

Determination of the unmet medical need in treating infections caused by resistant bacterial pathogens in Switzerland – and a Swiss Bacterial Priority Pathogens List

REPORT



CRE
Enterobacterales



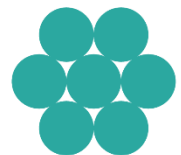
CRAB
A. baumannii



CRPA
P. aeruginosa



VRE
E. faecium



MRSA
S. aureus

Determination of the unmet medical need in treating infections caused by resistant bacterial pathogens in Switzerland – and a Swiss Bacterial Priority Pathogens List (Swiss BPPL)

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Preface

This report describes the procedure and outcome of a project conducted during 2024 and 2025 with the aim to identify the resistant bacterial pathogens causing infections whose adequate treatment with the antibiotics currently authorised in Switzerland is challenging, thereby highlighting an unmet medical need in the Swiss healthcare system.

The outcome of the project is a Swiss Bacterial Priority Pathogens List (BPPL). The methodology used for its development may serve as a blueprint for a national framework to guide the allocation of financial incentives to antibiotics that address high unmet medical needs in Switzerland.

The ongoing revision of the Epidemics Act, if adopted, will provide the legal basis for so-called subscription incentives. These incentives are designed to compensate for forgone revenue when antibiotics are used prudently—only when clinically indicated—thereby helping to slow the development of bacterial resistance.

This project, led by members of the Swiss Round Table on Antibiotics, could only be carried out thanks to the invaluable contribution of know-how and experience by the members of an expert team of renowned clinicians and scientists. The Round Table on Antibiotics expresses its deepest gratitude for their selfless support.

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Summary

Introduction: Antimicrobial Resistance (AMR) is a global phenomenon which also impacts countries like Switzerland with a well-resourced healthcare system: Clinicians are faced with significant challenges when infections caused by resistant bacterial pathogens cannot be adequately treated with the antibiotics authorised in our country.

Newly developed and older antibiotics available in other countries are often not authorised or no longer available in Switzerland. With fewer than 10 million residents and a reimbursement system currently not honouring the full value of antibiotics for public health, Switzerland is not a very attractive market for antibiotics.

The outcomes of this project shall contribute to improving the economic framework for antibiotics in Switzerland: Antibiotics effectively addressing high unmet medical needs and their causative bacterial pathogens shall qualify for subscription payments independently of the product volume sold, on top of the regular turnover. **(Chapter 1)**

Method: Applying a Delphi-type method, seven clinical experts and scientists were individually asked to determine relevant medical need criteria and their scoring, and to identify the pathogens causing the most critical unmet medical need in their clinical practice. In subsequent plenary sessions the anonymised responses were consolidated. This process was informed by the approach pursued by the World Health Organization (WHO) for the establishment of the 2024 update of the global WHO Bacterial Priority Pathogens List (WHO BPPL), national surveillance data provided by the Swiss Centre for Antibiotic Resistance (ANRESIS), and literature.

The outcome of this process was described in a consultation paper which was submitted to 40 medical, pharmaceutical, scientific, political, and investment/accelerator organisations in Switzerland. One feedback suggested a relative weighing of the selected medical need criteria and their tiered scoring, and the design of a composite score across the chosen medical need criteria. This should facilitate a systematic and consistent ranking of the shortlisted five resistant bacterial pathogens identified primarily from clinical experience. A possible approach to such an undertaking is provided in [ANNEX 2](#) for illustration purposes. **(Chapter 2)**

Selection and scoring of medical need criteria: The expert team selected three medical need criteria: treatability, trend of resistance, and incidence. Their proposed scoring for Switzerland partially deviates from the WHO's scoring definitions: Relevance for the Swiss healthcare system, availability of Swiss data, and ease of data access and use in Switzerland were given priority in the final design. **(Chapter 3)**

Results: Applying the proposed Swiss scoring definitions the three medical need criteria were scored for the shortlisted five resistant pathogens, using ANRESIS data. **(Chapter 4)**

Discussion and conclusion: The shortlist of pathogens primarily selected from medical experience was subjected to further assessment from a forward-looking scientific perspective. The assessment confirmed the following resistant pathogens as representing the greatest unmet medical need in the treatment of bacterial infections in Switzerland, and their ranking:

- Carbapenem-resistant Enterobacterales
- Carbapenem-resistant *Acinetobacter baumannii*
- Carbapenem-resistant *Pseudomonas aeruginosa*
- Vancomycin-resistant *Enterococcus faecium*
- Methicillin-resistant *Staphylococcus aureus*

These resistant pathogens are proposed to constitute the first Swiss BPPL. **(Chapter 5)**

Abbreviations

Abbreviation	Explanation
3GCR	Third-generation cephalosporin-resistant
AMR	Antimicrobial resistance
ANRESIS	Swiss Centre for Antibiotic Resistance, a nationwide, representative surveillance system and research instrument for antibiotic resistance and consumption
AWaRe	A classification system developed by the WHO to group antibiotics based on their potential for resistance and importance in human medicine. Three groups are defined: Access , Watch , and Reserve [1] ¹
BPPL	Bacterial Priority Pathogens List
CF	Cystic Fibrosis
COPD	Chronic Obstructive Pulmonary Disease
CRAB	Carbapenem-resistant <i>A. baumannii</i>
CRE	Carbapenem-resistant Enterobacterales
CRPA	Carbapenem-resistant <i>P. aeruginosa</i>
CSF	Cerebrospinal Fluid
ECDC	European Centre for Disease Prevention and Control
EMA	European Medicines Agency
EpidA	Federal Act on the Control of Communicable Diseases in Humans (Epidemics Act)
EOC	Ente Ospedaliero Cantonale
ESCR	Extended-Spectrum Cephalosporin-Resistant
FDA	US Food and Drug Administration
FOPH	Federal Office of Public Health
HAP	Hospital-Acquired Pneumonia
HAI	Healthcare-associated infections
HUG	Hôpitaux Universitaires de Genève
ICU	Intensive Care Unit
IPC	Infection Prevention and Control
IVDU	Intravenous Drug Use
LTCF	Long-Term Care Facility
MBL	metallo- β -lactamases

¹ Zanichelli et al. - 2023 - The WHO AWaRe (Access, Watch, Reserve) antibiot.pdf:

Access antibiotics are antibiotics with a narrow spectrum of activity, generally with fewer side-effects, a lower potential for the selection of antimicrobial resistance and of lower cost. They are recommended for the empiric treatment of most common infections and should be widely available.

Watch antibiotics generally have a higher potential for the selection of antimicrobial resistance and are more commonly used in sicker patients in the hospital facility setting. Their use should be carefully monitored to avoid overuse.

Reserve antibiotics are last-resort antibiotics that should only be used to treat severe infections caused by multidrug-resistant pathogens.

Abbreviation	Explanation
MCDA	Multi-Criteria Decision Analysis
MDR	Multidrug resistance / multidrug-resistant
MRSA	Methicillin-resistant <i>Staphylococcus aureus</i>
NARA	Nationales Referenzlaboratorium zur Früherkennung und Überwachung neuartiger Antibiotikaresistenzen / National reference laboratory for the early detection and monitoring of novel antibiotic resistance
NFHB	Non-Fatal Health Burden
OPAT	Outpatient Parenteral Antimicrobial Therapy
PAPRIKA	Potentially All Pairwise RanKings of all possible Alternatives
PMDA	Japanese Pharmaceuticals and Medical Devices Agency
R&D	Research and development
RKI	Robert Koch Institute
RTA	Swiss Round Table on Antibiotics
SARR 2024	Swiss Antibiotic Resistance Report 2024 [2]
VAP	Ventilator-Associated Pneumonia
VRE	Vancomycin-resistant Enterococci
WHO	World Health Organization
YLD	Years Lived with Disability

1 Introduction

1.1 Impact of antimicrobial resistance in Switzerland

AMR is a global phenomenon which also impacts countries like Switzerland with a well-resourced healthcare system: Clinicians are faced with significant challenges when infections caused by resistant bacterial pathogens cannot be adequately treated with antibiotics authorised in our country.

The WHO stated that the global clinical pipeline and recently approved antibiotics are insufficient to address the growing threat of antibiotic resistance [3]. Despite their critical role in health systems, antibiotics often fail to generate sufficient revenue to cover the costs of their development and post-market maintenance. Newly developed antibiotics tend to be launched in only a few high-income countries. With a market of fewer than 10 million residents and a reimbursement system not honouring the full value of antibiotics for public health, manufacturers do not always seek Swissmedic marketing authorisation for their antibiotics, despite a clear unmet medical need. The following examples illustrate the situation:

- Twelve of 18 (67%) antibiotics authorised by the US Food and Drug Administration (FDA), European Medicines Agency (EMA), Japanese Pharmaceuticals and Medical Devices Agency (PMDA), or Health Canada during 2010-2020 are not authorised in Switzerland [4], [5].
- Out of 42 antibiotics recommended by the Sanford Guide to Antimicrobial Therapy for treatment of 13 priority bacterial pathogens, 16 or 38% are not authorised in Switzerland. Among the “missing” antibiotics are also several older agents, including ampicillin, ampicillin/sulbactam, temocillin, intravenous fosfomycin, and polymyxin B.

