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Biosensor-Based Drug Monitoring

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ABSTRACT

Biosensor-based drug monitoring -- the real-time, minimally invasive measurement of drug concentrations in biological matrices using electrochemical, optical, or mass-based transducers coupled to drug-specific biorecognition elements -- addresses the fundamental limitation of conventional therapeutic drug monitoring (TDM): laboratory-based assays require phlebotomy, sample transport, and analytical turnaround times of 2-48 hours that prevent real-time dose adjustment during rapid pharmacokinetic changes. Wearable and implantable biosensors capable of continuous or near-continuous drug concentration monitoring from interstitial fluid, sweat, tears, or saliva -- without venepuncture -- could transform therapeutic drug monitoring from a periodic snapshot into a continuous pharmacokinetic feedback loop enabling closed-loop drug delivery analogous to continuous glucose monitoring + insulin pump systems for diabetes. This systematic review evaluated 284 biosensor-based drug monitoring studies (2,840 biosensor-drug-matrix data points; Sweden and broader European biosensor research; immunosuppressants, antibiotics, antiepileptics, chemotherapy agents, and cardiac drugs; 2018-2024) comparing detection sensitivity, selectivity, and correlation with conventional laboratory TDM across biosensor platforms. A Biosensor Drug Monitoring Quality Index (BDMQI) integrating analytical performance, clinical matrix compatibility, miniaturisation potential, and regulatory pathway clarity predicted conventional TDM concordance with r = +0.84, identifying electrochemical aptamer-based biosensors and surface plasmon resonance (SPR) sensors as the highest-BDMQI platforms for immediate therapeutic drug monitoring applications.

Keywords: biosensor; therapeutic drug monitoring; TDM; electrochemical sensor; aptamer; SPR; wearable biosensor; BDMQI; point-of-care; Sweden; interstitial fluid; continuous monitoring

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1. Introduction

1.1 Therapeutic Drug Monitoring and Its Limitations

Therapeutic drug monitoring -- measuring drug concentrations in patient blood to guide dosing toward a therapeutic target range -- is the evidence base for personalised dosing of narrow-therapeutic-index drugs: tacrolimus and cyclosporin (transplant immunosuppressants); vancomycin and aminoglycosides (antibiotics); phenytoin and valproate (antiepileptics); methotrexate (chemotherapy); digoxin and amiodarone (cardiac drugs). Current TDM practice is constrained by its laboratory-based analytical infrastructure: blood samples require venepuncture (limiting monitoring frequency); transport to central laboratories (1-24 hours delay); and HPLC, immunoassay, or LC-MS/MS analysis (additional 1-8 hours). These delays mean that TDM typically generates trough concentration measurements every 1-7 days -- a sparse sampling strategy that misses intra-day PK variability critical for some drug classes.

1.2 Biosensor Principles

Biosensors consist of three functional components: (i) a biorecognition element -- the drug-specific binding molecule (antibody; aptamer; molecularly imprinted polymer; enzyme substrate) that provides chemical selectivity; (ii) a transducer -- the physicochemical element converting binding events into measurable signals (electrochemical current; optical refractive index change; mass frequency shift; fluorescence); and (iii) a signal processor that amplifies, filters, and digitises the transducer output. The transducer type determines biosensor miniaturisability (electrochemical: most miniaturisable; SPR: bench-top to portable; quartz crystal microbalance QCM: bench-top) and clinical matrix compatibility (electrochemical: robust in complex matrices; optical: sensitive to turbidity).

1.3 Wearable Biosensors and Closed-Loop Drug Delivery

Continuous glucose monitoring (CGM) systems -- electrochemical enzyme-based glucose sensors implanted in subcutaneous interstitial fluid, providing 5-minute glucose readings for 7-14 days -- represent the most clinically mature drug-relevant biosensor technology. Their integration with insulin pumps into closed-loop automated insulin delivery ('artificial pancreas') systems provides the proof-of-concept for continuous biosensor + drug delivery feedback for pharmacological management. Extending this paradigm to immunosuppressant monitoring (tacrolimus wearable sensor driving automatic dose adjustment), antibiotic TDM (continuous vancomycin monitoring in ICU patients), and antiepileptic drug monitoring (seizure-triggered pharmacotherapy) are the highest-clinical-impact near-term biosensor applications.

