A three-level model for therapeutic drug monitoring of antimicrobials at the site of infection

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The silent pandemic of bacterial antimicrobial resistance is a leading cause of death worldwide, prolonging hospital stays and raising health-care costs. Poor incentives to develop novel pharmacological compounds and the misuse of antibiotics contribute to the bacterial antimicrobial resistance crisis. Therapeutic drug monitoring (TDM) based on blood analysis can help alleviate the emergence of bacterial antimicrobial resistance and effectively decreases the risk of toxic drug concentrations in patients' blood. Antibiotic tissue penetration can vary in patients who are critically or chronically ill and can potentially lead to treatment failure. Antibiotics such as β-lactams and glycopeptides are detectable in non-invasively collectable biofluids, such as sweat and exhaled breath. The emergence of wearable sensors enables easy access to these non-invasive biofluids, and thus a laboratory-independent analysis of various disease-associated biomarkers and drugs. In this Personal View, we introduce a three-level model for TDM of antibiotics to describe concentrations at the site of infection (SOI) by use of wearable sensors. Our model links blood-based drug measurement with the analysis of drug concentrations in non-invasively collectable biofluids stemming from the SOI to characterise drug concentrations at the SOI. Finally, we outline the necessary clinical and technical steps for the development of wearable sensing platforms for SOI applications.

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Introduction

Every year, about 5 million people die from causes related to the silent pandemic of bacterial antimicrobial resistance, making it a leading cause of death worldwide.[1] Bacterial antimicrobial resistance can result in prolonged hospital stays and substantially increased health-care costs.[2] The bacterial antimicrobial resistance crisis is exacerbated by the few efforts currently underway to develop new antimicrobial drugs[3] and by the inappropriate use of existing antibiotics, which serves to promote the further development of bacterial antimicrobial resistance.[4] Blood-based therapeutic drug monitoring (TDM) has the potential to optimise concentrations of antimicrobials (by tailoring dose regimens for each patient) and reduce the emergence of bacterial antimicrobial resistance, but is invasive and laborious.[5,6] Furthermore, the tissue penetration of antimicrobial drugs might vary, especially in patients who are critically or chronically ill, leading to treatment failure.[7,8]

We propose a three-level model that expands current TDM for antibiotics beyond blood analysis to include examination of antibiotic concentrations in non-invasive biofluids stemming from the site of infection (SOI). The three levels of the model are defined as: (1) upstream of the SOI (in the blood), (2) at the SOI (eg, epithelial lining fluid in cases of pneumonia), and (3) downstream of the SOI (eg, in the breath in cases of pneumonia). The advancements in wearable sensing technology offer a promising opportunity to accurately measure drug concentrations in various matrices in a simple, convenient, and low-cost manner. Wearables have the potential to realise this three-level model into a laboratory-independent and continuous TDM approach with a broad clinical applicability. To our knowledge, our model is the first to provide a complete and continuous picture of antibiotic tissue penetration.

Therapeutic antimicrobial monitoring

Timely application of appropriate and correctly dosed antimicrobials is essential for the effective treatment of sepsis and septic shock.[9] Traditionally, TDM was adopted for antibiotics with narrow therapeutic indices, such as aminoglycosides and vancomycin. Depending on the antibiotic, TDM has been shown to be cost effective, to reduce the incidence of infection, and to decrease exposure to toxic concentrations of aminoglycosides in the blood.[10,11] Due to increasing evidence linking subtherapeutic antibiotic concentrations with treatment failure, TDM is being used to identify underdosing and facilitate dose optimisation, with the aim of maximising the likelihood of antibiotic effectiveness.[12,13] TDM mainly analyses drug concentrations in patients' blood, but many infections occur outside of the bloodstream itself. Defining the optimal therapeutic range for antibiotics by specifying a lower concentration boundary to guarantee effectiveness and an upper boundary to prevent toxicity and adverse events is a necessary prerequisite to TDM.[14] Assessing interpersonal and intrapersonal pharmacokinetic and pharmacodynamic changes in relation to the in-vitro assessed minimal inhibitory concentration (MIC) of the pathogen are further key elements of TDM.[15] Pharmacokinetic and pharmacodynamic indices depend on the antibiotic applied; that is, whether it is a time-dependent agent (eg, β-lactam antibiotics), a concentration-dependent agent (eg, aminoglycosides), or both a time-dependent and concentration-dependent killing agent (eg, fluroquinolones).[16] Nevertheless, the antibiotic concentrations in plasma do not accurately reflect the concentrations in infected tissue (such as abscess fluid or

