

### **Online Supplementary Information 3**

**Article title:** Clinical value of emerging bioanalytical methods for drug monitoring: a scoping review of their applicability for medication adherence and therapeutic drug monitoring

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**Table 1. Overview of all included studies**

<b>Reported field</b>	<b>Study</b>	<b>Continent</b>	<b>Study population</b>	<b>Matrix measured</b>	<b>Analytical method</b>	<b>Drugs evaluated</b>	<b>Clinical applicability</b>
Asthma/ COPD	Salamzadeh et al., 2008[1]	Asia	Adult patients with asthma and COPD; N=86	Saliva*	HPLC	theophylline	TDM
Asthma/ COPD	Hassall et al., 2018[2]	Europe	Adults with stable COPD and/or asthma; N=200	Hair	LC-MS/MS	formoterol	Adherence
Cardiovascular disease	Peeters et al., 2019[3]	Europe	Outpatients from internal medicine, cardiology, and nephrology clinics; N=135	DBS*	UHPLC-MS/MS	enalapril, perindopril, losartan, valsartan, hydrochlorothiazide, amlodipine, nifedipine	Adherence
Cardiovascular disease	Foerster et al., 2018[4]	Europe	Patients (=18 years), regularly treated with apixaban, dabigatran, edoxaban, or rivaroxaban; N=33	DBS*	UPLC-MS/MS	rivaroxaban	TDM
Cardiovascular disease	Zalzstein et al., 2003[5]	Asia	Infants, children, and adolescents attending the paediatric cardiology unit and receiving digoxin for a variety of indication; N=18	Saliva*	FPIA	digoxin	TDM
Cardiovascular disease	Enderle et al., 2015[6]	Europe	Outpatients with pulmonary arterial hypertension or chronic thromboembolic pulmonary hypertension, receiving stable doses of tadalafil, sildenafil, ambrisentan, or bosentan for at least 4 weeks; N=84	DBS*	LC-MS/MS	sildenafil, tadalafil, ambrisentan, bosentan	TDM
Cardiovascular disease	Ghimenti et al., 2011[7]	Europe	Adult patients on warfarin therapy treated for atrial fibrillation, deep vein thrombosis, pulmonary embolism, and others; N=50	Saliva*	HPLC	warfarin	TDM
Cardiovascular disease	Lomonaco et al., 2014[8]	Europe	Adult patients with atrial fibrillation, deep vein thrombosis, or mechanical or biological heart	Saliva*	HPLC	warfarin	TDM

Reported field	Study	Continent	Study population	Matrix measured	Analytical method	Drugs evaluated	Clinical applicability
Cardiovascular disease	Richter et al., 2019[9]	Europe	valve bearers undergoing warfarin therapy; N=14 Hypertensive patients taking regularly cardiovascular drugs; N=57	Saliva and Urine*	LC-MS/MS	amlodipine, bisoprolol, spironolactone, hydrochlorothiazide, metoprolol, moxonidine, ramipril, torasemide, valsartan	Adherence
Chronic hyposmia	Henkin et al., 2012[10]	North America	Adult patients with smell loss (hyposmia) treated with oral theophylline; N=23	Saliva*	FPIA	theophylline	TDM
Chronic migraine	Ferrari et al., 2016[11]	Europe	Adults diagnosed with chronic migraine with self-reported triptan use; N=147	Hair	LC-MS/MS	almotriptan, eletriptan, frovatriptan, rizatriptan, sumatriptan	Adherence
Chronic migraine	Ferrari et al., 2017[12]	Europe	Primary headache patients with daily treatment for at least 3 months; N=93	Hair	LC-MS/MS	amitriptyline, citalopram, cloxazolam, duloxetine, topiramate	Adherence
Diabetes	Scherf-Clavel et al., 2019[13]	Europe	Adult patients with type 2 diabetes mellitus receiving a therapy with metformin and/or sitagliptin as fixed dose combination or monotherapy; N=154	DBS*	HPLC	metformin, sitagliptin	TDM
Epilepsy	Guo et al., 2019[14]	Asia	Epilepsy patients, aged 4 to 87years; N=29	DBS	GC-MS	valproic acid	TDM
Epilepsy	Brandt et al., 2018[15]	Europe	Adult epileptic inpatients prescribed lacosamide; N=25	Saliva*	-	lacosamide	TDM

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Epilepsy	Maldonado et al., 2008[16]	South America	Children treated for epilepsy, aged from 1 to 14 years; N=103	Saliva	FPIA	carbamazepine, valproic acid	TDM
Epilepsy	Tsatsakis et al., 2000[17]	Europe	Patients (aged 5 to 69 years) with epilepsy, using PHT for 2 months to several years; N=60	Hair*	HPLC FPIA	phenytoin	Adherence
Epilepsy	Williams et al., 2002[18]	Europe	26 pregnant women and 13 non-pregnant female controls with epilepsy; N=39	Hair	HPLC	carbamazepine, lamotrigine	Adherence
Epilepsy	Karas-Ruszczuk et al., 2017[19]	Europe	Outpatients and inpatients, have a 3-month history of stable Levetiracetam dosing;; N=51	Saliva and Hair*	LC-MS/MS	levetiracetam	TDM and Adherence
Epilepsy	Williams et al., 2001[20]	Europe	Closely supervised adult inpatients with epilepsy; N=37	Hair*	HPLC	carbamazepine	Adherence
Epilepsy	Rhoden et al., 2014[21]	South America	Patients from a neurology service affiliated to a public health care center, using valproic acid; N=17	DBS*	GC-MS	valproic acid	TDM
Epilepsy	Mecarelli et al., 2007[22]	Europe	Adult epileptic patients, taking levetiracetam as monotherapy or add-on therapy with other antiepileptic drugs for at least 3 months; N=30	Saliva*	GC-MS	levetiracetam	TDM
Epilepsy	Grim et al., 2003[23]	North America	Children and adults patients with epilepsy who attended the neurology clinic and treated with levetiracetam for a minimum of 4 weeks; N=40	Saliva*	HPLC	levetiracetam	TDM
Epilepsy	Linder et al., 2017[24]	Europe	Children and adolescents aged 2 to 18 years and treated with carbamazepine, lamotrigine, or valproic acid as a single or	DBS*	LC-MS/MS	carbamazepine, lamotrigine, valproic acid	TDM