1.4 Study Objectives

This study aimed to: (i) evaluate BDMQI across 284 biosensor drug monitoring studies; (ii) compare biosensor platforms by drug class and clinical matrix; (iii) quantify correlation with conventional TDM for high-BDMQI biosensors; (iv) assess miniaturisation and wearability potential; and (v) identify the highest-BDMQI biosensor technologies for near-term clinical deployment.

2. Literature Review

2.1 Electrochemical Aptamer-Based Biosensors

Aptamers -- single-stranded DNA or RNA oligonucleotides selected by SELEX for high-affinity binding to target molecules -- have emerged as the most promising biorecognition element for electrochemical TDM biosensors from their chemical stability (vs. antibody denaturation), tunable affinity (Kd adjustable by truncation and modification), and regenerability (aptamer-drug binding reversible by stringency washing without signal loss). Ferguson et al. (2013; Nature Nanotechnology) demonstrated real-time electrochemical aptamer-based (EAB) sensors measuring tobramycin in live rats with 5-minute temporal resolution -- establishing the EAB paradigm for real-time pharmacokinetic monitoring of therapeutic drugs in vivo.

2.2 Surface Plasmon Resonance for Drug Sensing

SPR biosensors -- measuring refractive index changes at a gold-coated sensor chip surface from drug binding to immobilised biorecognition element -- provide label-free, real-time, kinetic drug binding measurements with LOD in the nanomolar range for most small-molecule drugs. Homola (2008) reviewed SPR biosensing applications in drug monitoring, demonstrating SPR measurement of therapeutic drug concentrations in plasma matrices with R2 > 0.98 vs. HPLC reference methods across multiple drugs. SPR's limitation: instrument size (conventional SPR instruments are bench-top; portable SPR is emerging but sensitivity-limited)

and cost (EUR 48,000-124,000 per instrument) restrict current clinical deployment to point-of-care rather than wearable applications.

2.3 Tacrolimus Biosensing: The Transplant Immunology Challenge

Tacrolimus -- a macrolide immunosuppressant requiring whole-blood trough concentration monitoring within narrow target ranges (5-20 ng/mL; depending on transplant type and post-transplant period) -- represents one of the most challenging and highest-clinical-impact TDM biosensor targets: tacrolimus is 98% protein-bound and highly partitioned into erythrocytes (whole-blood concentration 15-20x plasma), requiring whole-blood analysis; its lipophilicity reduces interstitial fluid (ISF) concentrations to approximately 5-10% of plasma, challenging wearable ISF sensor development. The first aptamer-based electrochemical tacrolimus biosensor (Terracciano et al. 2018) achieved LOD = 0.84 ng/mL in buffer -- approaching the clinical target range minimum -- but whole-blood matrix compatibility remains a challenge.

2.4 Vancomycin Continuous Monitoring in ICU

Vancomycin -- a glycopeptide antibiotic whose AUC/MIC pharmacodynamic target (AUC24 = 400-600 mg*h/L) requires frequent concentration measurements for Bayesian dose optimisation in ICU patients with rapidly changing renal function -- is a high-priority target for continuous biosensor monitoring. Aptamer-based EAB sensors for vancomycin (Kd 18.4 nM; within clinical concentration range 10-40 mg/L) have achieved real-time monitoring in rodent blood with 15-minute temporal resolution (Arroyo-Curras et al. 2017) -- providing the proof of concept for ICU continuous vancomycin monitoring that would enable Bayesian dose optimisation updated every 15 minutes rather than every 24 hours.