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epithelial lining fluid).[17] Additionally, antibiotic concentrations might not be appropriate in patients with altered pharmacokinetics and pharmacodynamics (eg, patients who are critically ill) and in patients with diminished tissue penetration (eg, in peripheral artery disease), which can result in treatment failure.[8,18,19] Other key challenges to wider implementation of TDM include the needs for broad and continuous availability, easy operability, short turnaround times, and cost effectiveness, in combination with easy-to-interpret results.[20]

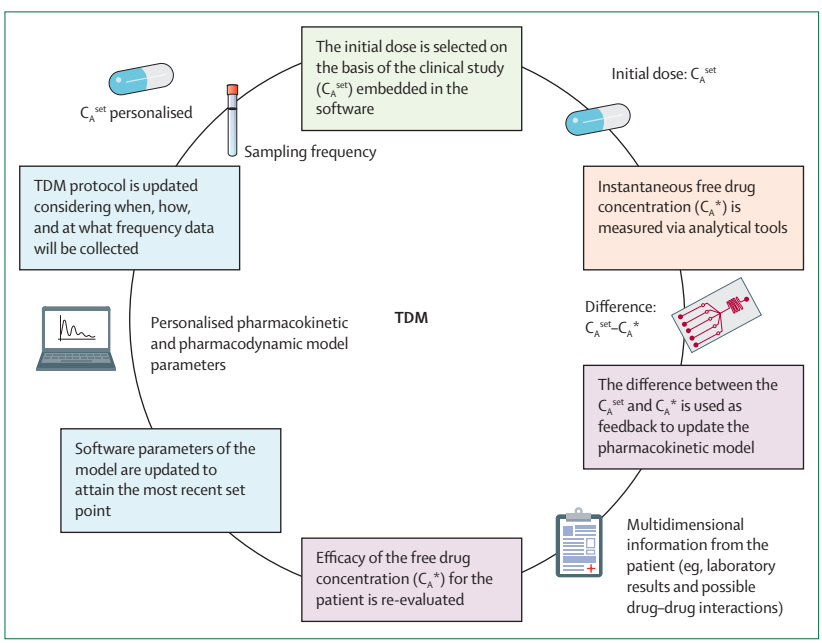


Figure 1: **What is therapeutic antibiotic management?**
The way we interpret the M in TDM has practical consequences for therapy: are we seeking monitoring or management?[21] Considering the variations in antimicrobial exposures across different patients, personalised antimicrobial dosing should be targeted to maximise therapeutic effectiveness. The dosage regimen should be tailored during treatment according to the requirements of each individual via a feedback control loop. The success of this loop depends on two factors: how representative the pharmacokinetic and pharmacodynamic studies are of drugs for the TDM, and the ability of current measurement techniques to access free drug concentrations. Ideally, initial pharmacokinetic and pharmacodynamic models should be built on the basis of large-scale studies, as the quality of the database determines the success of the dosage adjustment. In other words, the data used to construct the initial model should explicitly reflect pharmacokinetic variability according to the patient's physiological and pathological history, dietary habits, possible drug–drug interactions, and genetic factors. However, the underlying pharmacokinetic and pharmacodynamic model parameters in TDM software represent the average behaviour of the participants in the clinical study, and hence serve as an educated guess at best. Therefore, antimicrobial treatment should be conducted as a loop, with software parameters updated on the basis of a patient's clinical response. Such a loop starts with the selection of the set point (initial dose) based on the clinical study embedded in the software. Instantaneous free drug concentration (C_A*) is measured via an analytical tool (preferably one providing continuous measurement, such as a biosensor). The initial dose is selected on the basis of the clinical study (CA^{set}) and the measured value (C_A*) is used as feedback to update the pharmacokinetic model to correct the relationship between the dosage regimen and the free drug concentration. Simultaneously, the efficacy of the free drug concentration for the patient is continuously re-evaluated on the basis of multidimensional information collected through patient observation (eg, clinician judgement or laboratory results). Having multidimensional data is particularly important in the case of combined therapies—for example, when expert clinical judgement is required to decide the efficacy of a drug's concentration for the patient (C_A*) rather than adhering to the initial dose selected on the basis of the clinical study or pharmacodynamic algorithms only (CA^{set}). The pharmacokinetic and pharmacodynamic model is iteratively personalised by updating the software parameters of the model to attain the most recent set point (C_A*). If necessary, the TDM protocol is updated considering when, how, and with what frequency data will be collected. We believe TDM should evolve from passive drug concentration monitoring to the active management of free drug concentrations for the optimal benefit of each individual patient.[21] Adapted from Ates et al.[21] Figure created with BioRender.com.
TDM=therapeutic drug monitoring.