Reported field	Study	Continent	Study population	Matrix measured	Analytical method	Drugs evaluated	Clinical applicability
Epilepsy	Dwivedi et al., 2015[25]	Asia	combined therapy; N=46 Epileptic patients aged = 65 years taking either valproic acid alone or in combination for minimum 3 months;	Saliva*	HPLC	valproic acid	TDM
Epilepsy	Greenaway et al., 2011[26]	Europe	N=65 Epileptic patients treated with lacosamide as add-on therapy for at least 1 month;	Saliva*	HPLC	lacosamide	TDM
Epilepsy	Kaewdoun et al., 2015[27]	Asia	N=98 Epileptic outpatients aged 15 to 60 years old receiving carbamazepine monotherapy or in combination with other antiepileptic drugs for at least 1 month;	Saliva*	Fluorescence polarization immunoassay (FPIA)	carbamazepine	TDM
Epilepsy	Tsiropoulos et al., 2000[28]	Europe	N=42 Epileptic outpatients aged more than 14 years receiving stable doses of lamotrigine and comedication for at least 14 days;	Saliva*	HPLC	lamotrigine	TDM
Epilepsy	Kuczynska et al., 2019[29]	Europe	N=40 Epileptic patients on stable drug dosing for 3 months;	Saliva and Hair*	LC-MS/MS	lamotrigine	TDM and Adherence
Epilepsy	Shah et al., 2013[30]	Europe	N=85 Children (0.9-17 years) with epilepsy;	DBS	GC HPLC	valproic acid, levetiracetam, carbamazepine, lamotrigine	Adherence
Epilepsy	Li et al., 2016[31]	Asia	N=102 Inpatient and outpatient epileptic patients in the Pediatric Departments at the hospital taking oxcarbazepine as monotherapy or adjunctive therapy with other antiepileptic drugs;	Saliva*	HPLC	oxcarbazepine	TDM
Epilepsy	Miles et al., 2003[32]	North America	N=52 Epilepsy patients (2.5 to 25 years) attending the neurology clinic and	Saliva*	FPIA	topiramate	TDM

Reported field	Study	Continent	Study population	Matrix measured	Analytical method	Drugs evaluated	Clinical applicability
Epilepsy	Dordevic et al., 2009[33]	Europe	taking a constant dose of topiramate for at least 1 week; N=31 Epileptic patients on carbamazepine therapy at the clinic;	Saliva*	HPLC	carbamazepine	TDM
Epilepsy	Ryan et al., 2003[34]	North America	N=23 Epilepsy patients (2 to 46 years) attending the neurology clinic and taking lamotrigine;	Saliva*	HPLC	lamotrigine	TDM
Epilepsy	Linder et al., 2019[35]	Europe	N=31 Children (2-18 years) with epilepsy;	DBS*	LC-MS/MS	carbamazepine, lamotrigine, levetiracetam, valproic acid	TDM and Adherence
Epilepsy	Kongrit et al., 2014[36]	Asia	N=135 Outpatients aged 17 to 56 years with epilepsy and received topiramate either monotherapy or combination therapy with other antiepileptic drugs for at least 1 month;	Saliva*	turbidimetric immunoassay	topiramate	TDM
Epilepsy	Dwivedi et al., 2016[37]	Asia	N=26 Paediatric and adult outpatients (= 65 years) with epilepsy taking either of carbamazepine, phenytoin, phenobarbital alone or in combinations for a minimum of three months and their drug dosage reached to maximum tolerable levels;	Saliva*	HPLC	carbamazepine, phenytoin, phenobarbital	TDM
Epilepsy	Hamdan et al., 2017[38]	Asia	N=116 Paediatric outpatients (=18 years) diagnosed with epilepsy and had been prescribed levetiracetam for at least one month;	Saliva*	HPLC	levetiracetam	TDM and Adherence
Epilepsy	Kim et al., 2020[39]	Asia	N=15 Epileptic adult patients taking perampanel and whose dose was not changed for 2-3 weeks;	Saliva*	LC-MS/MS	perampanel	TDM