1.2 Patients at highest risk

The estimated mortality in Switzerland due to untreatable resistant bacterial infections amounts to 300 deaths every year [6].

The experts identified individuals in the groups or circumstances outlined in [Table 1](#) as being at highest risk of exposure to difficult-to-treat, resistance-related infections in Switzerland.

Table 1 Risk factors (The order of the listed items does not reflect their ranking for risk size.)

ID	Risk factors
A	Immunocompromised cancer or transplant patients
B	Patients undergoing haemodialysis, suffering from Chronic Obstructive Pulmonary Disease (COPD), bronchiectasis or Cystic Fibrosis (CF)
C	Individuals injecting drugs (intravenous drug use, IVDU)
D	Patients treated in intensive care units (ICU) and burn units, often affected by multiple organ failure, and patients with prolonged hospital stays
E	Individuals using in-dwelling devices / implants
F	Travellers returning from long stays in high-AMR-countries such as Algeria, Egypt and Asian countries – even if they were not hospitalised there
G	Individuals who previously used antibiotics, were colonised or infected

Considering the high life expectancy and prevalence of elderly persons in Switzerland, the experts did not list age or comorbidities as separate risk factors.

Because of the difficulty to assess long-term care facilities (LTCF) as a risk factor, the group of persons living in LTCF was not included in the list. LTCFs often do not have enough adequately trained medical personnel, medical control is often limited, screening is generally missing, and infection prevention and control measures (IPC) are not systematically applied. Test results of isolates taken in LTCFs cannot be traced back to the LTCF when the attending general practitioners send the samples to the laboratories in the name of their practices. Furthermore, generalising ANRESIS surveillance data to LTCFs is challenging due to the wide variation in institutional size and standards.

1.3 Remedial option

To enhance the antibiotics arsenal in Switzerland needed to treat infections where the currently available treatment options are inadequate, Article 51a of the revised Epidemics Act (EpidA) provides the legislative base for an innovative remuneration model that can attract new antibiotics to the Swiss market or help maintain existing antibiotics on the market. Their annual remuneration will consist of two components: the regular turnover, and a subscription payment independent of the product volume sold, which elevates the total annual revenue to a pre-determined maximum guaranteed level.

Not all antibiotics will benefit from the financial incentive. Only those that can demonstrate effectiveness in treating infections caused by officially prioritised resistant bacterial pathogens and address a defined unmet medical need may be eligible. The future Swiss Bacterial Priority Pathogens List (Swiss-BPPL) will guide the Authorities' decision about eligibility.

2 Method

We used several sources of information to determine the unmet medical need in Switzerland and the causative pathogens. They are described in sub-chapters 2.1-2.5.

2.1 Clinical experts' preferences and assessments

This project sought information about the unmet medical need as presented in the clinical practice, and particularly in clinical settings where high-risk patients are treated and where patients are exposed to infections with resistant pathogens. These situations present the biggest challenges which treating physicians and their patients are facing when relevant antibiotics are not regularly available on the Swiss market.

For this purpose, we chose an approach that has characteristics of Delphi-methods to elicit the expert team members' clinical experience, information, assessment, and prioritisation. Delphi methods are applied mainly in the exploratory or evaluative phases of a research process and have been established as a consensus method in the health sector.

Box 1 describes five main methodological characteristics of Delphi methods [7].

Box 1 Five main methodological characteristics of Delphi methods (copied from [7] and translated)

1. Experts are surveyed, and their anonymity is generally preserved.
2. The survey is conducted in at least two Delphi rounds, i.e. there is an initial round followed by (at least) one revision round.
3. The basis is a standardised questionnaire, sometimes supplemented by open questions to record arguments and rationales.
4. The statistical analysis is usually based on descriptive measures.
5. From the second Delphi round onwards, the experts receive feedback on the results of the previous round in addition to the questionnaire, enabling them to reconsider and, if necessary, revise their judgements.

The experts were selected to represent clinical experience in the three major language regions of Switzerland, in tertiary hospitals. They covered further relevant aspects including primary care, public health, AMR surveillance, and microbiology.

The RTA-team elicited the experts' assessments and prioritisation in two rounds of one-on-one interviews. The interviews were based on information provided in briefing documents prepared by the RTA-team.

The first round of interviews was dedicated to the selection of the medical need criteria deemed most relevant, and their scoring. The briefing document presented the medical need criteria and scoring systems used to generate the WHO BPPL (2024), and two additional criteria considered by the Robert Koch Institute (RKI).

The anonymised summary of the experts' responses, the three medical need criteria which the experts independently prioritised, as well as proposed scoring systems were described in the briefing document for the second round of interviews. There, the experts were requested to assess and comment on the proposals and describe alternatives if they did not agree with them. Furthermore, the experts were asked for information about the bacterial pathogens experienced to cause the most difficult-to-treat infections.

Again, the RTA-team anonymised and summarised the experts' responses and prepared the documentation for the face-to-face on-site plenary meeting which aimed to achieve a consensus. It is worth noting the strong consensus among the experts' responses, methodological criticism, and prioritisation of pathogens, both in the interviews and the on-site discussions. To accommodate the experts' critique of the way the attribute of the treatability criterion was built, a follow-up online plenary meeting was held, allowing time for the update of the treatability attribute values.

2.2 Consultation of approaches taken by WHO and Robert Koch Institute

To facilitate alignment with the global Bacterial Priority Pathogens List (WHO BPPL, 2024) [8], we studied the approach taken by the WHO to establish it, in full awareness of the different roles of the global and national BPPLs which are stated in the executive summary section of [8]. The WHO BPPL is a global tool and aims “to serve as a compass for AMR research and development (R&D) priority setting and investment, and for public health action. Its application requires adaptation and contextualization to account for regional differences in the distribution and ecology of bacterial pathogens, as well as variations in the vulnerable groups and the burden of AMR. Regionally tailored strategies and interventions are necessary for effective control of AMR in diverse geographical settings.”

Additionally, we reviewed the approach pursued by the RKI in a similar undertaking for Germany². The selection of the medical need criteria for Switzerland is described in sub-chapter 3.1.

2.3 Medical need criteria – scoring systems

While the expert team accepted the desirability of the Swiss scoring system to follow the concept of WHO’s definitions, the final choice was taken with a view on current availability of scoring data, their relevance for the Swiss healthcare system, and ease of access and use of the data.

The experts concluded that these three conditions are met by the ANRESIS surveillance data ([Home - ANRESIS](#)) for the selected medical need criteria treatability, trend of resistance, and incidence.

ANRESIS provided the susceptibility rates by pathogen-antibiotic combinations which we used to build the scoring of “treatability rate” for the clinical settings ICU, inpatient (all wards, excluding ICU), and outpatient. This dataset is available in the Supplementary Data ([Swiss Round Table on Antibiotics | Downloads](#)). It is not publicly accessible on the ANRESIS website.

[Table 2](#) provides an overview of the scope of data published on the ANRESIS website for resistance rates over time, and incidence time series.

ANRESIS’ selection of the seven pathogens follows the selection in pertinent literature for the WHO Europe area [9], the EU/EEA [10], and Switzerland [11]. The observed consistency of infection patterns and antibiotic resistance in Switzerland with European trends and beyond is plausible: Switzerland’s location at the heart of Europe, coupled with its open economy and affluence, encourages extensive travel, which in turn facilitates the cross-border spread of infections and resistance. Genetic analyses of resistant pathogens in Switzerland have identified similarities between resistance genes found in Switzerland and in neighbouring countries, as well as in countries beyond the Swiss neighbourhood [12].

ANRESIS also provides resistance rates over time data for *Salmonella spp.* and *N. gonorrhoeae*, however at present no incidence time series for these pathogens.

The scoring of the selected medical need criteria is described in sub-chapter 3.2.

² Robert Koch-Institut (RKI) und Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM), 01.02.2024, Version 2, Reserveantibiotika: Befreiung von der Nutzenbewertung durch standardisierte Kriterien gemäß § 35a Sozialgesetzbuch (SGB) V. Nicht erschöpfende Liste multiresistenter Bakterien und Kriterien für die Einstufung eines Antibiotikums als Reserveantibiotikum gemäß § 35a Absatz 1 Sozialgesetzbuch (SGB) V (für Deutschland)

Table 2: Pathogen-antibiotic combinations for which ANRESIS provides Resistance Rates over Time (“TR”) data and Incidence Time Series (“IN”) for Switzerland