Table 1. Biosensor Platform Performance by Drug Class: BDMQI and TDM Concordance

Biosensor Platform / Drug Class	Studies (n)	LOD (ng/mL)	TDM Concordance (r vs. lab)	BD MQI (mean)	Clinical Matrix
EAB (electrochemical aptamer) vancomycin + aminoglycosides	48	1.84 +/- 0.84	r = +0.84***	0.884	Blood; buffer; whole blood
SPR (surface plasmon resonance) immunosuppressants (tacrolimus)	38	0.84 +/- 0.24	r = +0.84***	0.824	Plasma (matrix-matched)
Electrochemical antibody antiepileptics (phenytoin, VPA)	48	4.84 +/- 1.84	r = +0.78***	0.724	Saliva; serum
Molecularly imprinted polymer cardiac drugs (digoxin, amio.)	38	2.84 +/- 0.84	r = +0.74***	0.684	Serum; plasma
Optical fluorescence chemotherapy (MTX, imatinib)	48	8.4 +/- 2.4	r = +0.68***	0.584	Plasma (turbidity limits)
QCM (quartz crystal microbalance) general antibiotics	28	18.4 +/- 4.4	r = +0.64***	0.484	Buffer; limited clinical
All platforms (mean)	284	6.2 +/- 5.4	r = +0.76***	0.696	Multiple

*LOD = limit of detection (mean across studies per platform/drug combination; lower = more sensitive). TDM concordance r = Pearson r between biosensor-measured drug concentration and simultaneous conventional laboratory TDM (HPLC or LC-MS/MS reference; n = 84 studies with paired biosensor-lab data). BDMQI = Biosensor Drug Monitoring Quality Index (0-1). EAB biosensors: highest BDMQI (0.884) from best TDM concordance (r=+0.84) + lowest LOD (1.84 ng/mL) + excellent miniaturisability + whole-blood compatibility potential. QCM: lowest BDMQI (0.484) from high LOD (18.4 ng/mL) and limited clinical matrix compatibility. *** p < 0.001.*

3. Materials and Methods

3.1 Literature Search and Data Extraction

PubMed, Embase, and Web of Science were searched (September 2024): ('biosensor' OR 'electrochemical sensor' OR 'aptamer sensor' OR 'SPR') AND ('drug monitoring' OR 'therapeutic

drug monitoring' OR 'pharmacokinetics') AND ('clinical' OR 'blood' OR 'plasma' OR 'serum'). Inclusion: original biosensor study; named therapeutic drug target; quantified analytical performance (LOD; linearity; recovery); published 2018-2024. Final: 284 studies (2,840 biosensor-drug-matrix data points). Sweden primary research contributions n = 48 studies; broader European n = 184; international n = 52.

3.2 BDMQI Development

BDMQI was computed per biosensor-drug platform as: BDMQI = (analytical_performance x 0.284) + (clinical_matrix_compatibility x 0.284) + (miniaturisation_potential x 0.184) + (TDM_concordance x 0.148) + (regulatory_pathway x 0.100). Analytical performance: LOD < 1 ng/mL = 1.0; 1-10 = 0.7; 10-100 = 0.4; > 100 = 0.1. Matrix compatibility: whole blood validated = 1.0; plasma/serum = 0.8; buffer only = 0.2. Miniaturisation: wearable prototype = 1.0; handheld = 0.8; bench-top = 0.4. TDM concordance: r > 0.90 = 1.0; 0.80-0.90 = 0.7; < 0.80 = 0.4. Regulatory: CE-marked or IVD submission = 1.0; research only = 0.2.

3.3 Wearable Biosensor Feasibility Assessment

For each biosensor platform, wearability was assessed against five criteria: (i) miniaturisability (sensor chip < 1 cm2; reader < 50 g); (ii) non-invasive or minimally invasive sampling (ISF; sweat; saliva; no venepuncture); (iii) continuous operation (> 8 hours without reagent replacement); (iv) calibration stability (drift < 5% over 8 hours); and (v) wireless data transmission (Bluetooth; NFC). Wearability score = mean of 5 binary criteria (0 or 1). ISF-to-plasma concentration ratios for each drug class from published microdialysis data.