Reported field	Study	Continent	Study population	Matrix measured	Analytical method	Drugs evaluated	Clinical applicability
Epilepsy	Franco et al., 2020[40]	Europe	N=30 Pediatric and adult patients with epilepsy receiving rufinamide as part of routine clinical management and being at steady state dose, at least 48 hours after the last rufinamide dose change (at least 96 hours for patients co-medicated with valproic acid);	Saliva*	HPLC	rufinamide	TDM
(Haemato)-Oncology	Willemsen et al., 2018[41]	Europe	N=26 Patients with any type of solid tumour;	DBS*	UPLC-MS/MS	everolimus	TDM
(Haemato)-Oncology	Braal et al., 2019[42]	Europe	N=22 Adult lung cancer patients;	Hair*	LC-MS/MS	erlotinib	TDM
(Haemato)-Oncology	Antunes et al., 2015[43]	South America	N=10 Adult patients with breast cancer;	DBS*	UHPLC-MS/MS	tamoxifen	TDM
(Haemato)-Oncology	Maring et al., 2009[44]	Europe	N=91 Adults with advanced non-small cell lung cancer;	Saliva*	HPLC	gemcitabine, epirubicin	TDM
(Haemato)-Oncology	Boucaud et al., 2003[45]	Europe	N=12 Adults with metastatic epithelial ovarian cancer;	Saliva*	HPLC with fluorescence detection	topotecan	TDM
(Haemato)-Oncology	Boons et al., 2017[46]	Europe	N=13 Adult patients (18 years or older) with CML on treatment with 300 mg nilotinib twice daily;	DBS*	LC-MS/MS	nilotinib	TDM
(Haemato)-Oncology	de Wit et al., 2015[47]	Europe	N=20 Patients =18 years with progressive disease from an advanced solid tumour;	DBS*	LC-MS/MS	pazopanib	TDM
(Haemato)-Oncology	Capron et al., 2016[48]	South America	N=12 Adult patients with chronic myeloid leukemia with imatinib treatment for >4 months;	Hair*	LC-MS/MS	imatinib	Adherence
(Haemato)-Oncology	Andriguetti et al., 2018[49]	South America	N=102 Outpatients prescribed with paclitaxel as a single chemotherapy or in combination with other	DBS*	LC-MS/MS	paclitaxel	TDM

Reported field	Study	Continent	Study population	Matrix measured	Analytical method	Drugs evaluated	Clinical applicability
(Haemato)-Oncology	Raymundo et al., 2018[50]	South America	chemotherapy drugs (carboplatin, gemcitabine, cisplatin, trastuzumab); N=34 Adults with prostate, breast, or lung cancer; N=31	DBS*	LC-MS/MS	docetaxel	TDM
(Haemato)-Oncology	Jager et al., 2014[51]	Europe	Female patients who underwent surgical treatment for early, ER-positive breast cancer, and subsequently received adjuvant tamoxifen for at least 2 months at the outpatient clinic; N=50	DBS*	LC-MS/MS	tamoxifen	TDM
(Haemato)-Oncology	Lee et al., 2020[52]	Asia	Outpatients aged 20 to 70 years with stable doses of radotinib taken at least for a week for the treatment of CML in chronic phase; N=50	DBS*	LC-MS	radotinib	TDM
(Haemato)-Oncology	Dillenburg et al., 2020[53]	South America	Prostate cancer patients; N=10	DBS*	LC-MS/MS	abiraterone	TDM
(Haemato)-Oncology	Antunes et al., 2015[54]	South America	Adult patients on chronic myeloid leukemia treatment with imatinib for at least 4 months; N=50	DBS*	LC-MS/MS	imatinib	TDM
HIV/AIDS	Courlet et al., 2019[55]	Europe	HIV patients participating in the Swiss HIV Cohort Study (SHCS) #815 study; N=73	Saliva*	LC-MS/MS	emtricitabine, lamivudine	Adherence
HIV/AIDS	Wu et al., 2018[56]	Asia	Female HIV positive patients, using lamivudine, tenofovir, or nevirapine over the past 12 months; N=33	Hair	LC-MS/MS	lamivudine, tenofovir disoproxil, nevirapine	Adherence
HIV/AIDS	Kromdijk et al., 2012[57]	Europe	HIV infected adults; N=80	DBS*	LC-MS/MS	nevirapine, efavirenz	TDM
HIV/AIDS	Alcaide et al., 2017[58]	Africa	HIV-infected women at week 32 of pregnancy; N=392	DBS	LC-MS/MS	tenofovir disoproxil, lamivudine,	Adherence



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HIV/AIDS	Van Zyl et al., 2011[59]	Africa	HIV infected adults on second-line treatment with lopinavir/ritonavir; N=93	Hair*	LC-MS/MS	efavirenz lopinavir	Adherence
HIV/AIDS	Gandhi et al., 2015[60]	North America	HIV-negative men who have sex with men and transgender women, enrolled in 3 prep trials; N=217	DBS and Hair	LC-MS/MS	tenofovir disoproxil, emtricitabine	Adherence
HIV/AIDS	Yamada et al., 2017[61]	Asia	HIV-1-infected outpatients, treated with abacavir, tenofovir, darunavir, raltegravir at least 1 month; N=30	Saliva*	LC-MS/MS	abacavir, tenofovir disoproxil	TDM
HIV/AIDS	Bernard et al., 2002[62]	Europe	HIV infected patients on HAART; N=89	Hair	HPLC	indinavir	TDM
HIV/AIDS	Duval et al., 2007[63]	Europe	HIV infected patients; N=43	Hair*	HPLC	indinavir	TDM
HIV/AIDS	Gandhi et al., 2009[64]	North America	Women with HIV initiating protease inhibitor therapy; N=224	Hair	LC-MS/MS	lopinavir, atazanavir	TDM and Adherence
HIV/AIDS	Gras et al., 2011[65]	Africa	Adult HIV patients being treated with zidovudine, lamivudine, and nevirapine; N=29	Saliva*	LC-MS	zidovudine, lamivudine, nevirapine	Adherence
HIV/AIDS	Gandhi et al., 2011[66]	North America	HIV infected and at-risk non-infected women; N=424	Hair	LC-MS/MS	atazanavir, ritonavir	TDM
HIV/AIDS	Hickey et al., 2014[67]	Africa	Adult patients on antiretroviral drugs; N=373	Hair	LC-MS/MS	nevirapine	Adherence
HIV/AIDS	Rakhmanina et al., 2007[68]	North America	Paediatric patients with HIV-1 infection (aged 4 to 14 years) receiving nevirapine for at least 4 weeks; N=19	Saliva*	LC-MS/MS	nevirapine	TDM and Adherence
HIV/AIDS	Wintergerst et al., 2000[69]	Europe	Asymptomatic HIV-infected male outpatients treated with antiretroviral containing indinavir; N=10	Saliva*	LC-MS	indinavir	TDM and Adherence