Antibiotics	<i>Acinetobacter</i> spp.	<i>E. faecalis</i> & <i>E. faecium</i>	<i>E. coli</i>	<i>K. pneumoniae</i>	<i>P. aeruginosa</i>	<i>S. aureus</i>	<i>S. pneumoniae</i>
Aminoglycosides (AMG)	TR, IN		TR, IN	TR, IN	TR, IN	TR, IN	
Aminopenicillins (AMPC)		TR, IN	TR, IN				
Amoxicillin-clavulanic acid (AMC)			TR, IN	TR, IN			
Carbapenems (CARB)	TR, IN		TR, IN	TR, IN	TR, IN		
Cefepime (CEF)					TR, IN		
Ceftazidime (CAZ)					TR, IN		
Ceftriaxone (CTX)							TR, IN
Cephalosporins 2 nd gen. (2G cephs)			TR, IN	TR, IN			
Cephalosporins 3 rd 4 th gen. (3-4G cephs)			TR, IN	TR, IN			
Ciprofloxacin (CIP)	TR, IN				TR, IN	TR, IN	
Clindamycin (CLI)						TR, IN	
Daptomycin (DAP)						TR, IN	
Erythromycin (ERY)							TR, IN
Fluoroquinolones (FQ)			TR, IN	TR, IN			
Fosfomycin (FOF)			TR, IN				
Fusidic acid (FUS)						TR, IN	
Gentamicin HLAR (GEN-HLRA)		TR, IN					
Levofloxacin (LVX)							TR, IN
Linezolid (LNZ)		TR, IN				TR, IN	
Macrolides (MAC)						TR, IN	
Methicillin (in ANRESIS: Flucloxacillin* (MRSA))						TR, IN	
Nitrofurantoin (NFT)			TR, IN				
Penicillin (PEN)						TR, IN	TR, IN
Piperacillin-tazobactam (PIP-TAZ)			TR, IN	TR, IN	TR, IN		
Rifampicin (RIF)						TR, IN	
Tetracycline (TET)		TR, IN				TR, IN	
Trimethoprim/sulfamethoxazole (TMP-SMX)	TR, IN		TR, IN	TR, IN		TR, IN	TR, IN
Vancomycin (VAN)		TR, IN				TR, IN	

* Flucloxacillin or methicillin are accepted as a marker for oxacillin resistance if oxacillin is not reported (ECDC)

2.4 Assessment from a forward-looking scientific perspective

The initial shortlist of resistant priority pathogens in Switzerland was further assessed by scientists from the National reference laboratory for the early detection and monitoring of novel antibiotic resistance (NARA). Their forward-looking perspective is mainly informed by the insights gained from monitoring of emergent resistance mechanisms. Their assessments are provided in Chapter 5, [Boxes 3-6](#).

2.5 Tiered scoring of resistant pathogens across the selected medical need criteria

Feedback from the consultation process suggested a relative weighing of the selected medical need criteria and their tiered scoring, and the design of a composite score across the selected medical need criteria by pathogen. The scoring should facilitate a systematic and consistent ranking of the pathogens which had been primarily identified by the clinical experts.

Applying a Multi-Criteria Decision Analysis (MCDA) methodology, we developed a first proposal of such a ranking. It may serve as illustration and stimulus for future work. Refer to [ANNEX 2](#) for the description of the procedure and the outcomes.

3 Selection and scoring of medical need criteria

This chapter provides justifications of the selection of three medical need criteria and describes their proposed scoring systems in Switzerland compared to the WHO scoring.

3.1 Selection of the medical need criteria

In the first round of interviews a majority of the experts considered four of the eight WHO criteria applicable for Switzerland: mortality, treatability, trend of resistance, and incidence. The other criteria were considered less relevant for the following reasons:

- *Preventability in healthcare setting and community:* The high standard of the Swiss healthcare system reduces the relevance of this criterion.
- *Non-fatal health burden, and transmissibility:* Challenges in providing scoring data of sufficient quality would put the objective assessment of these criteria at risk.
- *Pipeline:* Compounds currently in development may fail to reach the market even if they made it to late development stages (phases 2 and 3). Therefore, this criterion was not deemed relevant for the purpose pursued with the Swiss BPPL.

Although five of six members³ emphasised the relevance of mortality, the relatively low mortality in Switzerland reduces the weight of this criterion. The published mortality numbers represent estimates [13] rather than information from medical charts. Collecting mortality data from medical charts, and differentiation of whether a patient died from the infection or with an associated infection, would require a separate study. These considerations led the team to discard the mortality criterion, a decision shared by the RKI for similar reasons.

The two criteria described below have been used by the RKI. The expert team advised not to use them in the current project:

- *Reporting obligation* does not necessarily correlate with the relevance of the pathogens from an AMR perspective, as the example of the reporting obligation for *Clostridium botulinum* in Switzerland illustrates.
- *Clinical relevance:* The experts pointed to questions related to its definition: Particularly the consideration of how badly people live with the disease and its side effects may at least partly overlap with the WHO criterion of non-fatal health burden. Furthermore, a scoring of this criterion by expert opinion was suspected to be biased by recent clinical experience.

These considerations resulted in the following final set of medical need criteria recommended for use in Switzerland for the purpose of guiding (political) decisions about the selection and ranking of antibiotics for priority remuneration:

- Treatability
- Trend of resistance
- Incidence

[ANNEX 1](#) provides a more detailed justification for not considering the other WHO medical need criteria.

3.2 Scoring the medical need criteria

This sub-chapter describes and justifies the proposed scoring of the three selected medical need criteria in Switzerland, and its comparison with the scoring definitions applied by the WHO.

³ One of the seven experts only joined the project in the second round of one-on-one interviews.

3.2.1 Treatability

WHO definition of Treatability

Composite criterion which encompasses: number of molecule(s) listed in the guidelines, their efficacy ranking (1st or lower lines of treatment versus last resort), safety profile, availability of oral/ Outpatient Parenteral Antimicrobial Therapy (OPAT) formulation, presence of paediatric formulation, concomitant resistance, and cost

Experts' discussion

There are no national treatment guidelines for the inpatient setting in Switzerland. The expert team unanimously agreed with the use of “treatability rate” by pathogen which was created for the purpose of this project.

Information about further aspects of treatability may be accessed on the ANRESIS website by filtering the pathogen-antibiotic combinations by microorganism, antimicrobials, oral versus intravenous dosage forms, Swiss regions, AWaRe classification (AWaRe), sample type (blood, urine), and combinations thereof.

How treatability rates are built

Treatability rates inform about the scope of (potentially) effective pathogen-antibiotic combinations for treatment of infections caused by individual pathogens. The degree of the bacteria's susceptibility to the bactericidal or bacteriostatic effects of the antibiotic can give a hint at the potential effectiveness of the antibiotic treatment. Therefore, to provide a basis for the description of the treatability rate metric we first referred to ANRESIS' published **susceptibility rates** by pathogen-antibiotic combination: They are quotients of the number of isolates susceptible to the antibiotic in the dividend and the number of all isolates tested and reported to ANRESIS in the divisor. An appropriate susceptibility rate suggests that the antibiotic treatment may be effective.

Figure 1, copied from ANRESIS for illustration purposes, informs that 46 percent of *Shigella spp.* isolates showed susceptibility to Amoxicillin. To interpret this data with a view on gauging treatability the clinical experts accepted pathogen-antibiotic susceptibility rates $\geq 75\%$ as (potentially) effective first-line treatment options.

With a 46% susceptibility rate Amoxicillin, albeit a viable treatment option for *Shigella spp.* infections, will likely not be an effective treatment. Viability is inferred from the fact that the pathogen-antibiotic combination is listed by ANRESIS, at all.

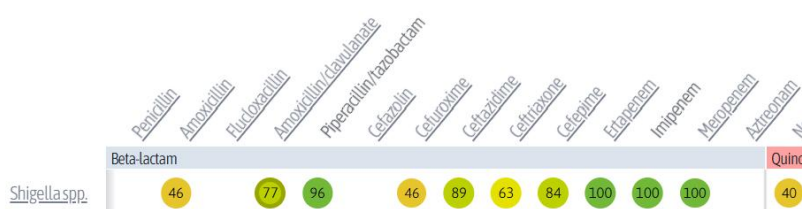


Figure 1 *Shigella spp.* susceptibility to β -lactam antibiotics

Source: ANRESIS

Box 2 provides information about the tiering of the susceptibility ranges in ANRESIS by means of the colour-coding of the disks. Following the interpretation in Table 3 in the Box, susceptibility rates $\geq 75\%$ would be expected to indicate medium to high probability of susceptibility of the bacterium to the antibiotic in a first-line treatment situation.

The cut-off values assigned to the colour codes are inferred from the observed ranges of susceptibility rates reported in the differently coloured disks. The interpretation texts were generated for the purpose of this project and are not officially stated in ANRESIS.

Susceptibility rates and the treatability score should not be applied uncritically or without taking the individual clinical context into account when making treatment decisions.

Table 3: Interpretation of ANRESIS colour-codes of pathogen-antibiotics susceptibility rate ranges

ANRESIS disk colour	Susceptibility rate range	Interpretation
dark-green	90 – 100%	high probability of susceptibility
olive-green	75 – 89%	medium probability of susceptibility
yellow	50 – 74%	low probability of susceptibility
orange & red	0 – 49%	medium – high risk of resistance

The **treatability rate** is a quotient built for a specific pathogen from the number of (potentially) effective pathogen-antibiotic combinations across all pathogen-antibiotic combinations for that pathogen in the dividend, and the number of all viable pathogen-antibiotic combinations for that pathogen in the divisor:

$$\frac{\text{No. of pathogen-antibiotic combinations with susceptibility rate } \geq 75\%}{\text{No. of all viable pathogen-antibiotic combinations for that pathogen}}$$

The treatability rate for *Shigella spp.* - illustrated in Figure 1 only for the pathogen-antibiotic combinations in the β -lactam group - is 70%: Out of the ten (10) viable pathogen-antibiotic combinations seven (7) qualify as (potentially) effective first-line treatment options.