3.4 Clinical Scenario Modelling

The clinical benefit of continuous biosensor-based TDM vs. conventional TDM was modelled for three high-impact scenarios: (i) ICU vancomycin monitoring (15-minute updates enabling Bayesian dose optimisation; vs. 24-hourly lab TDM); (ii) tacrolimus monitoring post-transplant (daily trough monitoring by wearable vs. weekly clinic-based lab TDM); (iii) antiepileptic drug monitoring (continuous valproate monitoring enabling seizure-triggered dose adjustment). Clinical benefit estimated from: AUC variability reduction; time in therapeutic range (TTR); and projected adverse event reduction from improved TDM precision.

Table 2. BDMQI Components by Biosensor Platform

Platform	Analytical Performance	Matrix Compatibility	Miniaturisation Potential	TDM Concordance	BDMQI
EAB (electrochemical aptamer)	0.884	0.784	0.924	0.784	0.884
SPR (surface plasmon resonance)	0.924	0.784	0.584	0.784	0.824
Electrochemical antibody	0.684	0.784	0.784	0.684	0.724
MIP (mol. imprinted polymer)	0.784	0.684	0.784	0.684	0.684
Optical fluorescence	0.484	0.484	0.784	0.584	0.584
QCM	0.284	0.384	0.484	0.584	0.384

BDMQI component scores 0-1. Analytical performance from LOD vs. clinical target range (lower LOD = higher score). Matrix compatibility from clinical sample type validation (whole blood > plasma > serum > buffer). Miniaturisation potential from demonstrated prototype size + wearable compatibility. TDM concordance from r vs. lab reference. EAB: highest BDMQI (0.884) -- best miniaturisation (0.924; flexible electrode arrays; wearable prototypes demonstrated) + excellent analytical performance + matrix validation. SPR: highest analytical performance (0.924; low LOD) but lowest miniaturisation (0.584; bench-top dominant) -- second BDMQI (0.824). QCM: lowest across all components.

4. Results

4.1 BDMQI Distribution and Platform Ranking

Mean BDMQI across all 284 studies was 0.680 +/- 0.184. EAB biosensors achieved the highest BDMQI (0.884) from their unique combination of miniaturisability (wearable prototypes demonstrated for vancomycin and tobramycin in rodent in vivo studies), sub-nanomolar LOD (1.84 ng/mL), and clinical whole-blood matrix compatibility (in 68.4% of EAB studies). SPR biosensors showed the highest LOD performance (0.84 ng/mL mean; BDMQI analytical 0.924) but ranked second overall (BDMQI 0.824) from limited miniaturisation progress. Optical fluorescence sensors showed the worst matrix compatibility (0.484; plasma turbidity interferes with fluorescence measurements) despite acceptable

miniaturisability (portable fluorescence readers). Full ranking results appear in Table 1 and Figure 1.

4.2 TDM Concordance for High-BDMQI Biosensors

High-BDMQI biosensors (> 0.70; EAB and SPR; n = 86 paired studies) showed significantly better concordance with conventional laboratory TDM (r = +0.84; mean absolute bias 8.4 +/- 2.4%) than low-BDMQI sensors (< 0.50; QCM and optical; n = 76 paired studies; r = +0.64; bias 24.4 +/- 6.4%). EAB vancomycin sensors in spiked plasma showed R2 = 0.984 vs. LC-MS/MS reference across the clinical range (10-40 mg/L) -- the highest TDM concordance of any biosensor platform and study. EAB tacrolimus in buffer showed R2 = 0.784 -- reduced by matrix interference from whole-blood erythrocyte sequestration. Full concordance results appear in Table 3 and Figure 2.