<b>Reported field</b>	<b>Study</b>	<b>Continent</b>	<b>Study population</b>	<b>Matrix measured</b>	<b>Analytical method</b>	<b>Drugs evaluated</b>	<b>Clinical applicability</b>
HIV/AIDS	van Heeswijk et al., 2001[70]	Europe	HIV-1-infected patients treated with nevirapine 200mg twice daily for at least 4 weeks; N=43	Saliva*	HPLC	nevirapine	TDM
HIV/AIDS	Johnston et al., 2019[71]	Africa	HIV-positive outpatients; N=135	Hair*	LC-MS/MS	efavirenz	TDM
HIV/AIDS	Murnane et al., 2019[72]	Africa	HIV-positive women that started ART during pregnancy and continued postpartuum; N=71	Hair	LC-MS/MS	tenofovir	Adherence
HIV/AIDS	Gandhi et al., 2019[73]	Asia	HIV-positive participants; N=75	Hair	LC-MS/MS	nevirapine, efavirenz	Adherence
HIV/AIDS	Chu et al., 2018[74]	Asia	HIV-positive adults; N=54	Hair	LC-MS/MS	zidovudine, efavirenz, lopinavir, ritonavir	Adherence
HIV/AIDS	Tabb et al., 2018[75]	Africa	HIV positive youngsters (age: 11-24y); N=227	Hair	LC-MS/MS	efavirenz, nevirapine, lopinavir, ritonavir	Adherence
HIV/AIDS	Hugen et al., 2000[76]	Europe	Adult outpatients infected with HIV who were treated chronically with indinavir 800mg q8h; N=14	Saliva*	HPLC	indinavir	TDM and Adherence
HIV/AIDS	Gandhi et al., 2017[77]	North America	HIV-negative men who have sex with men and transgender women using prep; N=280	Hair	LC-MS/MS	tenofovir	Adherence
HIV/AIDS	Pintye et al., 2017[78]	Asia	HIV infected children on standard second-line ART; N=244	Hair	LC-MS/MS	lopinavir	TDM and Adherence
HIV/AIDS	Chawana et al., 2017[79]	Africa	HIV-infected adolescents failing second-line ART; N=50	Hair	LC-MS/MS	atazanavir	TDM and Adherence
HIV/AIDS	Koss et al., 2017[80]	Africa	Samples were collected from men and transgender women that were enrolled in 2 open-label prep studies and from uninfected women participating in a randomized	Hair*	LC-MS/MS	tenofovir	Adherence

Reported field	Study	Continent	Study population	Matrix measured	Analytical method	Drugs evaluated	Clinical applicability
HIV/AIDS	Koss et al., 2015[81]	Africa	double-blind phase iib trial; N=1165 HIV-infected pregnant women at 12-28 gestation enrolled in ART trial;	Hair	LC-MS/MS	lopinavir, efavirenz	TDM
HIV/AIDS	Yan et al., 2016[82]	Asia	N=325 HIV infected adults;	Hair	LC-MS/MS	lamivudine	Adherence
HIV/AIDS	Prasitsuebsai et al., 2015[83]	Asia	N=287 Children with HIV infection on second-line ART regimens;	Hair*	LC-MS/MS	lopinavir	Adherence
HIV/AIDS	Olds et al., 2015[84]	Africa	N=149 Children with HIV infection (2-10 years of age);	Hair	LC-MS/MS	nevirapine	Adherence
HIV/AIDS	Baxi et al., 2015[85]	North America	N=74 HIV infected women;	Hair	LC-MS/MS	nevirapine	TDM
HIV/AIDS	Baxi et al., 2015[86]	Africa	N=271 HIV-negative serodiscordant couples and men who have sex with men using daily or intermittent prep in two phase II prep trials;	Hair*	LC-MS/MS	tenofovir , emtricitabine	TDM and Adherence
HIV/AIDS	Kromdijk et al., 2013[87]	Europe	N=88 HIV-infected adults;	DBS*	LC-MS/MS	efavirenz, nevirapine	TDM
HIV/AIDS	George et al., 2014[88]	Africa	N=50 HIV-infected adults;	Saliva	TLC	nevirapine	Adherence
HIV/AIDS	Lamorde et al., 2014[89]	Africa	N=101 HIV-infected adults;	Saliva*	TCL HPLC	nevirapine	TDM
HIV/AIDS	Duthaler et al., 2018[90]	Europe	N=297 HIV infected adults from Switzerland and Tanzania;	DBS*	LC-MS/MS	nevirapine, efavirenz, lopinavir	TDM
HIV/AIDS	Van Schooneveld et al., 2010[91]	North America	N=359 Adult HIV patients attending the HIV clinic, age >19 years, receipt of atazanavir (with or without ritonavir) for at least 7 days prior, and HIV RNA of <50 copies/ml for the last 90 days;	DBS*	UPLC	atazanavir	TDM
HIV/AIDS	ter Heine et al.,	Europe	N=48 Outpatients aged 18 years and older	DBS*	LC-MS/MS	ritonavir, darunavir,	TDM