Personalising antimicrobial drug dosing

TDM provides a feedback loop to ensure that antibiotic exposure remains therapeutic throughout the course of therapy. However, ensuring that prescribed doses are appropriate—whether they be for empirical or targeted therapy—requires further consideration of dose optimisation strategies (figure 1), particularly for population groups that are difficult to treat. Additionally, the reduced pathogen susceptibility commonly observed among patients in intensive care units (ICUs) presents added challenges to achieving pharmacokinetic and pharmacodynamic exposure targets.[22] Dose optimisation techniques, such as the use of continuous infusions for β-lactam antibiotics, have shown promise for improving patient outcomes and might be useful in treating infections caused by pathogens with reduced susceptibility.[23] Data from large clinical trials quantifying these potential clinical benefits are still forthcoming.[24]

Advances in dose optimisation strategies, such as the development of software applications that include model-informed precision dosing (MIPD), are important in expediting the dosing adjustments required to personalise antibiotic dosing.[25] Published models of antibiotic pharmacokinetics in specific population groups can now be integrated with relevant patient-specific information, such as kidney function and bodyweight, and with specific data for bacterial pathogens (eg, minimum inhibitory concentration) and TDM sample results (if using Bayesian forecasting) to generate tailored dosing regimens. Preliminary findings suggest that this personalised approach to antibiotic dosing results in improved attainment of pharmacokinetic and pharmacodynamic targets among patients who are at high mortality risk from infections.[26] In one study, approximately one in five patients received substandard antibiotic dosing regimens, which suggests that a more nuanced approach to dosing that considers patient, drug, and pathogen data might be required.[26]

An important consideration when looking to incorporate MIPD software into non-invasive antibiotic TDM is that existing pharmacokinetic models for antibiotic populations have been developed via intensive sampling from the central compartment. To apply these models to non-invasive samples, ideally from the SOI, further work describing differences in drug behaviour in the central and peripheral compartments will be required. Furthermore, as TDM information becomes available and is accumulated by use of innovative antibiotic surveillance tools, large volumes of data could further inform and continuously fine-tune existing pharmacokinetic models for populations such as critically ill patients. By harnessing artificial intelligence and machine-learning capabilities, personalised antibiotic dosing could become smarter, leading to improvements in initial empirical dosing and in the dose adjustments necessary due to intrapatient variability during treatment.

Wearable biosensors for personalised health monitoring

During the past six decades, biosensors have largely been used to replace conventional benchtop equipment as screening, monitoring, and diagnostic tools in centralised laboratories.[27] Commercial handheld analysers, such as glucose and lactate meters for the self-monitoring of metabolites, are successful examples of such applications. Although commercially available biosensors can reduce health-care costs and hospital visits, the majority are invasive and involve blood sampling, which raises the risk of infection and can result in reduced patient compliance. Research is therefore focused on developing biosensors (preferably in a wearable format) for non-invasive and minimally invasive analysis.[28]

Wearables are highly versatile, and their use can easily be expanded to provide a holistic approach to monitoring patients' health, beyond simply providing TDM. Metabolites, electrolytes, proteins, drugs, and hormones are detectable in non-invasively accessible biofluids, such as sweat,[29,30] saliva,[31] and tears,[32] and in interstitial fluid (ISF),[32,33] which is easily accessible with a minimum of invasiveness. These fluids could be used by wearable sensors as an alternative to blood.[34]

Sweat and sweat sensors

Sweat contains physiologically and metabolically rich analytical information that can be readily accessed and non-invasively retrieved. Several sampling sites are available for use, given the high number of sweat glands on the body (with densities of more than 100 glands per cm^2 in some locations).[35] A wide range of sweat-monitoring, wearable biosensor platforms have been developed, including temporary tattoos, patches, wristbands, and epidermal microfluidic devices.[36–39] Sweat is a dynamic biofluid; its pH can vary from 4·5 to 9·0, and its composition can vary depending on the skin's body localisation and how it is generated (ie, by exercising, thermal or chemical stimulation, or passively). Small molecular analytes, such as glucose, alcohol, uric acid, tyrosine, and cortisol, can be directly measured in sweat and these concentrations can—to some extent—correlate with those in blood.[30,37,40,41] Sweat has also been used for the detection of exogeneous molecules, including drugs.[42] However, the relationship between drug concentration in the blood versus the concentration measured in sweat is not well understood, which complicates prediction of the correlation between sweat and blood.