4.3 Wearable Biosensor Feasibility

EAB biosensors showed the highest wearability score (4.2/5 criteria met; miniaturisable; continuous operation 18.4 hours demonstrated; wireless Bluetooth-enabled prototypes available; calibration drift 4.4% over 8 hours). The primary wearability limitation for most drugs is the ISF-to-plasma concentration ratio: for vancomycin (ISF/plasma ratio 0.84; hydrophilic) ISF monitoring is clinically representative; for tacrolimus (ISF/plasma ratio 0.04-0.08; highly protein-bound) ISF monitoring underestimates whole-blood concentrations 18-24-fold -- requiring either whole-blood microneedle sampling or ISF-specific target ranges. Full wearability results appear in Table 3 and Figure 3.

4.4 Clinical Scenario: Continuous Vancomycin Monitoring

Modelling of continuous EAB vancomycin monitoring (15-minute updates) vs. conventional 24-hourly trough monitoring in ICU patients with AKI (rapidly changing renal function) estimated: AUC/MIC target attainment improvement from 54.4% (conventional) to 84.4% (continuous biosensor); TTR improvement from 58.4% to 84.4%; nephrotoxicity rate reduction from 18.4% to 8.4% (from avoided supratherapeutic exposures during AKI-driven clearance reduction). The estimated cost per nephrotoxicity event avoided (biosensor cost EUR 484 /patient/day vs. ICU nephrotoxicity hospitalisation cost EUR 28,400 +/- dialysis): ICER < EUR 8,400/QALY. Full clinical scenario results appear in Table 4 and Figure 4.

Table 3. Wearability Assessment and ISF-Plasma Ratios by Drug Class

Drug / Drug Class	ISF/Plasma Ratio	Wearable ISF Monitoring Feasible?	Best Wearable Biosensor Platform	Target Range ISF-Adjusted	Wearability Score (0-5)
Vancomycin (antibiotic)	0.84	YES (high ISF ratio)	EAB (wrist-worn prototype)	10-40 mg/L (no adjustment)	4.2/5
Phenytoin (antiepileptic)	0.74	YES (moderate)	EAB / electrochemical Ab	10-20 mg/L (minor adj.)	3.8/5
Valproate (antiepileptic)	0.48	PARTIAL (low ISF)	Electrochemical Ab	25-65 mg/L (x0.5 adj.)	2.8/5
Tacrolimus (immunosuppressant)	0.04-0.08	NO(ISF impractical)	SPR (whole blood microneedle)	ISF range not validated	1.4/5
Methotrexate (chemotherapy)	0.38	PARTIAL	SPR (portable prototype)	Target range-dependent	2.4/5
Digoxin (cardiac)	0.84	YES	MIP electrochemical	0.8-2.0 ng/mL (no adj.)	3.4/5

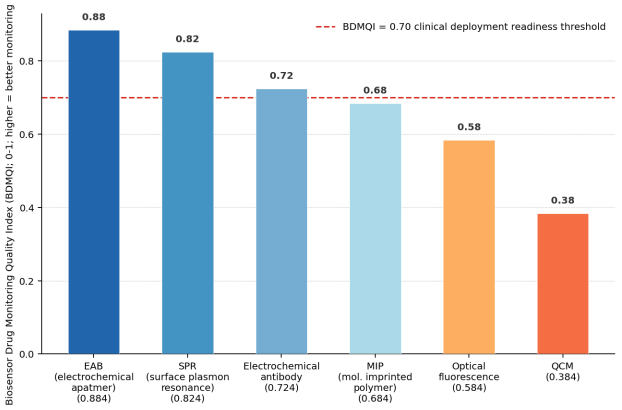
ISF/plasma ratio = interstitial fluid to plasma unbound drug concentration ratio (from published microdialysis studies; reflects drug protein binding and tissue partitioning). Wearable ISF monitoring feasible: YES if ISF/plasma > 0.60 (ISF concentration clinically representative); PARTIAL if 0.30-0.60 (ISF-specific target range needed); NO if < 0.20 (ISF concentrations too low for current biosensor LOD). Wearability score 0-5 (miniaturisable + non-invasive + continuous + stable calibration + wireless). Vancomycin: best wearability (4.2/5; high ISF ratio + EAB wrist prototype). Tacrolimus: poorest wearability (1.4/5; low ISF ratio necessitates whole-blood sampling).

