



# The IATDMCT COMPASS

News and Views on TDM and CT from around the World

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Dosing of Cancer Drugs:  
Hype or Reality?**

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## IATDMCT COMPASS

The *Compass* is published quarterly by the International Association of Therapeutic Drug Monitoring & Clinical Toxicology and distributed to the members by the Association. Letters to the Editor must be signed and should not exceed 200 words in length. Chairs of Committees are requested to submit announcements and reports of activities.

All IATDMCT members are encouraged to send contributions to the editorial team of COMPASS about professional achievements, new books in relation to the aims of the society, or workshops and symposiums related to TDMCT and held under the auspices of the IATDMCT.

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## DEAR FRIENDS AND COLLEAGUES!



It is with great excitement and gratitude that I welcome you to the September 2025 edition of *COMPASS*. Each issue is a journey we take together—a chance to learn, to reflect, and to inspire one another as we advance the science and practice of TDM and CT. This edition is filled with fresh perspectives, critical debates, and a shared passion for improving patient care.

We open with *Maaiké's* write-up on **“Optimizing Antibiotic Therapy in Critically Ill Patients: Addressing Pharmacokinetic Variability and Augmented Renal Clearance.”** This piece reminds us that critically ill patients are among the most vulnerable, and ensuring that antibiotics reach the right target, at the right dose, and at the right time can make all the difference. The complexities of augmented renal clearance highlight why our work in individualized therapy matters so deeply.

From there, we take a thoughtful look at *Eloïse* and colleagues' paper on **“Pros and Cons of Hair Analysis in Environmental Toxicology.”** Hair analysis has captured much attention for its promise in understanding long-term exposure to toxins—but as this article shows, science is as much about asking the right questions as it is about finding answers, while staying informed about the shortcomings.

The momentum around **Model-Informed Precision Dosing (MIPD)** is undeniable. In **“MIPD of Cancer Drugs: Hype or Reality?”** *Vikram and Ganessan* critically examine whether this approach has transcended theoretical promise to deliver tangible clinical outcomes. In the same vein, **“Is there a Room for Personalised Dosing of Trastuzumab Deruxtecan?”** *Dirk* and colleagues challenge us to envision how we can truly optimise treatment in breast cancer with antibody drug conjugates, balancing efficacy while safeguarding patients from harm.

We are also proud to feature **“Therapeutic Drug Monitoring: Transforming a Vision into Best Practice for Healthcare in Indonesia,”** an inspiring story of progress, perseverance, and the real-world impact of TDM in strengthening healthcare systems by *Jefman and Rovina*. It's a reminder of what can be achieved when dedication meets vision.

Looking ahead, we are thrilled about the **JSTDM-IATDMCT Young Scientist Joint Symposium 2025** at the **41st Annual Meeting of the Japanese Society of Therapeutic Drug Monitoring**. The future of our field depends on the curiosity, innovation, and energy of young scientists—and this collaboration is a wonderful platform to nurture just that.

Finally, we honor the legacy of scientific exploration with the **2025 Charles Lieber Memorial Satellite Symposium**, which delves into the fascinating connections between **alcohol, CYPs, inflammasome, microbiome, metabolome, and cardiovascular protection, but malignant transformation of hepatocytes**. It promises to broaden our horizons and spark meaningful discussions that transcend disciplines.

Thank you for being part of this vibrant community. Your passion, insights, and commitment make IATDMCT what it is today—a global family united by a shared purpose: to bring precision, compassion, and excellence to patient care.

**Together, let us continue to push boundaries, embrace innovation, and shape a future where every patient, everywhere, receives the right therapy at the right time.**

Looking forward to meeting some of you at the Singapore Congress !!