Breath and breath sensors

After the discovery that some volatile organic components in exhaled breath are associated with certain metabolic activities, research efforts have been dedicated to the analysis of these volatile organic components using gas sensors (electronic noses, which are analogous to receptor cells in the nose).[43] Breath analysis via electronic noses has so far been used for asthma management and treatment (both at home and in clinics) and in breath biopsies,[44] and has been used to diagnose diabetes, viral infections,[45] lung cancer,[46] and other lung diseases.[43] A more promising—yet challenging (due to sensitivity and selectivity issues)—application area is the detection of biomolecules. Monitoring of hydrogen peroxide (a biomarker for respiratory illnesses) has been shown by use of a paper-based sensor integrated into face masks.[47] A study in 2021 showed the possibility of detecting pathogens such as SARS-CoV-2 directly from breath by nucleic acid analysis via a face mask with a CRISPR-based biosensor.[48] Another study for temporal monitoring of antibiotics in exhaled breath condensate[49] showed that antibiotics behave similarly in breath and blood, supporting the idea that the analyte transportation from blood to the lungs bypasses the complex transport mechanisms involved in most non-invasive biofluids.

Saliva, urine, tears, stool, and ISF sensors

Saliva represents an attractive non-invasive alternative to blood as it is produced in large volumes.[50] Saliva analysis is a challenging process because of the numerous sources of contamination, ranging from mouth microbes to food and drinks debris, as well as ion-trapping of drugs. These challenges, as well as the issue of increased sensor biofouling, have previously hindered the development of wearable salivary sensors. Urine—as a byproduct of kidney metabolism—is composed of metabolites, easy to sample, and is mostly analysed by lateral flow devices.[51,52] Uncomplicated urinary tract infections frequently lead to the prescription of antibiotics, and recurrent urinary tract infections are difficult to treat as they are commonly caused by multidrug-resistant bacteria. Monitoring antibiotics in urine to optimise treatment could therefore have a substantial effect.

Compared with other biofluids such as saliva and urine, which present highly variable dilution effects, lachrymal fluid is kept at a low and relatively stable volume, is continuously replenished, and contains a variety of detectable biomarkers.[53] Tears are less prone to biofouling than saliva, ISF, and sweat; however, the difficulty of collecting tears remains a challenge. Contact lenses are commonly used as a platform for tear fluid analysis[54] and show great potential for use in the prevention, diagnosis, and treatment of eye-related infections. Similarly, analysis of stool samples in laboratory settings is excellent for the assessment of gut microbiota, monitoring probiotic bacteria, and diagnosing inflammatory bowel disease.[55] Therefore, stool analysis could be a potential application in patients with frequent bowel movements, such as those with diarrhoea who are treated with antibiotics.

Among alternative biofluids, ISF has the highest degree of correlation with blood; the composition of the two fluids is similar in terms of small molecules such