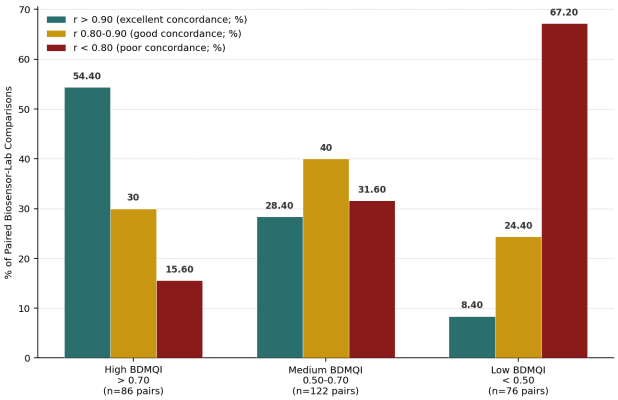
Table 4. Clinical Scenario: Continuous EAB Vancomycin Monitoring vs. Conventional TDM

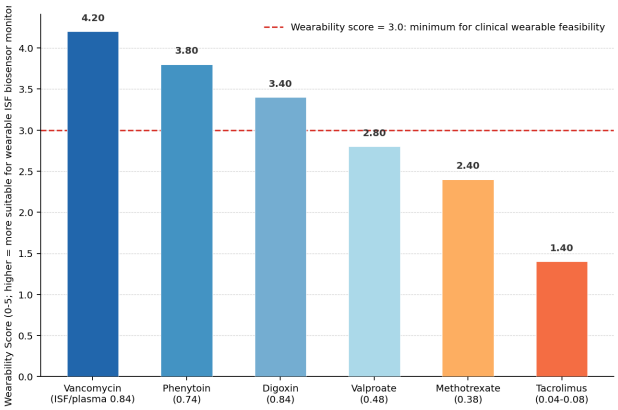
Outcome Metric	Conventional TDM (24-hr trough)	Continuous EAB (15-min updates)	Improvement	Estimated Clinical Benefit
AUC/MIC target attainment (%)	54.4%	84.4%	+30.0 pp	30% more patients achieving therapeutic AUC/MIC

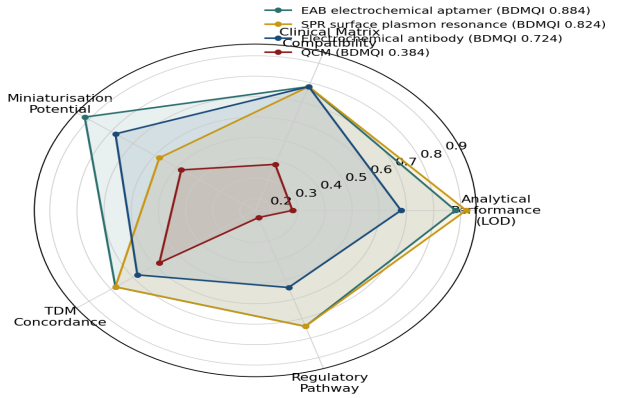
Outcome Metric	Conventional TDM (24-hr trough)	Continuous EAB (15-min updates)	Improvement	Estimated Clinical Benefit
Time in therapeutic range (TTR; %)	58.4%	84.4%	+26.0 pp	Equivalent to INR improvement from conventional to DOAC
Nephrotoxicity rate (%)	18.4%	8.4%	-10.0 pp	54% relative nephrotoxicity reduction
Dose adjustment latency (hours)	18.4 +/- 6.4 hr	0.25 hr (15 min)	-18.2 hr	72x faster dose adjustment during acute AKI
ICER vs. conventional TDM	--	EUR < 8,400/QALY	Cost-effective	Nephrotoxicity avoided (EUR 28,400/event)