Reported field	Study	Continent	Study population	Matrix measured	Analytical method	Drugs evaluated	Clinical applicability
	2011[92]		with confirmed HIV infection and used etravirine, darunavir/ritonavir or raltegravir for at least 2 weeks; N=11			raltegravir	
HIV/AIDS	de Truchis et al., 2016[93]	Africa	HIV-1 infected adults aged 18 years or older and had been treated with ART for 1 year; N=218	DBS	LC-MS	nevirapine, efavirenz	Adherence
HIV/AIDS	Yang et al., 2020[94]	Asia	HIV-infected adults; N=75	Hair	LC-MS/MS	nevirapine	Adherence
HIV/AIDS	Zhang et al., 2020[95]	Asia	HIV-infected adults; N=268	Hair	LC-MS/MS	tenofovir	Adherence
HIV/AIDS	Ngara et al., 2020[96]	Africa	HIV-infected adults on second-line treatment; N=50	Hair*	LC-MS/MS	atazanavir, ritonavir	TDM
HIV/AIDS	de Lastours et al., 2011[97]	Europe	Adult HIV-infected patients (<65 years old) receiving a stable antiretroviral regimen, including 245 mg TDF daily and/or 200 mg FTC daily for at least 3 months; N=41	Saliva*	LC-MS/MS	tenofovir , emtricitabine	TDM
HIV/AIDS	Gandhi et al., 2012[98]	North America	Women with or without HIV infection; N=111	Hair*	LC-MS/MS	efavirenz	TDM
IBD	Alsous et al., 2020[99]	Europe	Paediatric patients on AZA/6-MP treatment; N=29	DBS*	LC-MS/MS	azathioprine, mercaptopurine	TDM
IBD	Detrez et al., 2019[100]	Europe	Patients initiating or under maintenance golimumab for moderate-to-severe ulcerative colitis; N=10	DBS*	ELISA	golimumab	TDM
IBD	Bian et al., 2020[101]	Europe	Vedolizumab-treated outpatients with ulcerative colitis or Chron's disease; N=19	DBS*	ELISA	vedolizumab	TDM
Pain	Heiskanen et al., 2015[102]	Europe	Cancer patients on any dose of controlled-release (CR) oral	Saliva*	GC-MS	morphine, fentanyl, oxycodone	TDM

Reported field	Study	Continent	Study population	Matrix measured	Analytical method	Drugs evaluated	Clinical applicability
Pain	Hardy et al., 2012[103]	Australia/Oceania	morphine, CR oral oxycodone, or TD fentanyl; N=64 Patients with cancer, using sustained release oxycodone (Oxycontin); N=43	Saliva*	LC-MS/MS	oxycodone	TDM
Pain	Musshoff et al., 2007[104]	Europe	Adult patients with cancer pain; N=31	Hair	LC-MS/MS	tramadol, morphine, fentanyl	Adherence
Pain	Idkaidek et al., 2018[105]	Asia	Patients with neuropathic pain; N=44	Saliva*	LC-MS/MS	pregabalin	TDM
Pain	Miguez-Díez et al., 2015[106]	South America	Outpatients taking methadone for pain management; N=14	Saliva*	HPLC	methadone	TDM
Pain	Shaparin et al., 2017[107]	North America	Male and female chronic pain patients aged 18-72 years undergoing opioid treatment at pain management clinics; N=356	Saliva*	LC-MS/MS	oxycodone	Adherence
Parkinson	Kronstrand et al., 2003[108]	Europe	Patients with Parkinson's disease; N=16	Hair*	GC MS spectrophotometry for melanin quantitation	selegiline	Adherence
Psychiatric disorder	Sun et al., 2019[109]	Asia	Patients who were treated with risperidone for more than 3 months; N=34	Hair*	LC-MS/MS	risperidone	TDM
Psychiatric disorder	Preiskorn et al., 2018[110]	Europe	Children and adults diagnosed with attention-deficit/hyperactivity disorders, aged 7 to 48 years, undergoing medical treatment with methylphenidate; N=36	Saliva*	LC-MS/MS	methylphenidate	TDM
Psychiatric disorder	Ebert et al., 2018[111]	Europe	Inpatients or outpatients, aged 19 - 79 years, undergoing treatment with venlafaxine, citalopram, or quetiapine; N=75	Saliva*	LC-MS/MS HPLC-UV	venlafaxine, quetiapine, citalopram	TDM
Psychiatric disorder	Neumann et al., 2018[112]	Europe	Adult patients hospitalized for psychiatric disorders;	Saliva*	UPLC-MS/MS	aripiprazole, citalopram,	Adherence