To inform the determination of the Swiss BPPL, ANRESIS generated data panels for the proposed five resistant pathogens by clinical setting (ICU, inpatient (all wards, excluding ICU), and outpatient), thus facilitating a more granular localisation of the unmet medical need. These panels are available as Supplementary Data on the RTA website ([Swiss Round Table on Antibiotics | Downloads](#)) but are not publicly accessible on the ANRESIS website.

Note: These susceptibility rates may differ from the susceptibility rates ANRESIS publishes in the panels of multidrug-resistant (MDR) microorganisms (ESCR *E. coli*, ESCR *K. pneumoniae*, VRE, MRSA). This is due to several factors including but not limited to the calculation of the susceptibility rates from the test results of resistant isolates only, different time periods (two years in the published ANRESIS data versus one year (2024) only in the Swiss BPPL-panels), inpatient data including ICU in the published ANRESIS data versus separated for ICU and inpatients (all wards, excluding ICU) in the Swiss BPPL panels.

The treatability rates per pathogen and clinical setting are presented in column AO of the Supplementary Data panels.

It has to be reiterated that pathogen-antibiotic combinations with susceptibility rates $\geq 75\%$ should not be interpreted as (potentially) effective treatment options without further consideration of the individual medical situation, as well as economic, and administrative restrictions. This advice is illustrated by the following comments of the clinical experts and comments received from the consultation process:

- While the 75% susceptibility cut-off rate looks appropriate for first-line treatment of uncomplicated infections, it would be too low for treatment of serious infections, such as meningitis caused by *S. pneumoniae*.
- Treatability rates do not account for contraindications to the use of certain antibiotics in specific populations, e.g. tetracyclines for young infants and pregnant women. Furthermore, availability of a suitable oral formulation and licensing status for children is not reflected.
- An administrative restriction is present when mandatory health insurances do not reimburse OPAT drugs used in outpatient settings or LTCFs, even when they may be potentially effective treatments.
- Furthermore, one clinician noted that susceptibility rates refer to the wild type rather than mutated forms of bacteria. The latter are observed in colonised travellers returning from high-resistance countries and often do not respond to certain antibiotics (see [Table 1](#), risk group F).

A word of caution also needs to be said about the use of treatability rates: They can only provide a rough assessment of the appropriateness of the available arsenal of antibiotics per pathogen. They do not support an assessment of treatability of specific syndromes or infections affecting certain groups of patients.

Proposed Swiss scoring system for treatability in comparison with the WHO scoring

Concluding from the information about the building of the treatability rate score in the previous section, the proposed Swiss scoring of treatability is described in [Table 4](#).

Table 4: Swiss scoring system for the *TREATABILITY* criterion

#	WHO scoring	Proposed Swiss scoring
1	Number of first-line antibiotic options recommended by guidelines	Treatability rates by clinical setting (ICU, inpatient (all wards, excluding ICU), and outpatient), generated from resistant isolates as provided in the Supplementary Data (updated from time to time). ANRESIS disclaimer: “Although ANRESIS data is intended to be used to guide and support an optimal empirical antimicrobial therapy, its use does not substitute a thorough investigation of patients’ signs and symptoms, or sound diagnostic and therapeutic reasoning.”
2	Concomitant resistance reported for first-line options	The susceptibility data provided in the Supplementary Data reflect concomitant resistance. These data panels are created for the purpose of treatability scoring and are not publicly accessible on the ANRESIS website.
3	Availability of alternative option(s) for the most typical infectious syndrome	The published ANRESIS pathogen-antibiotic combinations may be filtered for a selection of syndromes. The data panels in the Supplementary Data cannot be filtered for syndromes.
4	Availability of various formulations (e.g. oral, OPAT, paediatric)	The published ANRESIS pathogen-antibiotic combinations may be filtered by intravenous and oral administration modes. In the Supplementary Data the share of oral formulations within the set of (potentially) effective therapies per pathogen and clinical setting is provided in column AS.
5	Accessibility of treatments based on cost	This score is not deemed relevant in this context because in Switzerland, antibiotics are reimbursed by the compulsory health insurance and cantons.

3.2.2 Trend of resistance

WHO definition of Trend of resistance rate

10-year trend of resistance rate data, where resistance rate is defined as percentage of resistant isolates out of the total number of isolates tested.

Experts’ discussion

Identification of the national unmet medical need is best informed by data from the national surveillance system. However, given the high cross-border people traffic to and from neighbouring and more distant countries for work, travel and trade, these countries’ AMR situation has a strong impact on Switzerland and should therefore be consulted as indicator of future trends of resistance in Switzerland.

Therefore, in this context, trend of resistance rates in WHO regions are less relevant indicators of the future AMR development in Switzerland than the AMR situation in countries heavily involved in the people traffic with Switzerland.

Proposed Swiss scoring system for trend of resistance in comparison with the WHO scoring

For the scoring of trend of resistance rates in Switzerland we propose using ANRESIS “resistance rates over time” data for the pathogen-antibiotic combinations listed in [Table 2](#). The data reflects percentages of resistant isolates out of all isolates tested (blood and CSF) on the national level and in different regions of Switzerland.

The data is currently available for the period of 2004 – 2025). The experts suggested that data of the most recent years may represent the fast-changing resistance patterns more accurately than long-term data.

Any trend may be gauged only visually from the line charts on the ANRESIS website. However, the Swiss Antibiotic Resistance Report 2024 (SARR 2024) [2] provides trend indicators, described by upward and downward directed arrows or a minus sign to describe the 4-year and 10-year increasing, decreasing and stable trends by 2023. This information is updated every two years, following the frequency of updates of the SARR report.

Refer to [Table 5](#) for the description of the proposed Swiss scoring.

Table 5: Swiss scoring system for the TREND OF RESISTANCE RATE criterion

#	WHO scoring	Proposed Swiss scoring
		ANRESIS: Resistance rates over time by pathogen-antibiotic combination, derived from resistant isolates, on the national level and, where available, by region. Furthermore, trend of resistance data generated in neighbouring and relevant more distant countries and/or relevant literature should be consulted.
1	Level 5: Increasing trend in ≥ 3 WHO regions (or in most regions with data)	less relevant in the Swiss context
2	Level 4: Increasing trend in 2 WHO regions	less relevant in the Swiss context
3	Level 3: Increasing trend in one WHO region	less relevant in the Swiss context
4	Level 2: Stable trend in all WHO regions	less relevant in the Swiss context
5	Level 1: Significantly decreasing trend in at least one WHO region, with no increase in any of the other regions	less relevant in the Swiss context

3.2.3 Incidence

WHO definition of Incidence

Global incidence of cases associated to resistance per 1 million population (all ages, all sexes, associated to resistance)

Experts' discussion

Some experts preferred the prevalence metric to the incidence metric. However, because antibiotic treatment courses per case are relatively short, the two metrics are expected to yield similar values for bacterial infections. Accordingly, the experts agreed to use incidence rather than prevalence data.

Proposed Swiss scoring system for incidence in comparison with the WHO scoring

For the scoring of incidence in Switzerland we propose using “incidence data series” data provided by ANRESIS for the pathogen-antibiotic combinations listed in [Table 2](#). To facilitate alignment of the Swiss scoring with the WHO’s definition we propose the following adaptations to the way how the ANRESIS data is selected and presented:

- While ANRESIS provides incidence data from resistant and from all (resistant and susceptible) isolates, we use data from resistant isolates only.
- For alignment with WHO’s scoring of cases per 1 million population we multiply the number of cases in the Swiss population and the denominator of 100,000 population used by ANRESIS by a factor of 10 to allow their direct comparison with the WHO scoring.
- Because WHO’s definition does not foresee the granularity of incidence data by pathogen-antibiotic combination we added the number of resistant isolates across all pathogen-antibiotic combinations, by pathogen.

ANRESIS does not distinguish isolates from patients with infections attributable to resistance from isolates from patients with infections associated to resistance. However, the number of isolates is deemed a fair proxy of the number of cases associated with resistance which is used by the WHO.

ANRESIS data is currently available for the period of 2010–2022 on the national and regional levels.

Refer to [Table 6](#) for the description of the proposed Swiss scoring.⁴

Table 6: Swiss scoring system for the INCIDENCE criterion

#	WHO scoring	Proposed Swiss scoring
1	Global Incidence of cases per 1 million population	Time series of the number of resistant isolates per 1 million inhabitants across all pathogen-antibiotic combinations, by pathogen, on the national level and, where available, by regions.
	High: > 10,000	
	Medium-High: 5,001–10,000	ANRESIS’ more granular information of incidence by pathogen-antibiotic combination, by pathogen, will support a better understanding of the major drivers of incidence.
	Medium: 1,001–5,000	
	Medium-Low: 100–1,000	
	Low: < 100	Furthermore, incidence data from neighbouring and relevant more distant countries should be consulted as indicators of future developments in Switzerland.

⁴ ANRESIS uses data from blood and cerebrospinal fluid (CSF) isolates.

4 Results

This chapter presents the scores of the three medical need criteria resulting from application of the proposed Swiss scoring systems.