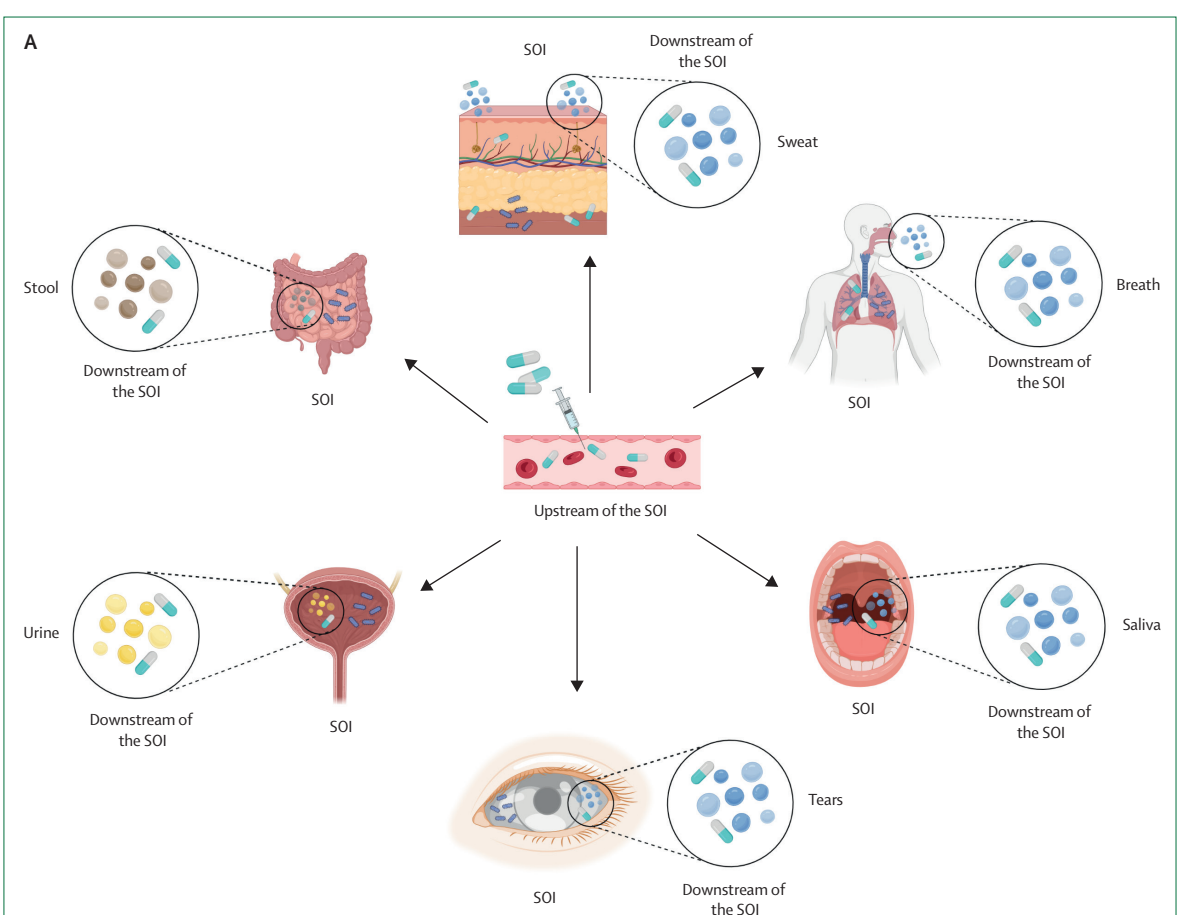
as electrolytes, metabolites, and proteins. Successful examples of ISF-based biosensing include commercialised, wearable devices for continuous glucose monitoring. Even though alternative, non-invasive approaches for ISF collection and analysis exist, such as reverse iontophoresis,[56] and despite the great advantages of using ISF for biomarker monitoring, the effective development of wearable ISF sensors is limited by the sampling protocol, which involves minimally invasive microneedles being used to puncture the epidermis.[57]

A three-level model for TDM of antimicrobials at the SOI

Clinical application

We propose a novel three-level model for TDM of antimicrobials at the SOI (figure 2A). Our model offers a non-invasive, laboratory-independent approach to TDM using wearables (potentially at the SOI) and, more generally, could improve overall understanding of antimicrobial tissue penetration. Level 1 represents blood as a surrogate matrix upstream of the infected tissue; level 2 refers to the SOI and pharmacological target, where adequate antimicrobial exposure is needed; and level 3 represents non-invasively collectable biofluids stemming from the relevant infected tissue (eg, sweat in soft tissue infections and breath in pneumonia, figure 2B), which are considered to be surrogate matrices downstream of the site of SOI.

Four clinical implementation strategies can be envisaged for this TDM model. First, drug monitoring at the SOI is likely to be the most appropriate strategy for TDM. Second, measuring the difference between antimicrobial concentrations upstream of the SOI and downstream of the SOI could indicate an antimicrobial gradient, which could provide a deeper understanding of antimicrobial flow (ie, antimicrobial penetration from blood through the SOI into the biofluid stemming from the SOI). Third, TDM upstream of the SOI could serve as a calibration measure for TDM downstream of the SOI, either at the beginning of treatment or continuously during treatment. The antimicrobial concentrations in blood follow well investigated pharmacokinetic and pharmacodynamic models, and are more stable than concentrations in biofluids stemming from the SOI, which show high variability.[58] Finally, calibration measures could be used to establish a continuous,



(Figure 2 continues on next page)