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			N=96			escitalopram, duloxetine, mirtazapine, pipamperone, venlafaxine, quetiapine	
Psychiatric disorder	Kloosterboer et al., 2018[113]	Europe	Patients aged 18 years or older who used either risperidone, paliperidone (the active metabolite of risperidone), aripiprazole, or pipamperone; N=81	DBS*	LC-MS/MS	risperidone, paliperidone, aripiprazole, pipamperone	TDM and Adherence
Psychiatric disorder	Geers et al., 2017[114]	Europe	Schizophrenia patients aged 18-55 years, treated with clozapine, on a stable dose for at least 2 weeks, and had Caucasian ethnicity; N=15	DBS*	LC-MS/MS	clozapine	TDM
Psychiatric disorder	da Silva et al., 2018[115]	South America	Outpatients on fluoxetine treatment for > 6 months; N=30	DBS*	UHPLC-MS/MS	fluoxetine	TDM
Psychiatric disorder	Böttcher et al., 2019[116]	Europe	ADHD patients on Elvanse therapy, of which the oral fluid samples were sent to the laboratory for analysis; N=70	Saliva	UPLC-MS/MS	lisdexamfetamine	Adherence
Psychiatric disorder	Sticht et al., 2007[117]	Europe	Children (7-16 years of age) with ADHD; N=17	Hair	GC-MS	methylphenidate	Adherence
Psychiatric disorder	Marchei et al., 2008[118]	Europe	Children diagnosed with ADHD; N=11	Hair	LC-MS	methylphenidate	Adherence
Psychiatric disorder	Fucci et al., 2007[119]	Europe	Patients on stable methadone maintenance therapy; N=10	Hair	GC MS	methadone	Adherence
Psychiatric disorder	Cirimele et al., 2000[120]	Europe	Schizophrenic patients with refractory psychosis; N=26	Hair*	GC-MS	clozapine	TDM
Psychiatric disorder	Pirro et al., 2014[121]	Europe	Patients treated for opiate addiction; N=79	Hair	LC-MS/MS	buprenorphine	TDM

<b>Reported field</b>	<b>Study</b>	<b>Continent</b>	<b>Study population</b>	<b>Matrix measured</b>	<b>Analytical method</b>	<b>Drugs evaluated</b>	<b>Clinical applicability</b>
Psychiatric disorder	Skopp et al., 2011[122]	Europe	Participants in a maintenance program; N=18	Hair	LC-MS/MS	buprenorphine	TDM
Psychiatric disorder	Weber et al., 2017[123]	Europe	Depressive patients over 20 years old receiving citalopram or mirtazapine; N=36	DBS*	LC-MS	citalopram, mirtazapine	TDM
Psychiatric disorder	Dziurkowska et al., 2013[124]	Europe	Women with major depressive disorder treated with venlafaxine; N=14	Saliva	HPLC	venlafaxine	TDM
Psychiatric disorder	Mercolini et al., 2014[125]	Europe	Schizophrenic patients treated with ziprasidone at the mental health centres; N=10	DBS*	HPLC-F	ziprasidone	TDM
Psychiatric disorder	Wang et al., 2019[126]	Asia	Schizophrenic patients with fixed drug use for >6 months; N=46	Hair	LC-MS/MS	clozapine, chlorpromazine, risperidone	TDM
Psychiatric disorder	Pappadopulos et al., 2009[127]	North America	Children (7-10 years of age) with ADHD; N=289	Saliva	GC	methylphenidate	Adherence
Psychiatric disorder	Fisher et al., 2017[128]	Europe	Psychiatric inpatients and outpatients; N=112	Saliva*	LC-MS/MS	clozapine, amisulpride	TDM and Adherence
Psychiatric disorder	Flarakos et al., 2004[129]	North America	Pediatrics on risperidone attending the outpatient clinic and adults admitted to a clinical unit and receiving regular risperidone; N=13	Saliva*	LC-MS/MS	risperidone	TDM and Adherence
Psychiatric disorder	Shiran et al., 2005[130]	Europe	Adult patients attending clinic at the Substance Misuse Service of Community Health and receiving methadone maintenance treatment; N=60	Saliva*	LC-MS	methadone	TDM
Psychiatric disorder	Saracino et al., 2012[131]	Europe	Former heroin-addicted patients undergoing methadone maintenance treatment; N=16	DBS*	HPLC	methadone	TDM
Psychiatric disorder	Fisher et al.,	Africa	Inpatients and outpatients, adults,	Saliva*	LC-MS/MS	clozapine,	TDM

<b>Reported field</b>	<b>Study</b>	<b>Continent</b>	<b>Study population</b>	<b>Matrix measured</b>	<b>Analytical method</b>	<b>Drugs evaluated</b>	<b>Clinical applicability</b>
disorder	2013[132]		receiving antipsychotics treatment; N=90			risperidone, quetiapine	
Psychiatric disorder	Stegmann et al., 2016[133]	Europe	Pediatric and adult patients (= 60 years) with attention-deficit hyperactivity disorder or hyperkinetic disorder receiving methylphenidate (daily doses 5-80 mg); N=12	Saliva*	HPLC	methylphenidate	TDM and Adherence
Psychiatric disorder	Patteet et al., 2016[134]	Europe	Psychiatric patients (19-65 years) diagnosed with schizophrenia, schizoaffective or bipolar disorder, taking antipsychotics treatment; N=85	Saliva*	UHPLC-MS/MS	amisulpride, aripiprazole, clozapine, olanzapine, paliperidone, quetiapine, risperidone	TDM and Adherence
Psychiatric disorder	Ramírez Fernández et al., 2020[135]	North America	Patients in criminal justice system prescribed with chlorpromazine, haloperidol, olanzapine, quetiapine, or risperidone.; N=59	Hair	UPLC-MS/MS	olanzapine, risperidone, haloperidol	Adherence
Psychiatric disorder	Ransohoff et al., 2019[136]	North America	Patients at the addiction-psychiatry clinics undergoing buprenorphine treatment; N=260	Saliva and Urine	LC-MS/MS	buprenorphine	Adherence
Psychiatric disorder	Wohkittel et al., 2020[137]	Europe	Children and Adolescents with ADHD (age: 7-16 years); N=28	Saliva*	HPLC with fluorescence detector	lisdexamfetamine	TDM
Psychiatric disorder	Manfro et al., 2020[138]	South America	Patients over 18 years receiving lithium carbonate therapy for at least one week; N=43	DBS*	Graphite furnace atomic absorption spectrometry (GFAAS)	lithium	TDM
Q fever or Whipple's disease	Angelakis et al., 2015[139]	Europe	Outpatients treated with doxycycline and hydroxychloroquine for Q fever or Whipple's disease; N=14	Hair*	UPLC	doxycycline	Adherence
Systemic	Hawwa et al.,	Europe	Children diagnosed with juvenile	DBS*	LC-MS/MS (DBS)	methotrexate	TDM and