4.1 Scoring results of treatability

Given the national BPPL's aim to guide (political) decisions about the selection of antibiotics for priority remuneration, and the limited availability of antibiotics in Switzerland, the treatability criterion got the greatest attention, similar to the highest relative weight which the WHO team assigned to this criterion in the generation of the global BPPL (2024).

Table 7 provides the treatability rates by clinical setting for the five resistant pathogens shortlisted by the experts. The data is sourced from the Supplementary Data ([Swiss Round Table on Antibiotics | Downloads](#)).

Table 7 Treatability rates by pathogen and clinical setting

Pathogen	ICU	Inpatient	Outpatient
<i>E. coli</i> as reference strain for Carbapenem-resistant Enterobacterales (CRE)	1/24 (4%)	2/24 (8%)	6/20 (30%)
Carbapenem-resistant <i>Acinetobacter baumannii</i> (CRAB)	0/13 (0%)	1/13 (8%)	0/9 (0%)
Carbapenem-resistant <i>Pseudomonas aeruginosa</i> (CRPA)	2/12 (17%)	4/12 (33%)	1/9 (11%)
Vancomycin-resistant <i>Enterococcus faecium</i> (VRE)	4/19 (21%)	3/19 (16%)	1/14 (7%)
Methicillin-resistant <i>Staphylococcus aureus</i> (MRSA)	13/31 (42%)	12/31 (39%)	11/28 (39%)

The data indicates limited availability of (potentially) effective antibiotics for first-line treatment mainly for CRE (in all clinical settings), and CRAB and CRPA (in the ICU and inpatient settings), with a most scary paucity for CRAB.

An illustrative tiered scoring of treatability rate is described in ANNEX 2.

4.2 Scoring results of trend of resistance

Refer to Figure 2 for an illustration how the increasing, stable, and decreasing trend indicators are presented in the SARR 2024 report [2], (here for *E. coli*).

The trend data on the ANRESIS website and in the SARR 2024 report reflect averages from resistant isolates across all clinical settings. The number of antibiotics by pathogen listed in the data panels of the Supplementary Data is higher than in the SARR 2024 report which focuses on the clinically most relevant antibiotics according to the ANRESIS Advisory Board's assessment.

Table 6. a: Resistance rates of invasive *Escherichia coli* isolates in humans in 2023.

Antimicrobial	West*		North-East*		South*		Total		95% CI***	Trend**	
	n	%	n	%	n	%	n	%		4y	10y
Aminopenicillins	1063	51.8	4207	49.2	243	41.2	5513	49.4	48.7–50.1	–	↓
Amoxicillin-clavulanic acid	1042	32.3	4325	27.7	243	18.5	5610	28.1	27.5–28.7	↑	↑
Piperacillin-tazobactam	1295	10.9	4415	8.6	555	3.1	6265	8.6	8.2–9.0	↑	↑
Cephalosporin 2 nd gen.	314	38.2	3243	15.9	444	14	4001	17.4	16.8–18.0	↑	↑
Cephalosporin 3 rd /4 th gen.	1375	14	4663	11.9	555	8.5	6593	12.1	11.7–12.5	↑	↑
Carbapenems ¹	1176	0.2	4394	0	555	0	6125	0.1	0.1–0.1	–	–
Aminoglycosides	1162	11.8	4532	10	555	6.3	6249	10	9.6–10.4	–	↑
Trimethoprim-sulfamethoxazole	1369	29.1	4283	26.5	555	23.8	6207	26.8	26.2–27.4	–	↓
Fluoroquinolones ²	1371	24	4647	17.9	555	16	6573	19	18.5–19.5	↑	↓
Nitrofurantoin	602	1.3	1124	0.2	99	0	1825	0.5	0.3–0.7	–	↓
Fosfomycin	600	5	1713	1.2	99	2	2412	2.2	1.9–2.5	↑	↑

¹ Carbapenems: imipenem, meropenem

² Fluoroquinolones: ciprofloxacin, norfloxacin, ofloxacin

*West (GE, NE, VD, JU, FR), South (TI), North-East (other cantons) according to linguistic regions. **Trends were modelled with logistic regressions.

Arrows represent a significant effect ($p < 0.05$) of the year on the corresponding outcome (increase, decrease). ***95% confidence intervals (CI) were calculated by the Wilson score method.

Figure 2 Resistance rates of invasive *E. coli* isolates in humans in 2023. Source: [2], pg 88

Table 8 provides the rates of pathogen-antibiotic combinations by type of trend for the five shortlisted resistant pathogens. Source: SARR 2024 report [2]

Table 8 Rates of pathogen-antibiotic combinations by 10-year trend indicator

Pathogen	Increasing trend	Stable trend	Decreasing trend
<i>E. coli</i> as reference strain for Carbapenem-resistant Enterobacterales	6/11 (55%)	1/11 (9%)	4/11 (36%)
Carbapenem-resistant <i>Acinetobacter baumannii</i>	1/4 (25%)	3/4 (75%)	-
Carbapenem-resistant <i>Pseudomonas aeruginosa</i>	1/6 (17%)	5/6 (83%)	-
Vancomycin-resistant <i>Enterococcus faecium</i>	1/5 (20%)	3/5 (60%)	1/5 (20%)
Methicillin-resistant <i>Staphylococcus aureus</i>	4/13 (31%)	7/13 (54%)	2/13 (15%)

Except for *E. coli*, the stable 10-year trend is dominant. With 6/11 or 55% of the *E. coli*- antibiotic combinations showing an increasing resistance trend, *E. coli* stands out in this trend category.

An illustrative tiered scoring of trend of resistance is described in ANNEX 2.

4.3 Scoring results of incidence

The adaptations proposed in sub-chapter 3.2.3 to the way ANRESIS data is selected and presented to align with the WHO scoring definition results in the scoring data shown in Table 9: Column A reflects the

denominator of 100,000 used by ANRESIS, and column B reflects the denominator of 1 million used by the WHO.

Table 9 Incidence of resistant isolates by pathogen

Pathogen	A: No. of resistant isolates per 100,000 inhabitants across all antibiotics by pathogen in 2022	B: No. of resistant isolates per 1 million inhabitants across all antibiotics by pathogen in 2022
<i>E. coli</i> <i>E. coli</i> as reference strain for Carbapenem-resistant Enterobacterales	114.97	1,149.7
<i>S. aureus</i>	29.94	299.4
<i>E. faecium</i>	7.69	76.9
<i>P. aeruginosa</i>	4.17	41.7
<i>Acinetobacter spp.</i>	0.46	4.6

The mapping of incidence rates of the shortlisted resistant pathogens to the WHO scoring tiers is provided in [Table 10](#).

Table 10 Incidence of resistant isolates by pathogen per 1 million inhabitants in Switzerland, by WHO scoring tiers

WHO scoring tiers	Scoring of the pathogens in Switzerland
High: > 10,000	-
Medium-High: 5,001–10,000	-
Medium: 1,001–5,000	<i>E. coli</i>
Medium-Low: 100–1,000	<i>S. aureus</i>
Low: < 100	<i>P. aeruginosa</i> , <i>Acinetobacter spp.</i> , <i>E. faecium</i>

Not surprisingly, the incidence rates in Switzerland fall within the WHO’s low to medium categories, with *E. coli* distancing the other pathogens by far: This pathogen’s incidence is four times higher than the closest follower, *S. aureus*, and 230 times higher than *Acinetobacter spp.*

An illustrative tiered scoring of incidence is described in [ANNEX 2](#).

5 Discussion and conclusion

While the values of the three medical need criteria in the sub-chapters 4.1-4.3 show a clear focus on *E. coli* (as reference strain for the Enterobacterales), the information shared by the experts in the one-on-one interviews and further discussed in the plenary sessions provided more detail. Further detail and justification of the selection of pathogens for the proposed Swiss BPPL was also provided by scientists from the National reference laboratory for the early detection and monitoring of novel antibiotic resistance (NARA). Sub-chapters 5.1-5.6 provide a summary of their contributions to the discussion. Sub-chapter 5.7 justifies why certain pathogens were not considered for inclusion in the Swiss BPPL. Sub-chapter 5.8 provides the proposed first version of a Swiss BPPL.

5.1 Carbapenem-resistant *E. coli* / Enterobacterales (CRE)

The NARA scientists identified the major threat to treatability of Enterobacterales in isolates belonging to the so-called metallo- β -lactamases (MBLs) being insensitive to the inhibitory action of clinically available β -lactamase inhibitors. Refer to [Box 3](#) for more details.

Box 3 Lack of therapeutic options for isolates with metallo- β -lactamase mechanism

Carbapenem resistance can be mediated either by enzymes (carbapenemases) or other mechanisms (permeability defects mainly). For treatment of infections caused by carbapenem-resistant strains, several therapeutic options are currently available, including Ceftazidime-avibactam, Meropenem-vaborbactam, Imipenem-relebactam*, or Cefiderocol*.

Among carbapenemase-producers, the major threat is related to those producing metallo- β -lactamases (MBL), corresponding infections being extremely difficult to treat due to a critical lack of therapeutic options, considering reduced susceptibility or even resistance to Cefiderocol being commonly observed for such strains. Next to Cefiderocol*, only the highly effective Aztreonam-avibactam* combination option remains available.