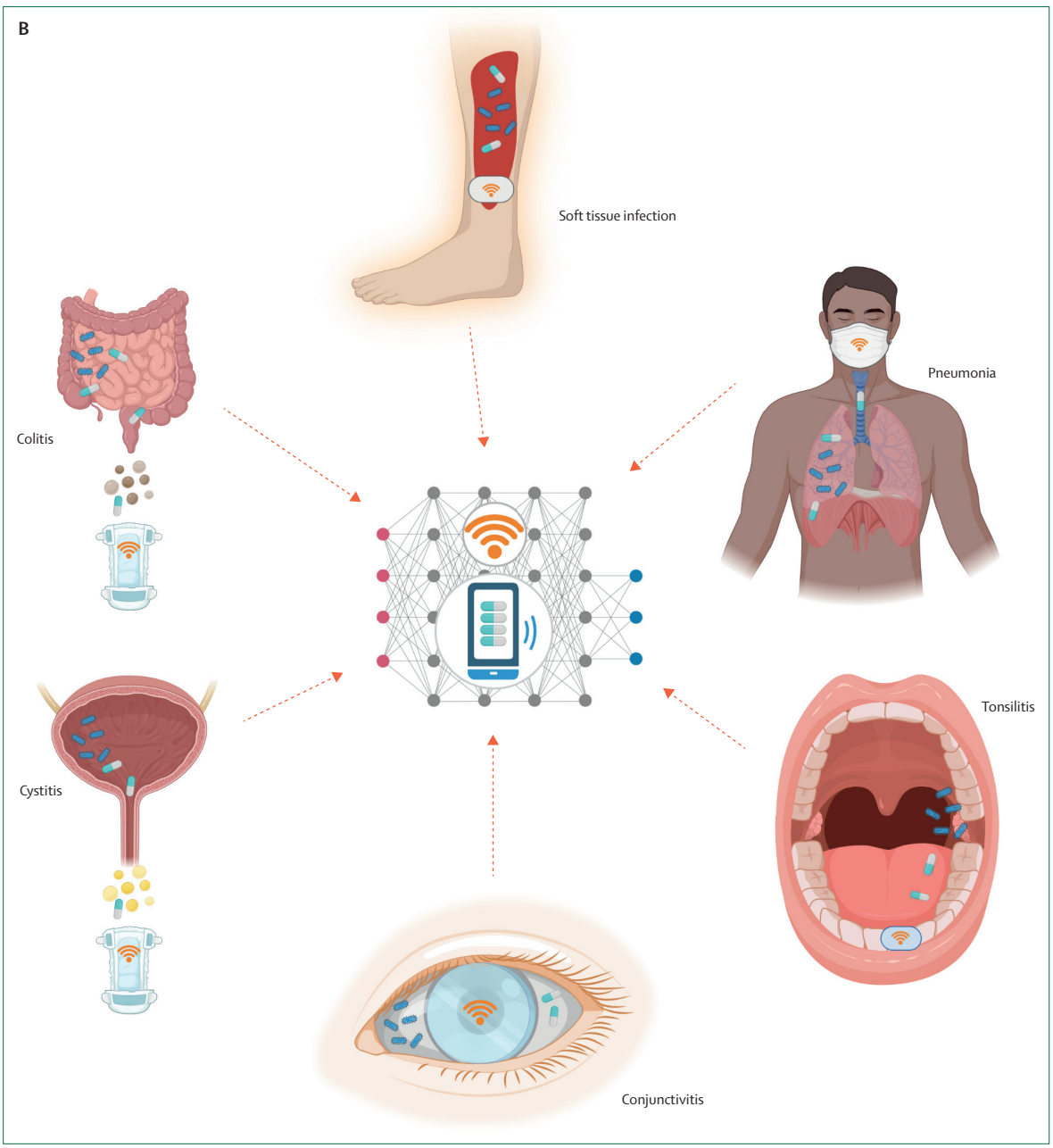


Figure 2: **The novel TDM model**
(A) Applying three levels of TDM to the human body. Level 1: antibiotics are introduced to the bloodstream upstream of the SOI. Level 2: antibiotics reach the SOI in the infected tissues. Level 3: antibiotics are excreted into non-invasive biofluids downstream of the SOI. (B) Wearable biosensors for TDM downstream of the SOI detect antibiotic concentrations continuously (or semi-continuously) and non-invasively via a smart sweat patch for soft tissue infections, a smart face mask for pneumonia, a smart tooth-mounted biosensor for tonsillitis, a smart lens for conjunctivitis, and smart diapers for cystitis and colitis. The sensor data could be sent to a smart device (or secure server) and analysed by artificial intelligence algorithms. Figure created with BioRender.com. TDM=therapeutic drug monitoring. SOI=site of infection.

non-invasive, stand-alone evaluation of antimicrobials at the SOI; to assess concentration changes over time; or to potentially indicate adequate dosing for a personalised therapy.