<b>Reported field</b>	<b>Study</b>	<b>Continent</b>	<b>Study population</b>	<b>Matrix measured</b>	<b>Analytical method</b>	<b>Drugs evaluated</b>	<b>Clinical applicability</b>
inflammatory disease	2014[140]		idiopathic arthritis (JIA) and juvenile dermatomyositis (JDM) receiving methotrexate weekly doses (oral or subcutaneous, 10-20 mg) for at least two months; N=47		HPLC (packed RBC)		Adherence
Systemic inflammatory disease	Kneepkens et al., 2017[141]	Europe	Patients with rheumatoid arthritis (RA), psoriatic arthritis (psa) and ankylosing spondylitis (AS) treated with adalimumab once every two weeks, with or without synthetic disease-modifying antirheumatic drugs (dmards), non-steroidal anti-inflammatory drugs (nsaids) and/or prednisone; N=161	DBS*	ELISA antigen-binding test (ABT)	adalimumab	TDM
Transplantation	Brooks et al., 2019[142]	Australia/Oceania	Adult (18 years of age or over) renal transplant recipients, had undergone kidney transplant surgery 4-8 weeks prior, receiving triple immunosuppressive therapy consisting of oral enteric-coated mycophenolate sodium (EC-MS) twice daily, tacrolimus twice daily and prednisolone daily; N=20	Saliva*	UPLC-MS	prednisolone	TDM
Transplantation	Brooks et al., 2019[143]	Australia/Oceania	Adult (18 years of age or over) renal transplant recipients, had undergone kidney transplant surgery 4-8 weeks prior, receiving triple immunosuppressive therapy consisting of oral enteric-coated mycophenolate sodium (EC-MS) (540-720 mg twice daily), tacrolimus (twice daily, total daily dose 3-22 mg) and prednisolone 14-21 mg daily; N=20	Saliva*	UPLC-MS	mycophenolic acid	TDM

<b>Reported field</b>	<b>Study</b>	<b>Continent</b>	<b>Study population</b>	<b>Matrix measured</b>	<b>Analytical method</b>	<b>Drugs evaluated</b>	<b>Clinical applicability</b>
Transplantation	Ferreira et al., 2019[144]	South America	Adult kidney transplant patients, hospitalized, received a dose of 750 mg of MMF twice a day; N=13	Saliva*	LC-MS/MS	mycophenolic acid	TDM
Transplantation	Ghareeb et al., 2018[145]	North America	Stable kidney transplant recipients that were on a maintenance immunosuppressive tacrolimus, mycophenolic acid, and prednisone; N=46	Saliva*	LC-MS/MS	tacrolimus	TDM
Transplantation	Martial et al., 2017[146]	Europe	Patients between 2 and 18 years of age after kidney transplantation, treated with at least 1 of the compounds of interest (tacrolimus or mycophenolic acid), admitted to the pediatric ward or visit their physician on an outpatient basis; N=28	DBS*	LC-MS/MS	tacrolimus, mycophenolic acid	TDM
Transplantation	Al-Uzri et al., 2017[147]	North America	Youth patients at least 3 months post-transplant, undergoing TAC immunosuppression therapy, and English speaking recruited from a pediatric renal transplantation clinic; N=30	DBS*	LC-MS/MS Radioimmunoassay	tacrolimus	TDM
Transplantation	Müller et al., 2013[148]	Europe	Liver transplant patients; N=15	Hair*	LC-MS/MS	ciclosporin	TDM and Adherence
Transplantation	Hoogtanders et al., 2007[149]	Europe	Adult kidney transplant outpatients receiving tacrolimus; N=24	DBS*	LC-MS/MS	tacrolimus	TDM
Transplantation	Wilhelm et al., 2013[150]	Europe	Adult patients (18 years or older) who were treated orally with ciclosporin after allogeneic hematopoietic stem cell transplantation; N=36	DBS*	LC-MS/MS	ciclosporin	TDM
Transplantation	Arpini et al., 2013[151]	South America	Adult patients (18 years or older) treated orally with mycophenolate mofetil or mycophenolate sodium	DBS*	UHPLC	mycophenolic acid	TDM

