Table 1. An overview of current clinical implementation studies and programmes across the United States and Europe.

Implementation Initiative	Objectives	Clinical sites (Country)	Strategy	N^{O} PGx genes tested	Platform	Drug-gene combinations implemented in clinical care (clinical guidelines)	Population (n)
Cleveland Clinic's Personalized Medication Program (30, 47)	-Implementing a CDSS to guide pharmacogenetics test ordering and provide gene-based dosing recommendations at the point-of-care. In parallel a PGx consultation service is available	-Cleveland Clinic (USA)	-Implementing alerts which recommend ordering a PGx test at the point-of-care -Implementing drug-gene pairs one at a time	n/a	n/a	*HLA-B*57:01/*abacavir *TPMT/*thiopurines (as per the CPIC guidelines)	Patients treated in a tertiary care adult hospital, children's hospital regional hospitals or ambulatory locations across Ohio
CLIPMERGE PGx (48, 49)	-Provide insight into the mechanisms, tools and processes that will best support the use of PGx in clinical care -Contribute to the emerging body of data needed for forthcoming larger studies that will assess the utility of PGx in medication safety and efficacy	-Icahn School of Medicine at Mount Sinai (USA)	Implementing pre-emptive genotyping and real-time CDSS deployed through the EHR into routine care using a bio-bank derived cohort	36 (20)	Sequenom iPLEX ADME PGx (20)	*CYP2C19*/clopidogrel *CYP2C9*/warfarin *VKORC1*/warfarin *SLOCO1B1*/simvastatin *CYP2D6*/TCAs *CYP2C19*/TCAs *CYP2D6*/SSRIs (as per CPIC guidelines)	Pilot study: primary care patients who consented to Bio*ME* biobank (N=1,500). Eventual aim is to recruit all Bio*ME* participants
eMERGE-PGx (50-52)	-Install a NGS sequencing platform assessing sequence variation in patients likely to be prescribed a drug of interest in a 1 to 3 year time frame -Integrate clinically validated genotypes into the EHR and CDSS and to assess the impact on clinical outcomes and process of implementation -Develop a repository of variants of unknown significance linked to clinical phenotype data to expand PGx understanding	-Boston Children's Hospital -Children's Hospital of Philadelphia -Cincinnati Children's Hospital -Geisinger Health System -Group Health/University of Washington -Marshfield Clinic -Mayo Clinic (RIGHT) -Icahn School of Medicine at Mount Sinai (CLIPMERGE) -Northwestern University -Vanderbilt University Medical Center (PREDICT) (all above in USA)	Multi-center project evaluating pre-emptive sequencing and pre-emptive genotyping	84	PGRNseq	Varies across clinical sites (as per CPIC guidelines)	Individuals likely to be prescribed drugs of interest within a 1- to 3- year timeframe, specific therapeutic focus amongst all sites (N=9,000)
INGNITE (PGx initiatives) (54)		-University of Florida (USA) -Vanderbilt University (USA) -Indiana University (USA)					
INGENIOUS (55, 56)	-To assess whether PGx testing for a panel of clinically relevant markers impacts annual healthcare costs and adverse event incidence	-Indiana Institute of Personalized Medicine at Indiana School of Medicine (USA)	Operational implementation of pre-emptive genotyping of a panel of clinically relevant markers in routine care, in a safety-net hospital	14	Open Array	Clinically relevant pharmacogenes associated with the response of 28 drugs (as per CPIC guidelines)	Adult patients receiving care at the Eskenazi Health System (n=6,000)

Personalized Medicine Program (57, 58)	-Developing a pre-emptive, chip-based genotyping approach that is cost-effective, initially for implementation of a single drug/gene pair but eventually expanding to many others	-University of Florida and Shands Hospital (USA)	Implementing pre-emptive genotyping in routine care	120 (20)	Life Technologi-es Quant Studio Open Array (20)	*CYP2C19*/clopidogrel (as per CPIC guidelines)	Patients receiving antiplatelet therapy and undergoing percutaneous coronary intervention (n=800)
PG4KDS (59, 60)	-Ultimately migrate all CPIC drug-pairs into the EHR and CDSS	-St. Jude Children's Research Hospital (USA)	Research protocol implementing pre-emptive genotyping	230	Affymetrix DMET Plus Array	*TPMT, CYP2D6, SLOC1B1* and *CYP2C19* coupled to 12 high-risk drugs (as per CPIC guidelines)	St. Jude (paediatric) patients with a primary medical record at St. Jude Hospital (n=1,559)
PGRN (52)							
PREDICT (21, 61)	-To establish a framework and infrastructure for pre-emptive incorporation of genomic information into the EHR.	-Vanderbilt University Medical Center (USA)	Operational implementation of pre-emptive genotyping in routine care	34	VeraCode ADME Core Panel	*CYP2C19*/clopidogrel *CYP2C9*/warfarin *VKORC1*/warfarin (as per CPIC guidelines)	Patients receiving antiplatelet therapy following placement of cardiovascular stent (N=10,000)
RIGHT (62, 63)	-Develop best practices for the implementation of genetic sequence data into clinical systems .	Mayo Clinic (USA)	Implementing pre-emptive sequencing and genotyping in routine care	84	PGRNseq and Luminex CYP2D6 ASPE kit	*SLOCO1B1*/simvastatin *CYP2C19*/clopidogrel *IFNL2*/interferon *CYP2D6*/tramadol *CYP2D6*/tamoxifen *CYP2D6*/codeine *HLA-B*1502*/carbamazepine *HLA-B*1501*/abacavir *TPMT*/thiopurines (as per CPIC guidelines)	Patients likely to receive statin therapy within 3 years, recruited from the Mayo Clinic Biobank (N=1,013) (20)
The 1200 Patients Project (64-66)	-To determine the feasibility and utility of incorporating pre-emptive pharmacogenomics testing in clinical care. -Future aims include examining the impact of providing PGx results on prescribing decisions and patient outcomes.	University of Chicago (USA)	Observational study implementing pre-emptive genotyping	n/a	Sequenom ADME and Sequenom custom panel	n/a	Adults receiving outpatient medical care and using 1-6 prescription medications (N=1,200)
U-PGx and the PREPARE Study	-Implementation of pre-emptive PGx testing, of a panel of clinically relevant markers -Assessing the impact on incidence of adverse event incidence and	-Leiden University Medical Center (NLD) -Royal Liverpool University Hospital (UK) -University of Patras (GRC)	Block-randomized clinical study to implement pre-emptive genotyping of a panel of clinically relevant markers. Additional NGS sequencing amongst those	13	LGC Group SNPLine	Clinically relevant pharmacogenes associated with the response of 43 drugs (see Table 2 for actionable drug-gene	Individuals who receive a first prescription of a drug of interest. First line, oncology,

	healthcare costs -Performing exploratory analyses to expand understanding of PGx	-University of Ljubljana (SVN) -Medical University of Vienna (AUT) -National Cancer Institute Aviano (ITA) -University Hospital Granada (ESP)	presenting extreme phenotypes	combinations) (as per DPWG guidelines)	renal and liver transplant, cardiology, and psychiatric patients (N=8,100)

EHR: Electronic health record; CDSS: Clinical decision support system; ADME: Absorption, distribution, metabolism, elimination; TCA: Tricyclic antidepressants; SSRI: Serotonin reuptake inhibitors; USA: United States of America; NLD: The Netherlands; UK: United Kingdom; GRC: Greece; SVN: Slovenia; AUT: Austria; ITA: Italy; ESP: Spain