Furthermore, recent studies, including one conducted by the NARA Swiss Reference Centre, showed effectiveness of Sulbactam-Durlobactam* against MBL-producing *Escherichia coli* resistant to both Aztreonam-avibactam and Cefiderocol [14].

* antibiotics not authorised in Switzerland

Furthermore, the clinical experts experience a lack of oral treatment options for ESBL-producing *E. coli* and *K. pneumoniae* as a most critical unmet medical need.

A clinical expert in paediatric medicine reminded that the implications of the lack of oral treatment options are of particular concern in the treatment of infants and children: The mere availability of oral treatment options does not address whether these can be dispensed in child-appropriate formulations and whether a label dose is available for this patient group. She suggested that future iterations of the Swiss BPPL should consider an incorporation of the paediatric perspective.

5.2 Third-generation Cephalosporin-resistant Enterobacterales

Some responses to the consultation suggested considering inclusion of 3GCR Enterobacterales in the Swiss BPPL.

While the NARA scientists agreed that there is a need for development of oral options for the treatment of infections caused by 3GCR Enterobacterales in the long term, they assessed this need as less

important than the need for more treatment options for carbapenem-resistant Enterobacterales. Refer to [Box 4](#) for more details.

Box 4 Assessment of treatability of 3GCR Enterobacterales

We agree that there are currently not many options available for outpatient (oral) treatment of infections associated with 3GCR-Enterobacterales. And the recently approved β -lactam therapeutic options will not address this issue because they are only IV molecules requiring multiple daily administrations.

These infections are generally treatable with intravenous therapeutic options. However, their administration requires hospitalisation of the patients, which comes with a significant cost to public health.

Several interesting molecules are currently in phase I/II development which meet the need for oral treatment options (tebipenem, ceftibuten-avibactam, etc.), however they are not yet available.

While the development of oral treatment options is suggested in the future, the medical need is less important than that for carbapenem-resistant Enterobacterales.

5.3 Carbapenem-resistant *Acinetobacter* spp. (CRAB)

The clinical experts see the treatability of this pathogen at risk.

Please refer to [Box 5](#) for the NARA scientists' assessment of treatability and new treatment options for *A. baumannii*-associated infections, as well as *E. coli*.

Box 5 Assessment of unmet medical need and new treatment options for A. baumannii

Isolates of carbapenem-resistant *Acinetobacter baumannii* are most often resistant not only to all β -lactams, but also to many other molecules belonging to distinct antibiotic classes.

Sulbactam-Durlobactam is a great therapeutic option, currently only available in the USA. Even if this drug combination remains ineffective against MBL-producing isolates, the predominance of OXA-23-producing isolates in Europe (including Switzerland) which are most often susceptible to Sulbactam-Durlobactam therefore highlights the great value of this therapeutic option for *Acinetobacter baumannii*-associated infections.

Availability of Sulbactam-Durlobactam should be considered as a priority.

5.4 Carbapenem-resistant *P. aeruginosa* (CRPA)

The low treatability rates in all clinical settings shown in [Table 7](#) made the experts conclude that treatability of this pathogen is at risk.

5.5 Vancomycin-resistant *Enterococcus faecium* (VRE)

VRE scores relatively well in all three medical need categories. However, the experts voiced concerns that increasing resistance to Daptomycin will leave Linezolid and Tigecycline as the last resort treatment options. They pointed to Germany where resistance to Linezolid is already highly prevalent.

5.6 Methicillin-resistant *S. aureus* (MRSA)

As the NARA scientists outline in [Box 6](#) the lack of β -lactam options and the toxicity potential of the available treatment options, when used in long-term treatment, may present a risk to the patients and cause higher costs when negative side-effects occur.

Box 6 Assessment of medical need caused by infections with MRSA

MRSA incidence rates have been stable in Switzerland for many years at relatively low levels, and there are several effective treatment options available for this pathogen.

However, many of these treatments (non- β -lactams) have increased toxicity when used over the long term and have numerous contraindications. The lack of β -lactam options is therefore a cause for concern.

MRSA is associated with many serious infections of all types (abscessed pneumonia, chronic abscesses, bacteraemias, osteoarticular infections, and more) which may require long-term treatment, hence the issue of toxicity.

Finally, as MRSA spreads both in hospitals and the community, controlling its spread is more difficult.

Given the availability of effective, albeit potentially toxic non- β -lactam treatment options, the inclusion of this pathogen in the Swiss BPPL can be justified, but probably with a lower degree of importance compared to the other pathogens mentioned.

Probably with cases such as the ones described in [Box 6](#) in mind the clinical experts did not hesitate to include MRSA in the Swiss BPPL, nor did any participant of the consultation question the decision. However, compared to the other pathogens or pathogen groups of the proposed Swiss BPPL the scores of the three medical need criteria for MRSA showed the least worrying situation compared to the other pathogens:

- In [Table 7](#), MRSA's treatability rates – albeit all below 50% – are the highest in all clinical settings compared to the scores of the other listed pathogens.
- [Table 8](#) shows the highest share of MRSA-antibiotic combinations in the “stable” trend of resistance category. However, three other pathogens in this list show higher “stable” trend of resistance rates.
- In [Table 9](#) MRSA's incidence ranks second behind *E. coli*, in the medium-high tier.

The relatively good scores of MRSA compared to the scores of the other resistant pathogens in the proposed Swiss BPPL is also reflected in the composite score in [Table A7](#) at the end of [ANNEX 2](#).

5.7 Pathogens not recommended for inclusion in the initial version of the Swiss BPPL

The experts did not recommend including the following pathogens in the initial version of the Swiss BPPL:

- *S. pneumoniae*: Penicillin-resistant cases are still very rare in Switzerland. The availability of vaccines and hence an effective prevention made the experts refrain from assessing this pathogen for treatability.

- *N. gonorrhoeae*: Culture-based susceptibility testing is rarely performed, and the more widely applied PCR-testing for identification of the genotype does not provide information about resistance. The currently rare cases with low susceptibility to ceftriaxone may still be treated by increased dosing.
- *Salmonella spp.*: ANRESIS does not currently report incidence of (resistant and susceptible) isolates of *Salmonella spp.* in Switzerland. Although there are cases of infections in the clinic, resistant pathogens are rare. Infections with *Salmonella spp.* (and with *Shigella spp.*) can still be appropriately treated with the current arsenal of antibiotics in Switzerland.
- *H. influenzae*: Although the treatment options may be limited due to the lack of oral dosage forms, the currently low number of cases does not justify claims of an unmet medical need in the context of this report.
- *Stenotrophomonas maltophilia*, *Campylobacter jejuni*, and *Mycobacterium abscessus* were mentioned by some experts during the one-on-one interviews but not further assessed during the course of the project.

5.8 Conclusion

The scorings of the three medical need criteria and the assessments by scientists confirmed the preselection of pathogens, and their ranking, which was primarily informed by clinical experience. The following list of resistant pathogens is therefore proposed as the initial version of the Swiss BPPL.

- Carbapenem-resistant Enterobacterales
- Carbapenem-resistant *Acinetobacter baumannii*
- Carbapenem-resistant *Pseudomonas aeruginosa*
- Vancomycin-resistant *Enterococcus faecium*
- Methicillin-resistant *Staphylococcus aureus*

This ranking of the pathogens is also confirmed by the outcome of the tiered scoring of the selected medical need criteria, and the composite score across these criteria, as proposed in [ANNEX 2, Table A7](#).

Annexes

- | | |
|---------|---|
| ANNEX 1 | Reasons for excluding certain WHO medical need criteria |
| ANNEX 2 | Tiered scoring of resistant pathogens across the selected medical need criteria |

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ANNEX 1 Reasons for excluding certain WHO medical need criteria

The justifications provided in this annex originate from one-on-one interviews with the members of the expert team.

Mortality

WHO definition	Justification of non-consideration
Case Fatality Ratio (Pooled prevalence of all-cause mortality (%) among patients with infections caused by antibiotic-resistant pathogens)	The relatively low mortality in Switzerland reduces the weight of this criterion. Furthermore, collecting mortality data from medical charts implies a significant effort, and differentiating whether a patient died from the infection or with an associated infection will pose a huge challenge and impair data quality.