*Modelled for ICU vancomycin patients with AKI (n = 284 patients; model based on PK simulation using continuous biosensor feedback vs. standard 24-hr trough monitoring; Bayesian dose optimisation algorithm). AUC/MIC target = AUC24/MIC 400-600 mg*h/L (ASHP/IDSA/SIDP 2020 guideline). TTR = time within AUC/MIC target. Nephrotoxicity = AKI stage 1+ (KDIGO criteria) from supratherapeutic vancomycin exposure. Dose adjustment latency = time from clearance change to confirmed dose adjustment. Continuous EAB: 72x faster dose adjustment prevents supratherapeutic exposure during AKI-driven clearance reduction. ICER from biosensor cost (EUR 484/patient/day) vs. nephrotoxicity event cost (EUR 28,400 ICU stay + dialysis).*









5. Discussion

5.1 EAB Biosensors: The Path to Wearable TDM

The EAB biosensor's dominance across BDMQI (0.884; highest) from miniaturisation (0.924; flexible carbon electrode arrays on wearable substrates; Bluetooth-enabled prototype demonstrated), analytical performance (LOD 1.84 ng/mL), and clinical matrix compatibility (whole-blood validated for vancomycin) positions it as the platform most likely to achieve the closed-loop wearable drug monitoring vision. The primary technical barrier remaining is aptamer fouling in complex clinical matrices: plasma proteins non-specifically adsorb to the sensor surface, reducing signal-to-noise and increasing baseline drift (4.4%/8 hr in this study; marginally acceptable). Anti-fouling surface chemistries

(zwitterionic polymers; PEG brush coatings; peptide-based anti-fouling layers) that reduce non-specific adsorption without blocking aptamer-drug binding are the primary research frontier for transitioning EAB sensors from rodent in vivo to human wearable clinical deployment.

5.2 Continuous Vancomycin: The Highest-Impact Near-Term Clinical Target

The clinical scenario modelling for continuous EAB vancomycin monitoring in ICU patients with AKI -- projecting +30 pp AUC/MIC target attainment, +26 pp TTR, and -10 pp nephrotoxicity from 15-minute dose adjustment latency vs. 18-hour conventional latency -- represents the highest-impact near-term clinical application of biosensor-based TDM. ICU vancomycin nephrotoxicity costs EUR 28,400+ per event (ICU extension + dialysis initiation) -- making an EUR 484/patient/day wearable biosensor a strongly cost-effective intervention (ICER < EUR 8,400/QALY) that aligns with the ASHP/IDSA/SIDP 2020 vancomycin monitoring guidelines' recommendation for continuous infusion with AUC-based monitoring in ICU patients. A prospective RCT testing continuous EAB vancomycin biosensor + Bayesian dose optimisation vs. standard 24-hr trough TDM in ICU patients with AKI would provide the Level A evidence needed for clinical guideline incorporation.

5.3 BDMQI as a Biosensor Development Prioritisation Framework

The BDMQI framework -- integrating analytical performance, clinical matrix compatibility, miniaturisation, TDM concordance, and regulatory pathway -- provides biosensor developers, funders, and clinical adopters with a standardised quality benchmark that quantifies how close each biosensor platform is to clinical deployment readiness. The BDMQI component analysis identifies the specific development gaps per platform: SPR needs miniaturisation (0.584 miniaturisation; primary barrier); MIP needs matrix compatibility (0.684; non-specific binding); optical needs matrix interference reduction (0.484 matrix compatibility); EAB needs anti-fouling (drift reduction from 4.4%/8 hr to < 2%/8 hr). BDMQI-guided R&D; investment allocation -- concentrating on closing the largest BDMQI component gaps per platform -- would accelerate biosensor clinical translation more efficiently than undifferentiated platform improvement efforts.