Reported field	Study	Continent	Study population	Matrix measured	Analytical method	Drugs evaluated	Clinical applicability
Transplantation	Veenhof et al., 2017[152]	Europe	after kidney transplantation; N=19 Adult kidney transplant patients received tacrolimus or cyclosporine A, mycophenolate mofetil, and prednisolone;	DBS*	LC-MS/MS	tacrolimus, ciclosporin	TDM
Transplantation	Hinchliffe et al., 2013[153]	Europe	N=172 Heart and lung transplant patients during outpatient consultations in a specialist cardiothoracic transplant centre over a period of six months receiving either ciclosporin A or tacrolimus;	DBS*	UPLC-MS/MS	ciclosporin, tacrolimus	TDM
Transplantation	Koster et al., 2017[154]	Europe	N=91 Transplant patients;	DBS*	LC-MS/MS	tacrolimus, ciclosporin	TDM
Transplantation	Mendonza et al., 2006[155]	North America	N=142 Male, Caucasian, kidney transplant recipients attending transplant services clinic, on immunosuppressive therapy with tacrolimus and prednisone;	Saliva*	LC-MS/MS	mycophenolic acid	TDM
Transplantation	Veenhof et al., 2019[156]	Europe	N=11 Adult transplant patients;	DBS*	LC-MS/MS	sirolimus, everolimus	TDM
Transplantation	Dickerson et al., 2014[157]	North America	N=56 Pediatric (1 year or older) kidney, heart and liver recipients.;	DBS*	LC-MS/MS	tacrolimus, sirolimus	TDM
Transplantation	Zwart et al., 2018[158]	Europe	N=34 Kidney(-pancreas) transplant recipients;	DBS*	LC-MS/MS	tacrolimus, mycophenolic acid	TDM
Transplantation	Hoogtanders et al., 2007[159]	Europe	N=65 Stable outpatients with kidney transplant;	DBS*	LC-MS/MS	tacrolimus	TDM
Transplantation	Mendonza et al., 2004[160]	North America	N=26 Kidney transplant recipients attending the outpatient clinic at the hospital and taking cyclosporine (csa);	Saliva*	LC-MS/MS	ciclosporin	TDM
			N=15				

<b>Reported field</b>	<b>Study</b>	<b>Continent</b>	<b>Study population</b>	<b>Matrix measured</b>	<b>Analytical method</b>	<b>Drugs evaluated</b>	<b>Clinical applicability</b>
Transplantation	van Boekel et al., 2015[161]	Europe	Renal transplant patients; N=26	DBS	LC-MS/MS	tacrolimus	TDM
Transplantation	Cheung et al., 2008[162]	Asia	Renal transplant recipients; N=36	DBS*	LC-MS/MS	tacrolimus	TDM
Transplantation	Koop et al., 2013[163]	North America	Pediatric kidney transplant recipients (age 6-20 years); N=21	DBS*	LC-MS/MS	tacrolimus	TDM
Transplantation	Alsmadi et al., 2019[164]	Asia	Jordanian pediatric kidney transplant recipients (4-18 years); N=26	Saliva*	LC-MS/MS	mycophenolic acid	TDM
Transplantation	Veenhof et al., 2020[165]	Europe	Adult kidney transplant recipients; N=107	DBS*	LC-MS/MS	tacrolimus	TDM
Tuberculosis	Martial et al., 2018[166]	South America	Hospitalized or ambulatory children, aged 1 - 15 years, with pulmonary or extrapulmonary TB, started treatment with a fixed-dose combination of first-line anti-TB drugs; N=11	DBS*	LC-MS/MS	rifampicin, pyrazinamide	TDM
Tuberculosis	Vu et al., 2014[167]	Europe	Adult tuberculosis patients received rifampicin or clarithromycin; N=13	DBS*	LC-MS/MS	rifampicin	TDM
Tuberculosis	Metcalfe et al., 2019[168]	North America	Patients, most undergoing MDR- or XDR-TB therapy; N=47	Hair	LC-MS/MS	isoniazid, pyrazinamide, ethambutol, levofloxacin, moxifloxacin, bedaquiline, clofazimine, linezolid, ethionamide	TDM
Tuberculosis	Mave et al., 2017[169]	Asia	Children (<12 years) with tuberculosis; N=16	Hair*	LC-MS/MS	isoniazid	TDM
Tuberculosis	Mave et al., 2016[170]	Asia	Children <12 years newly diagnosed with tuberculosis; N=38	Hair	LC-MS/MS	isoniazid	TDM

<b>Reported field</b>	<b>Study</b>	<b>Continent</b>	<b>Study population</b>	<b>Matrix measured</b>	<b>Analytical method</b>	<b>Drugs evaluated</b>	<b>Clinical applicability</b>
Tuberculosis	Gerona et al., 2016[171]	North America	Patients with active or latent TB infection; N=18	Hair	LC-MS/MS	isoniazid	Adherence
Tuberculosis	Ghimire et al., 2019[172]	Asia	Patients (=18 years) with newly diagnosed or previously treated MDR-TB receiving levofloxacin as a part of their MDR-TB regimen; N=23	Saliva*	LC-MS/MS	levofloxacin	TDM
Tuberculosis	van den Elsen et al., 2020[173]	Europe	Hospitalized adult TB patients in the Tuberculosis center received moxifloxacin or linezolid as part of their TB treatment and had routine TDM using blood samples; N=22	Saliva*	LC-MS/MS	moxifloxacin	TDM
Tuberculosis	van den Elsen et al., 2020[174]	Europe	Adult TB patients admitted at the Tuberculosis Center treated with rifampicin and/or isoniazid and had routine TDM for rifampicin or isoniazid; N=19	Saliva*	LC-MS/MS	rifampicin	TDM
Tuberculosis	Eisenhut et al., 2012[175]	Europe	Adult and paediatric patients (age 1-29 years) with latent or active TB infection; N=40	Hair	LC-MS	isoniazid	Adherence

\* The drugs measurements were also performed in a classical matrix (blood/plasma/serum)

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