However, the following considerations for these strategies exist and warrant further investigation. First, the SOI is usually inaccessible with non-invasive methods, meaning a direct TDM strategy cannot be pursued with the current sampling and sensing technologies in a simple, fast, and low-cost way. With our three-level model, the antimicrobial concentrations at the SOI could become estimable through derivation from

antimicrobial flow. Second, determining antimicrobial concentrations at the SOI is of specific interest to optimise and guide antibiotic target attainment, especially when the specific minimum inhibitory concentration is established. The antimicrobial flow upstream of the SOI could be estimated through the distribution of blood to the respective organs (by percentage) in relation to cardiac output. However, measuring antimicrobial concentrations downstream of the SOI in dynamic biofluids represents a novel approach, which comes with challenges relating to sampling and interpretation. For example, assessing the body's entire volume of sweat to discover the amount secreted from the skin during a given amount of time is highly challenging. The sweat rate can vary within and between individuals, and local sweat rates differ depending on the anatomical sampling site.[59,60] Finally, calibrating sensors at the beginning of—or continuously during—a monitoring period by simultaneously measuring the antimicrobial concentrations upstream of the SOI is an opportunity to link a validated analysis with dynamic measures to foster reliable predictions.[61] However, the need for blood-based TDM analysis before the measurement makes this approach more complex than TDM downstream of the SOI and restricts its broad application, especially in low-income and middle-income countries. A countermeasure for the costly, non-continuous, and laborious blood analysis could be an additional wearable sensor module for ISF analysis, as ISF's molecular composition correlates well with blood.[62]

Technological application

Wearables could provide a shift from blood-based TDM to multilevel TDM, including non-invasive analysis of antimicrobials at the SOI and integrative therapy management. During sepsis treatment, for example, a network of multiple wearable sensors could enhance therapeutic success by enabling the simultaneous and rapid monitoring of supplementary information, such as concentrations of cytokines, pH, C-reactive protein, or procalcitonin, together with TDM. Moreover, such a network of multiple wearable biosensors could be further modified to enable on-site pathogen detection (eg, targeting amplification-free nucleic acid testing by use of CRISPR–Cas technology[48]) in primary care. These wearable devices can cost a few to hundreds of US$ depending on their development and production costs, and they represent an affordable diagnostic tool.

Various matrices, such as sweat, breath, tear fluid, and urine, are being produced and collected in different physical forms, and sample compositions are affected by how collection is conducted.[63] Therefore, defining and standardising the sampling approach is essential. Identifying the underlying secretion mechanisms of biofluids is also important for understanding the pharmacokinetics and pharmacodynamics of antimicrobials in these biofluids.[34] Antibiotic concentrations in breath have been shown to correlate well with blood in healthy pigs. However, in lung diseases such as pneumonia, the effect of pathophysiological changes, such as increased extravasation and a reduction of exchange area and time, needs to be explored.[17,49] Nevertheless, once sufficiently high time-resolution data are collected and the molecule secretion by each biofluid is better understood, direct correlation could be possible, but not necessarily needed. Artificial intelligence-based smart applications that can be implemented into wearables could aid understanding of these dynamic biofluids and support data standardisation.[64] Wearable biosensing devices for non-invasive analysis harbour great potential for driving the P4 (predictive, preventive, personalised, and participatory) medicine concept, as they can directly engage patients with their own health management.[65] As wearables are integrable into secure streaming platforms for health data, they provide an interoperable public health surveillance tool at the individual and societal level, with great potential in remote and resource-restricted settings.[66]

Next steps

Needs

A structured assessment to define the needs of different stakeholders—especially patients—should be conducted. A variety of frameworks exist that define the multiple stakeholder groups involved in health research. These stakeholders include patients, the public, and consumers; providers such as clinicians and health-care institutions; payers such as organisations that pay for health-care goods and services; product makers, such as manufacturers; policy makers and regulators; training institutions; and researchers and research funders.[67] The formulation of a stakeholder engagement plan will foster an expedient and successful development of wearables for monitoring patients' health.