Preventability in healthcare setting and community

WHO definition	Justification of non-consideration
The existence and effectiveness of preventive measures in containing the transmission of the target AMR pathogen and reducing disease burden. This criterion encompasses two distinct aspects of preventability: 1. Individual-based infection prevention and control (IPC) measures, including hand hygiene and standard and transmission-based precautions (such as contact, isolation, and barrier precautions). 2. Community-based IPC measures, including vaccination, water sanitation, access to health services, and food safety.	<p>Preventative measures are well established in the clinical practice in Switzerland. While infection prevention and control (IPC) measures are easily applicable, decolonisation measures are difficult to apply.</p> <p>However, despite many preventative measures in hospitals including surveillance of outbreaks, certain problems do occur on a recurring basis, such as hospital-acquired pneumonia (HAP), ventilator-associated pneumonia (VAP), and the pop-up of opportunistic pathogens, particularly pathogens also prevalent in other than the human domain.</p> <p>The NOSO strategy was established in the frame of the National Health Strategy 2020. Its aims include a reduction of the national prevalence of healthcare-associated infections (HAI) from 6% in 2022 to 5% in 2030 and 4% in 2035.</p> <p>Implementation of the first measures started at the end of 2016, and progress is monitored and assessed in published annual reports. Between 2017 and 2024 the national prevalence of HAI has been stable at around 6%. (Source: <i>Swissnoso Jahresbericht Epidemiologie und Prävention von health-care-assoziierten Infektionen in Schweizer Akutspitälern 2024</i>, BAG, 2025)</p> <p>Public health interventions in the Swiss community are well established and accessible.</p>

Non-fatal health burden

WHO definition	Justification of non-consideration
Years Lived with Disability (YLDs) per million inhabitants, including all ages and all sexes, attributable to infections by each resistant pathogen	<p>Non-fatal health burden (NFHB) is relevant in the general healthcare cost discussions. Usually, the treatment outcome for infections is dichotomous: full recovery or death. NFHB due to complications associated with antibiotic treatment may be lifelong. Such cases would mainly be seen in the rare cases of survivors of resistant infections.</p> <p>NFHB data is not consistently defined nor generally collected in Switzerland. Its systematic generation would imply a significant effort and the need for collaboration across administrative areas of responsibility.</p>

Transmissibility

WHO definition	Justification of non-consideration
<p>Evidence of transmission of the AMR pathogen among different pathways. Two distinct domains are considered:</p> <p>Human-to-human transmission: outbreak capability in healthcare / community setting.</p> <p>Transmission between humans and animal, food, and environment compartments</p>	<p>Compared to outbreaks caused by viruses, most dangerous bacterial pathogens do not have a relevant outbreak potential, at least in the human domain. Transmissibility is specific for each pathogen. While MDR tuberculosis pathogens transmit relatively easily in case of open pulmonary tuberculosis, others such as carbapenem-resistant intestinal pathogens are not easily transmissible but still have the potential to paralyse entire hospital wards, including ICUs. Good transparency and reporting in Switzerland prevent outbreaks from becoming an epidemic. Solid data about transmission pathways (one of the WHO scoring criteria) for Switzerland and Europe are missing. Its documentation would require complex classification, which is hardly feasible, and it would be difficult to maintain the data up to date.</p>

Pipeline

WHO definition

The criterion assesses the extent to which the antibacterial pipeline, both currently and over the next 5–7 years, can effectively meet clinical needs for treating each resistant bacterial pathogen.

The criterion considers the number of newly approved antibiotics in the last 5–7 years, as well as the number of candidates in the clinical developmental pipeline that meet WHO innovation criteria, such as new chemical classes, novel targets, and absence of cross-resistance. Additionally, it evaluates the availability of oral formulations for both the new candidates and those under development.

Justification of non-consideration

All experts agreed that this criterion is not relevant for the aim pursued by this project which is different from the aim pursued by the WHO BPPL. The Swiss BPPL aims to identify medical need areas in Switzerland that lack an adequate arsenal of antibiotic treatment options. Therefore, it focuses on drugs already available in other countries. The observed high attrition rates even in late stages of drug development do not allow to predict whether the compounds will become marketable products.

ANNEX 2 Tiered scoring of resistant pathogens across the selected medical need criteria

Background

Feedback from the consultation process suggested that the identification of the pathogens for the Swiss BPPL should be complemented by a tiered scoring of the selected medical need criteria and a composite score across these criteria. This should facilitate their systematic and consistent ranking with regard to the unmet medical need they can cause if not addressed by an appropriate arsenal of antibiotics.

We herewith present a proposal which may serve as illustration and stimulus for future work using a systematic method (e.g. a Multi-Criteria Decision Analysis (MCDA)). Yet, it shall be kept in mind that even in a structured scoring process like MCDA “decision-makers’ objectives are within the panel’s personal discretion and not normatively determined by hard quantitative or qualitative evidence” [15].

Model structure

In the next sections we present a conceptual illustration of a possible scoring system following a basic MCDA approach whose structure is laid out in [Figure A1](#).

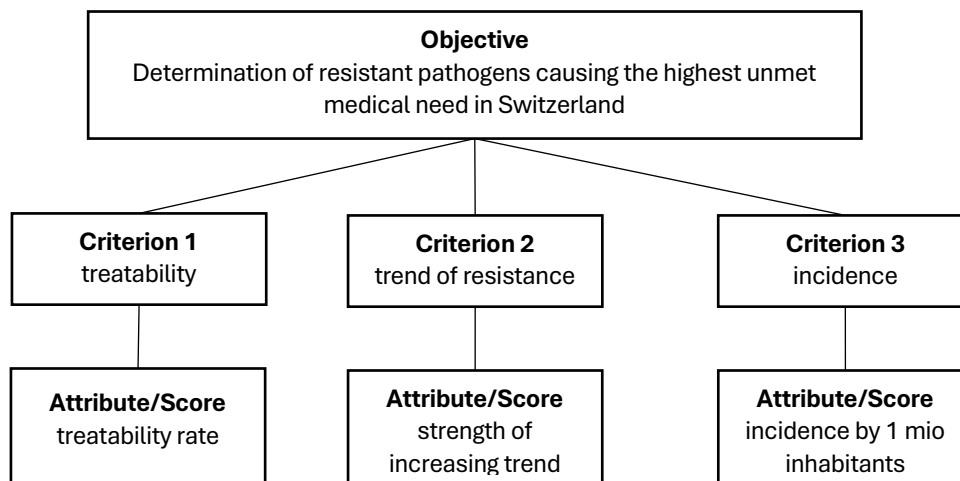


Figure A1 Model structure

Applying relative weights to the selected medical need criteria

For the purpose of this illustrative scoring of the selected medical need criteria, we used the respective weights that were elaborated by the WHO’s expert panel by means of the PAPRIKA procedure as a starting point. The weights represent the scale and relative importance of a criterion under consideration. See [Figure A2](#).

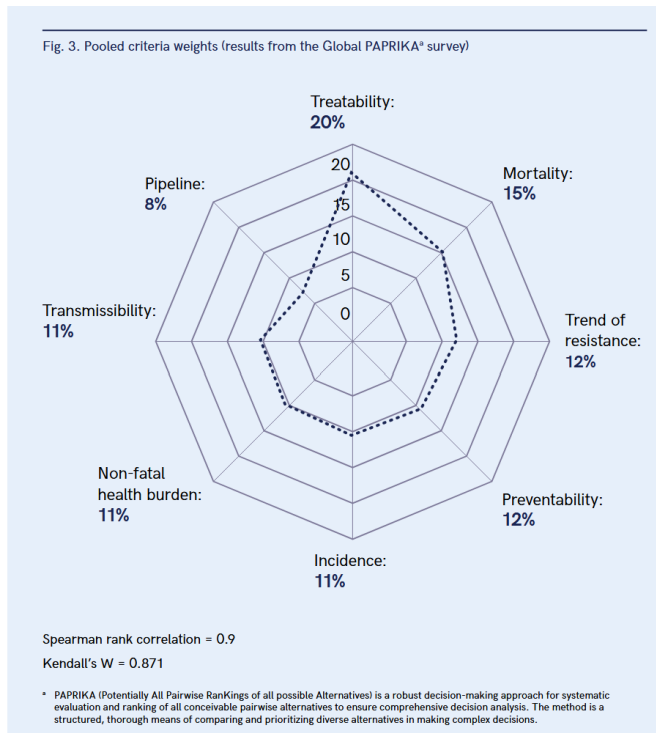


Figure A2 Pooled criteria weights from the Global PAPRIKA survey, WHO BPPL (2024), page 8

Given that the Swiss project used only three and not eight criteria, we extrapolated the WHO weights for the three selected criteria. The result is provided in Table A1. The calculation is demonstrated here for the treatability criterion: WHO weight of treatability (20%) divided by the sum of WHO - weights of the three criteria selected for Switzerland (43%) multiplied by 100 = 47%.

Table A1 Weights of the medical need criteria used in the Swiss context

Criterion	Relative weight
Treatability	47%
Trend of resistance	28%
Incidence	26%
Total	100%

NB: This weighing was developed for illustration purposes and should not pre-empt a different final version.

Definition of the attributes and their scoring

For the purpose of this illustration, we used direct rating scales with numeric values from 1 – x. Lower values identify worse outcomes than higher values. Because we applied the simplest, namely the additive way of aggregation, the proposed scoring tiers have to meet the requirement that equal increments reflect equal quantitative distances within the criterion.

Treatability

As a quantitative measure of treatability, we created the “treatability rate” attribute which provides high-level information about the adequacy of the available arsenal of (potentially) effective first-line treatment options by pathogen and clinical setting (ICU, inpatient (all wards, excluding ICU), outpatient).

Table A2 copies the treatability rates of the shortlisted resistant pathogens in the ICU setting provided in Table 7.

Table A2 Scoring of the attribute “treatability rate”

Pathogens	Treatability rate numbers (ICU setting)	Treatability rate percentages (ICU setting)
<i>A. baumannii</i> *	0/13	0%
<i>E. coli</i> **	1/24	4%
<i>P. aeruginosa</i>	2/12	17%
<i>E. faecium</i>	4/19	21%
<i>S. aureus</i>	13/31	42%

Legend: *, reference for *Acinetobacter* spp.; **, reference for Enterobacterales

The treatability rate percentages by pathogen in Table A2 informed the choice of five tiers in Table A3. We chose the treatability rates in the ICU setting where the most critical-stage patients are treated.

