearly twofold that in Kimpese). In Kisantu, medicine stores and clinics are widely present, with different types of medicine stores for every budget or illness. In its official healthcare facilities, a flat rate per consultation or hospital admission is applied. Kimpese is probably more similar to most zones in DRC, with difficult access to health care and exclusively out-of-pocket payments, curtailing timely consultation and treatment.

Considering the increasing prevalence of bacterial resistance against Watch antibiotics [5,6], we were particularly interested in the use of Watch antibiotics. The fraction of Watch antibiotics (31.9% of DID in Kisantu, 21.1% in Kimpese) was lower than that observed in most countries with data available (worldwide 38.6%) [14]. Watch antibiotic use was higher in urban health areas, explained by their frequent use in private clinics and over-the-counter in medicine stores.

Combining two surveys, we measured antibiotic use in settings where antibiotic use cannot be routinely estimated from sales data or medical records and where healthcare and medicines are in large part offered by an unregulated private sector. The inclusion of all healthcare provider types and the random sampling of households provided unique healthcare utilisation data that standalone provider-based antibiotic use surveys cannot offer. Healthcare visit exit surveys could be regularly repeated in a number of sentinel sites where population healthcare utilisation data are available, offering a feasible way to monitor trends in antibiotic use and measure the effectiveness of efforts to optimize antibiotic use.

Study limitations

Antibiotic use could be underestimated as a result of difficulties recalling visits during healthcare utilisation surveys. The pre-defined number of healthcare visit exit surveys at traditional healers and religious leaders was not attained because of infrequent patient visits, which limited comparisons of their indictors. The appropriateness of the antibiotic courses used cannot be assessed from patient visit exit surveys without full anamnesis and clinical/diagnostic examination. Our findings underscore widely differing antibiotic use between two geographically close areas and hence cannot draw any conclusions on nationwide antibiotic use.

Conclusion

The surprisingly high antibiotic resistance prevalence among bloodstream infections in DRC, of chiefly community-acquired pathogens [5,6], could be the result of an interaction between poorly controlled bacterial infections and frequent exposure of these bacteria to antibiotics. Both factors relate to difficulties accessing appropriate diagnostic capacity and resulting self-medication with (underdosed) antibiotics from private providers. Optimizing antibiotic use also involves ensuring sufficient access to the appropriate antibiotic treatment [18].

Antibiotic dispensing by private providers is not overseen by health authorities, nor are we aware of existing antibiotic stewardship interventions targeting private providers those in DRC or elsewhere in Central Africa. Intervention bundles to optimize antibiotic use, including training of medicine store staff and other community-level providers, have shown to improve clinical care and in some occasions to decrease antibiotic use [20,21] and should be considered on a wider scale, albeit adapted to the local health care landscape.

Transparency declaration

All authors declare no competing interests. This work was part of the Bacterial Infections in the Tropics research cluster at the Institute of Tropical Medicine, funded by the InBev-Baillet-Latour Fund. Kimpese Health Research Center, Kimpese and Institut National de Recherche Biomédicale, Democratic Republic of Congo, received funding by the Belgian Directorate of Development Cooperation for Antimicrobial Resistance projects. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. Pseudonymized individual data collected for the study, study protocol, questionnaires, and analysis scripts are available on https://github.com/ingelbeen/cabu.

Author contributions

BI, PM, and MABvdS designed the study; BI, DMP, MFP, MYNB, FKK, LK, BM, JI, LH, and OL collected the data and contributed to writing; FKK and LH provided insights from the preceding qualitative study in questionnaire design and interpretation; BI and NMB verified, curated, and analyzed the data; BI, RIDL, MJMB, OL, JJ, and MABvdS interpreted the results and contributed to the writing; all authors critically reviewed and contributed revisions to the final version of the paper. PM and MABvdS contributed equally.

Acknowledgement

We would like to thank Esther Van Kleef for reviewing statistics used in a revision of the manuscript.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cmi.2022.04.002.

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