Cheers,

Smita, COMPASS Editor-In-Chief

# THERAPEUTIC DRUG MONITORING: TRANSFORMING A VISION INTO BEST PRACTICE FOR HEALTHCARE IN INDONESIA

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Over recent decades, Therapeutic Drug Monitoring (TDM) has significantly improved patient outcomes and minimized adverse effects by optimizing doses of medications that have narrow therapeutic windows. This clinical practice involves measuring drug concentrations in blood or plasma, adjusting dosages accordingly, and monitoring the patient's condition afterwards to ensure therapeutic efficacy while reducing risks such as toxicity.<sup>1</sup> TDM implementation faces substantial barriers, including limited trained personnel, high costs of laboratory equipment and drug analysis, and inadequate interdisciplinary collaboration among healthcare professionals.<sup>2</sup> Despite its benefits, TDM remains underutilized in many healthcare settings, particularly in the Asia-Pacific region.<sup>3</sup> Though Indonesia lags behind other countries, there is still hope for the advancement of TDM services in spite of persistent obstacles. Addressing these challenges is critical to integrating TDM into routine clinical practice, enhancing patient safety, and optimizing therapeutic outcomes in healthcare facilities in Indonesia.

## Setting up TDM service

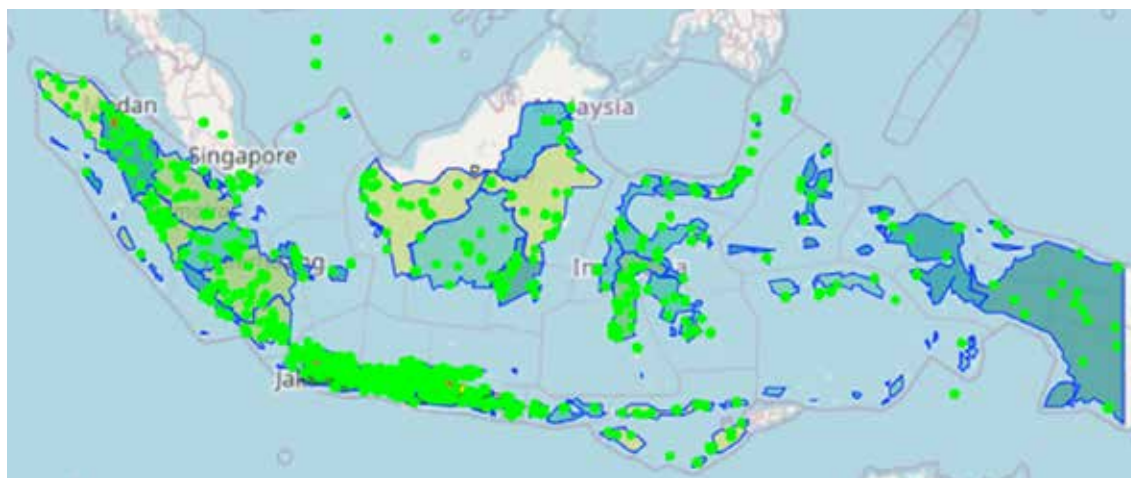
Initiating TDM services requires careful consideration of three critical components: (1) infrastructure (laboratory facilities and equipment), (2) a multidisciplinary expert team, and (3) a sustainable financing system.<sup>4</sup> Implementing TDM faces significant barriers, particularly related to infrastructure costs. Establishing and maintaining advanced laboratory facilities for TDM entails substantial expenses.<sup>5</sup> The expert team must

comprise professionals with diverse expertise capable of delivering holistic TDM services, including clinicians, clinical pharmacologists, clinical pharmacists, nurses, and laboratory personnel.<sup>6</sup> High costs of drug analyses contribute to the high expense of TDM services, which should ideally be covered by health insurance schemes to ensure accessibility, especially in low-middle income countries.<sup>5,7</sup>

## Healthcare System in Indonesia

As one of the world's most populous nations, Indonesia faces complex challenges in delivering comprehensive healthcare to its diverse population.<sup>8</sup> Currently there are 3,269 hospitals distributed across its 1.9 million km<sup>2</sup> archipelago (Figure 1), ensuring broad access to medical facilities.<sup>9</sup> The healthcare system in Indonesia is a referral system, starting from primary care facilities such as primary health care and private clinics, followed by district referral hospitals (secondary hospitals), and provincial or national referral hospitals (tertiary hospitals).<sup>10</sup> The majority of hospitals in Indonesia are private hospitals (62%). Approximately ~72% of the Indonesian population is covered by health insurance, with 66% covered by National Health Insurance (NHI).<sup>11</sup>