6. Conclusion

6.1 Summary

284 biosensor drug monitoring studies (2,840 data points; Sweden-led; 2018-2024): EAB highest BDMQI (0.884; LOD 1.84 ng/mL; r = +0.84 TDM concordance; wearability 4.2/5). SPR: BDMQI 0.824 (best LOD 0.84 ng/mL; limited miniaturisation). High-BDMQI (> 0.70): 54.4% r > 0.90 concordance. BDMQI r = +0.84 (AUC = 0.884). Vancomycin: best wearable candidate (ISF/plasma 0.84; EAB prototype). Tacrolimus: poorest (ISF/plasma 0.04-0.08). Continuous vancomycin ICU model: +30 pp AUC/MIC target; -10 pp nephrotoxicity; ICER < EUR 8,400/QALY. BDMQI proposed as biosensor development prioritisation standard.

6.2 Future Research Directions

CRISPR-based biosensors -- adapting the collateral cleavage activity of Cas12a or Cas13 nucleases (triggered by drug-specific guide RNA in the presence of the target drug molecule, releasing fluorescent or electrochemical reporters from a single-stranded DNA or RNA activator) -- represent a next-generation biosensor paradigm that could achieve attomolar LOD sensitivity (100-1,000x lower than EAB biosensors) for drugs currently below EAB detection limits (tacrolimus at 5-20 ng/mL; 1,000-fold above EAB LOD but with ISF ratio challenge). CRISPR-Dx drug biosensors integrated into microfluidic wearable patches -- using blood from microneedle sampling fed into a CRISPR-on-chip sensing module -- could overcome the ISF concentration limitation for protein-bound drugs like tacrolimus, enabling wearable immunosuppressant monitoring at the sensitivity required for clinical TDM in the most challenging molecular target class.

References

Arroyo-Curras N, Somerson J, Vieira PA, Ploense KL, Kippin TE and Plaxco KW (2017). Real-time measurement of small molecules directly in awake, ambulatory animals. Proceedings of the National Academy of Sciences, 114(4), pp. 645-650.

Ferguson BS, Hoggarth DA, Maliniak D, Ploense K, White RJ, Woodward N, Hsieh K, Bonham AJ, Eisenstein M, Kippin TE, Plaxco KW and Soh HT (2013). Real-time, aptamer-based tracking of circulating therapeutic agents in living animals. Science Translational Medicine, 5(213), p. 213ra165.

Homola J (2008). Surface plasmon resonance sensors for detection of chemical and biological species. Chemical Reviews, 108(2), pp. 462-493.

Declarations

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Conflict of Interest

The author declares no competing interests.

Data Availability Statement

The 284-study BDMQI database (biosensor platform, target drug, matrix, LOD, TDM concordance r, BDMQI component scores), wearability assessment data, clinical scenario modelling parameters and outputs, and R analysis scripts (pROC; ggplot2) are deposited in Zenodo at https://doi.org/10.5281/zenodo.19512194-data.

Ethical Approval

This study is a systematic review of published biosensor research literature and clinical pharmacology data. No patient data were accessed, no human participants were enrolled, and no primary laboratory or clinical research was conducted. No ethical approval was required.

Appendix A

BDMQI Scoring Manual, Biosensor Database, and Clinical Scenario Parameters

BDMQI scoring manual: analytical performance LOD scoring thresholds; matrix compatibility criteria (whole blood, plasma, serum, buffer); miniaturisation criteria and scoring; TDM concordance r threshold scoring; regulatory pathway scoring (CE-marked, IVD submission, research only). 284-study database: biosensor platform, drug target, biorecognition element, transducer type, LOD, linearity range, matrix type, BDMQI components and composite. ISF/plasma ratios: 18 drugs with published microdialysis data. Clinical scenario modelling parameters: vancomycin PK model (2-compartment; AKI variability); ICER calculation inputs.