Execution

Biosensors have been shown to be capable of detecting low antibiotic concentrations in non-invasive and minimally invasive biofluids, but integrating these sensors with different sampling approaches on a common wearable platform needs further engineering.[49,68] This technological development must be followed by a regulatory framework to implement standards set by the International Organization for Standardization and to create the necessary conditions for scaling up device manufacturing in the long term. For downstream biofluid collection and analysis, various forms of sensors are needed to adapt to the different body sites, such as patch-based, on-skin sweat sensors; sensor-integrated face masks for exhaled breath analysis;[69] mouth guard-based saliva analysis; tear analysis via contact lenses; diaper-based urine testing; and stool analysis (figure 2B). ISF is a good surrogate for blood for

establishing reliable correlations between measured drug concentrations. When coupled with closed-loop drug delivery systems for automated dose adjustment, ISF could hold the potential for future wearable TDM applications.

Additionally, the cross-connection of wearable sensors with smart devices and algorithms should be established to incorporate physiological and clinical information into analyses. Data interoperability and data integrity are of utmost importance. Special attention should also be given to data privacy, by implementing two-factor authentication—an additional credential (such as a biometric measure) to the password—to access health data. This additional security measure empowers the patient to provide access to proprietary data that are stored within their respective health-care institution. Data security should be addressed further as internet connectivity exposes the patient to potential cyber harm, a new risk in digital health.[70] Overall, technological achievements should be thoroughly implemented and investigated within a clear development plan that provides full clinical validation. Thus, investigating the value of this three-level model for non-invasive TDM at the SOI by considering clinical endpoints, such as overall survival, disease severity, safety, length of ICU stays, and quality of life after ICU discharge, will be essential. Although there are no conclusive data to date supporting the use of MIPD software in combination with TDM, further clinical trial data, including cost-effectiveness analyses, are required to robustly evaluate the use of MIPD for TDM as meaningful clinical interventions.[71] Future work will need to ensure that MIPD software with TDM is applied early in clinical therapy using prompt adaptive feedback mechanisms. Importantly, patient groups at high risk who are likely to benefit most from dose optimisation, such as patients who are critically ill with a high severity of disease, patients with a pulmonary source of infection, and patients who are likely to be infected with bacterial organisms with reduced antimicrobial susceptibility, should be targeted in clinical interventional studies.[72–74]

Further applications

In addition to providing a novel key element for the quantitative assessment of antimicrobials in TDM, the qualitative detection of antimicrobials in non-invasive biofluids provides further advances for patient care. Non-compliance has been shown to affect up to 20% of paediatric patients and can lead to treatment failure.[75] Screening for the presence of antimicrobial agents at the bedside within minutes and at low cost would provide important information about treatment compliance. Poor compliance is a well known reason for treatment failure in patients with tuberculosis. Directly observed therapy has therefore become standard practice for the treatment of multidrug-resistant tuberculosis; however, this successful strategy is costly and labour intensive. Similarly, if broadly detectable β-lactam antibiotics cannot be targeted in samples downstream from the SOI, non-compliance could explain treatment failure rather than ineffective antibiotic treatment.

Our three-level concept of TDM is potentially applicable in other fields. For example, monitoring oncological drugs at the site of cancers or immunosuppressants at the site of suppression could provide highly promising approaches for improving treatment efficiency and the outcomes of patients with cancer or patients who have had transplantation surgery. Moreover, our model could also be implemented into the drug development process by providing continuous information about pharmacokinetics.

Conclusion

We have proposed a three-level model for TDM of antimicrobials, which links antimicrobial concentrations from the analysis of blood with non-invasive biofluids stemming from the SOI. This model will provide a thorough understanding of antimicrobial flow and concentrations at the SOI. For this purpose, wearables offer a promising solution for continuous and point-of-care biofluid analysis to access molecular biomarkers. Combining our three-level model with wearable sensors will help to overcome the limitations of traditionally invasive and laboratory-dependent analysis. Furthermore, our model would foster continuous and non-invasive TDM by implementing the non-invasive collection of biofluid from the respective infected site. The next steps in the development of wearable platforms are assessing the stakeholder needs, executing full technological development, conducting clinical investigations to support the clinical value of our model, and obtaining permission from patients to monitor their treatment.

Contributors

NB and CD conceptualised this Personal View. NB, HCA, JAR, and CD reviewed the conceptualisation. NB, HCA, and CD created the figures. NB, HCA, JRS, MOC, JAR, WG, and CD wrote the original draft, with review and editing input from AFW, JE, and JG.

Declaration of interests

We declare no competing interests.

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