Figure 1. Distribution of Hospitals in Indonesia<sup>9</sup>



According to the report by the World Health Organization, infectious diseases and kidney disorders are among the top ten causes of mortality in Indonesia. Infectious diseases, such as tuberculosis, rank fourth, with a mortality rate of 48.9 deaths per 100,000 population.<sup>12</sup> Based on the Institute for Health Metrics and Evaluation (IHME), there were an estimated 36,500 deaths attributable to antimicrobial resistance (AMR) and 147,000 deaths associated with AMR in Indonesia, predominantly due to pathogens such as *Acinetobacter baumannii*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Mycobacterium tuberculosis* (TB).<sup>13</sup> Moreover, kidney disorders account for 15.8 deaths per 100,000 population.<sup>12</sup> From 1991 to 2018, Indonesia reported an increasing demand for renal transplantation.<sup>14</sup>

Indonesia has one of the highest rates of hospital-acquired infections in Southeast Asia, with a prevalence of 30.4%.<sup>15</sup> Mortality from hospital-acquired infections in intensive care units (ICUs) is twice as high as non-infected patients.<sup>16</sup> A potential key challenge is the failure to achieve bactericidal antibiotic targets due to pharmacokinetic changes in critically

ill patients, particularly when treating multidrug-resistant (MDR) infections.<sup>17</sup> Vancomycin, as an example, a potent antimicrobial used to treat methicillin-resistant *Staphylococcus aureus* (MRSA), has a narrow therapeutic index, requiring careful monitoring to prevent toxicity and ensure efficacy.<sup>18</sup> Our preliminary study shows that the prevalence of vancomycin-induced acute kidney injury (VIAKI) is significantly higher than that in other countries: 21% vs ~15% (a manuscript is currently being prepared for publication). Implementing vancomycin TDM in Indonesia could significantly enhance patient safety.<sup>19</sup> These findings highlight the urgent need for establishing TDM for vancomycin in Indonesia.

Indonesia is one of the countries with the highest burden of multidrug-resistant *Mycobacterium tuberculosis* (MDR-TB) globally. The rising prevalence of MDR-TB and extremely-resistant *Mycobacterium tuberculosis* (XDR-TB) in Indonesia is a critical concern.<sup>20</sup> Treatment of MDR-TB and XDR-TB requires complex antibiotic regimens, necessitating a comprehensive management approach, including TDM.<sup>21</sup>

Another example is the use of tacrolimus - an immunosuppressant used in renal transplant patients. It requires careful monitoring of its levels to prevent organ rejection and toxicity.<sup>22</sup> In Indonesia, tacrolimus level measurements have been conducted for years. However, our preliminary study highlights the need for optimization of pre-analytical and post-analytical aspects of tacrolimus level measurement (unpublished data). Based on these findings, we initiated a TDM service for tacrolimus in June 2025 at a private hospital in collaboration with a private laboratory.<sup>23</sup> This service is currently self-funded by patients.

Both AMR and renal transplantation in Indonesia further highlight the need for TDM to optimize antimicrobial and immunosuppressant therapies.<sup>17,24,25</sup>

## Challenges and Opportunities for TDM in Indonesia

Currently, TDM services are not available in Indonesian government hospitals. Although most patients treated at these hospitals are covered by NHI, bureaucratic processes in public institutions often cause significant delays in initiating TDM due to the high costs of laboratory procurement and testing.<sup>5</sup> However, the predominance of private hospitals in Indonesia provides opportunities to establish TDM services, as private hospitals can collaborate with private laboratories, which can more readily procure necessary laboratory infrastructure.

Numerous cases of infections in Indonesia, including hospital-acquired infections, require potent antibiotics such as vancomycin, linezolid, and aminoglycosides, which have safety concerns necessitating TDM to treat MDR infections.<sup>26</sup> This presents an opportunity to initiate TDM services for antimicrobials. To include TDM in the NHI coverage, evidence that implementation of TDM is cost-effective, as well as data on unit cost, are required. Currently, such data are unavailable, necessitating further research.

The vast and archipelagic geography of Indonesia presents challenges in delivering TDM services across the country. However, by dividing Indonesia into three zones (western, central, and eastern), establishing at least one TDM service per zone and developing an effective referral system among healthcare facilities can address these challenges.