Table A3 Definition of the scoring tiers of the attribute “treatability rate”

Tiers for illustration purposes (ICU setting)	Scoring for illustration purposes (ICU setting)
0% - 10%	1
11% - 20%	2
21% - 30%	3
31% - 40%	4
41% - 50%	5

NB: These scoring tiers were developed for illustrative purposes and should not pre-empt a different final version.

Note: The valuation of the treatability rate attribute entailed the need for judgmental decision: The choice of the cut-off susceptibility rate of $\geq 75\%$ that segregates (potentially) effective first-line treatment options from treatment options with lower probability of susceptibility and medium-high resistance greatly influences the treatability rate: The higher the cut-off susceptibility rate, the lower the treatability rate and hence the more urgent the perceived need of further treatment options.

Depending on the research interest, treatability rates may be generated for further selections, such as but not limited to the average across all clinical settings, antibiotic classes (e.g. β -lactams only), dosage forms (oral, OPAT, iv), and more.

Trend of resistance

There are two sources of information about trend of resistance: ANRESIS website and the SARR 2024 report.

On its website ANRESIS provides resistance rates (% R) over time for the period of 2004-2025 derived from invasive blood culture data from susceptible and resistant isolates (refer to sub-chapter 3.2.2 in the report). Data is currently provided for the pathogen-antibiotic combinations identified in Table 2 of the report.

SARR 2024, chapter 6, provides trend indicators, described by upward and downward directed arrows or a minus sign to describe the 4-year and 10-year increasing, decreasing and stable trends by 2023. This information is updated every two years, following the frequency of SARR updates. See Figure A3 for *E. coli* as an illustration.

Table 6. a: Resistance rates of invasive *Escherichia coli* isolates in humans in 2023.

Antimicrobial	West*		North-East*		South*		Total		Trend**		
	n	%	n	%	n	%	n	%	95% CI***	4y	10y
Aminopenicillins	1063	51.8	4207	49.2	243	41.2	5513	49.4	48.7–50.1	–	↓
Amoxicillin-clavulanic acid	1042	32.3	4325	27.7	243	18.5	5610	28.1	27.5–28.7	↑	↑
Piperacillin-tazobactam	1295	10.9	4415	8.6	555	3.1	6265	8.6	8.2–9.0	↑	↑
Cephalosporin 2 nd gen.	314	38.2	3243	15.9	444	14	4001	17.4	16.8–18.0	↑	↑
Cephalosporin 3 rd /4 th gen.	1375	14	4663	11.9	555	8.5	6593	12.1	11.7–12.5	↑	↑
Carbapenems ¹	1176	0.2	4394	0	555	0	6125	0.1	0.1–0.1	–	–
Aminoglycosides	1162	11.8	4532	10	555	6.3	6249	10	9.6–10.4	–	↑
Trimethoprim-sulfamethoxazole	1369	29.1	4283	26.5	555	23.8	6207	26.8	26.2–27.4	–	↓
Fluoroquinolones ²	1371	24	4647	17.9	555	16	6573	19	18.5–19.5	↑	↓
Nitrofurantoin	602	1.3	1124	0.2	99	0	1825	0.5	0.3–0.7	–	↓
Fosfomycin	600	5	1713	1.2	99	2	2412	2.2	1.9–2.5	↑	↑

¹ Carbapenems: imipenem, meropenem

² Fluoroquinolones: ciprofloxacin, norfloxacin, ofloxacin

*West (GE, NE, VD, JU, FR), South (TI), North-East (other cantons) according to linguistic regions. **Trends were modelled with logistic regressions.

Arrows represent a significant effect ($p < 0.05$) of the year on the corresponding outcome (increase, decrease). ***95% confidence intervals (CI) were calculated by the Wilson score method.

Figure A3 Trend information of resistance rates of invasive *E. coli* isolates in humans in 2023. Source: SARR 2024

For the purpose pursued by this project, namely to provide guidance for (political) decisions about the selection of antibiotics for priority remuneration, various scoping options may be considered when defining the attribute(s)/score(s) for trend of resistance: the length of the time period of trend data (e.g. 4 or 10 years), whether trend data for certain antibiotics (e.g. Carbapenems, Vancomycin, Methicillin/Flucloxacillin or antibiotics classified by WHO as Reserve antibiotics) should be weighted higher than others, or whether additional attributes/scores should be defined informing about the most recent level of resistance or extent of change in the chosen time period, and further options.

In the illustrative approach presented here, we defined an attribute/score “increasing trend” from SARR 2024 trend data across all antibiotics by a pathogen, with a built-in relative weighing of the numbers of pathogen-antibiotic combinations with increasing, stable, and decreasing trends as percentage of the

total number of antibiotics by pathogen. The final attribute/score uses the relative percentage of the increasing trend. The building of the attribute/score is explained below and demonstrated for *E. coli* in Table A4.

- Because the number of antibiotics by pathogen varies, the scoring values need to be provided as percentages to enable comparison across pathogens.
- We created the attribute/score on the basis of 10-year trend data (column A) and applied a simple weighing by adding the number of antibiotics with the same increasing, stable or decreasing trend in the 4-year horizon (column B). The sum of the two values is shown in column C.
- The summary percentage score in column D is calculated by dividing the value in column C by the total number of antibiotics for the pathogen under consideration.

Table A4 Building the trend of resistance value, illustrated with *E. coli*

Qualitative trend per SARR 2024	10-y trend; no. of antibiotics	4-y trend - if same as 10-y trend; no. of antibiotics	(A)+(B)	% of Total
	(A)	(B)	(C)	(D)
increasing	6	5	11	65%
stable	1	1	2	12%
decreasing	4	0	4	24%
TOTAL	11	6	17	100%

NB: This scoring was developed for illustrative purposes and should not pre-empt a different final version.

We chose to use four tiers for the relative percentages of the increasing trend.

Table A5 provides the outcome of the scoring for seven pathogens for which SARR 2024 provides trend of resistance data. The current cluster of five pathogens in tier 4 may become smaller with evolving trend developments.

Table A5 Tiered scoring trend of resistance

Tier range	Tier score	Pathogens
76%-100%	1	-
51%-75%	2	<i>E. coli</i> , <i>K. pneumoniae</i>
26%-50%	3	-
0%-25%	4	<i>S. aureus</i> , <i>P. aeruginosa</i> , <i>Acinetobacter spp.</i> , <i>E. faecium</i> , <i>S. pneumoniae</i>

NB: These scoring tiers were developed for illustrative purposes and should not pre-empt a different final version.

Incidence

Table 10 in sub-chapter 4.3 of the report suggests that the WHO scoring tiers are not suitable for our illustrative scoring exercise because they cater for much larger incidence numbers than currently seen in Switzerland. We therefore adapted the scoring of incidence in Switzerland as illustrated in Table A6.

Table A6 Swiss incidence scoring tiers reflecting equal quantitative distances

Swiss incidence interval tiers	Nominal scores	Scoring of pathogens in Switzerland
1,000 – 1,499	1	<i>E. coli</i>
501 – 999	2	
0 – 500	3	<i>S. aureus</i> , <i>K. pneumoniae</i> , <i>E. faecium</i> , <i>P. aeruginosa</i> , <i>S. pneumoniae</i> , <i>Acinetobacter spp.</i>

NB: These scoring tiers were developed for illustrative purposes and should not pre-empt a different final version.

The huge difference in incidence order of magnitude of *E. coli* compared to all other pathogens results in the seven listed pathogens falling into only two tiers, fewer than if we used the WHO tiers. We checked the impact on the composite score (see next section) if we applied 100- or 200-interval tiers. We found that the smaller intervals had no impact on the sequence of the pathogens in the composite score.

Composite score across the three medical need criteria, by pathogen

To generate a composite score by pathogen, we multiplied the numeric scores of the attributes of treatability, trend of resistance, and incidence by the weights of these criteria. See Table A7.

Table A7 Composite score by pathogen (lowest scores identifying worst outcomes)

Pathogen	Treatability (*1.47)	Trend of resistance (*1.28)	Incidence (*1.26)	Composite score
<i>E. coli</i>	1.47	2.56	1.26	5.29
<i>Acinetobacter spp.</i>	1.47	5.12	3.78	10.37
<i>P. aeruginosa</i>	2.94	5.12	3.78	11.84
<i>E. faecium</i>	4.41	5.12	3.78	13.31
<i>S. aureus</i>	7.35	5.12	3.78	16.25

These composite scores and their ranking are the outcome of a scoring approach developed for illustration purposes. Its development unveiled the challenges we had to accept in taking discretionary

decisions about the assignment of relative weights to the individual criteria, the design of their attributes/scores, their valuation, the scaling of scoring tiers, and the building of the composite score.

The composite scores by pathogen and their ranking confirm the priority ranking by the experts on the basis of the experience in their clinical practice. Further work will be needed to develop a scoring system deemed appropriate for use in the politically informed selection of antibiotics eligible for preferred remuneration in Switzerland.