## Conclusion

Awareness of TDM services is emerging in Indonesia, signaling increased recognition of their value in optimizing patient care. Despite numerous challenges, there are significant opportunities to expand TDM

services in Indonesia. More research is required to show that TDM is cost-effective and to provide reasonable unit costs for drug analysis. Furthermore, robust collaboration among government, the private sector, and academic institutions is needed to accelerate the implementation of TDM as best practice for healthcare services in Indonesia.

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## 2025 CHARLES LIEBER MEMORIAL SATELLITE SYMPOSIUM: ALCOHOL, CANNABIS, INFLAMMASOME, MICROBIOME, METABOLOME & CHRONIC DISEASES

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On Saturday June 21 2025, the 16<sup>th</sup> Research Society on Alcoholism (RSA) and 2<sup>nd</sup> International Society for Biological Research on Alcoholism (ISBRA) – **Charles Lieber Memorial Satellite Symposium** – took place in New Orleans. Organized by Drs. Manuela G. Neuman and Helmut Seitz, this year's symposium was titled: "*Alcohol, Cannabis, Inflammasome, Microbiome, Metabolome & Chronic Diseases.*"

This satellite symposium was dedicated to Charles S. Lieber who was a pioneer in the field of alcohol-induced liver and gastrointestinal diseases and whose unparalleled contributions to the field were groundbreaking. Dr. Lieber was a passionate and well-respected clinical investigator, physician and educator. He was a devoted clinician who treated patients for 50 years, as well as a researcher in areas such as hepatic cirrhosis and fibrosis.

The symposium addressed the mechanisms and biomarkers of alcohol-induced damage to different organs, as well as the role of other substances of misuse in this dialogue. Participants learned about the relationship between alcohol intake and several chronic diseases, in the presence or absence of viruses, as well as the interactions of alcohol with medications and drugs of misuse. Conversely, participants also learned about the role of alcohol consumption in metabolic diseases. Finally, nutrition as a therapeutic intervention in microbiota was discussed. Attendees actively and enthusiastically engaged with the speakers following their presentations.

The symposium thus provided a platform for researchers in all stages of their careers to discuss clinical and basic research ideas with this assembly of experts. The intention of this symposium was to advance the international profile of scientific meetings both in terms of faculty,



young scientists and student participation. Our mission was to provide a forum to progress scientific research in alcohol and metabolic diseases.

Dr. **Helmut Seitz**, of the *University of Heidelberg*, who was one of Charles Lieber's fellows, started the symposium by educating everyone on Dr. Lieber's legacy. His presentation centred around the role of cytochrome P450 (CYP) 2E1 and reactive oxygen species in alcohol-induced liver damage. Other factors such as age, degree of fitness, nutrition, and related cardio-metabolic risk factors, autoimmune diseases, sex, and genetics influence the severity of the disease.

Dr. **Amitava Dasgupta (Ph.D)**, a long-time member of IATDMCT from the *Department of Pathology & Laboratory Medicine, University of Kansas Medical Center, Kansas City*, presented the role of alcohol in cardiovascular diseases. He explained that the current guidelines in the U.S. for moderate consumption of alcohol is up to one standard drink per day for women, and up to two for men. Interestingly, the well-established relationship between reduced risk of cardiovascular disease and moderate consumption of alcohol may not be evident until middle age (35-49) or older (50-64) in men. However, women may benefit from moderate consumption of alcohol in a much younger (18-34) age. The plausible mechanisms for the cardioprotective effects of consuming alcohol in moderation include increased levels of high-density lipoprotein, decreased levels of low-density lipoprotein, prevention of clot formation, reduction in platelet aggregation and lowering of plasma apolipoprotein(a) concentration.

The next presentation was by Dr. **Rainer Spanagel** from the *Department of Pharmacology, University of Heidelberg*, who addressed how the reproducibility and translation of preclinical alcohol research can be improved. He offered recommendations such as the execution of an *a priori* power calculation prior to the study. Additionally, negative findings should be published to counteract publication bias. The application of these recommendations, especially for preclinical confirmatory studies, will ultimately improve the reproducibility and translation of animal research.