Evidence Requirements in the Regulatory and Reimbursement Processes of Digital Therapeutics: Insights from the US, EU4 and UK

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Introduction

Digital Therapeutics (DTx) are software-based programmes increasingly used to diagnose, manage and prevent chronic and behaviour-modifiable diseases. We characterise the pathways and evidence supporting the regulatory approval and reimbursement/HTA of DTx in the United States, EU4 (France, Italy, Spain and Germany) and the UK.

Methods

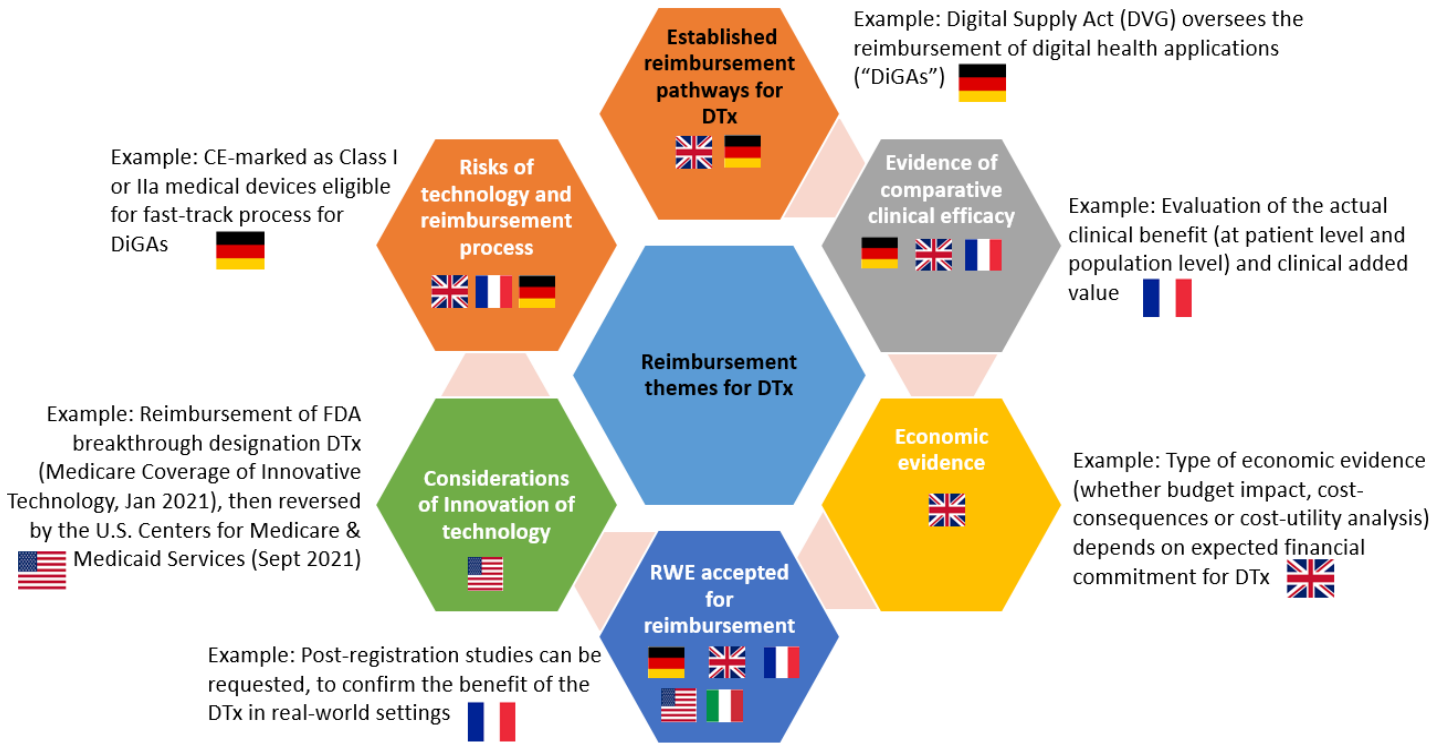
A pragmatic literature review was conducted in BIOSIS Previews®, Embase®, MEDLINE®, QUOSA®, using keywords related to DTx, regulatory and reimbursement frameworks (January 2010 to June 2021). Searches were supplemented with grey literature, official guidance documents and websites (e.g., FDA, ICER). Databases were searched for DTx approved to date, using Python.

Regulatory pathways usually not specific to DTx and shaped by provisions on medical devices

FDA Centralised processes	EU Regulation on Medical Devices (MDR), 2017/745 (entered into force on 26 May 2021)	2002 UK Medical Device Regulation (MDR)
Class I, II and III (resp. low, moderate and high-risk) categorization	(National) Notified Bodies issue a Conformité Européenne (CE) status.	CE marks recognised until 30 June 2023
Premarket approval (PMA) for Class III devices; 510(k) marketing clearance for DTx claiming equivalence to existing (predicated) device	Medical Device Coordination Group guidance on clinical evidence on devices in MDR	MHRA "Clinical investigations of medical devices "guidance (May 2021)": clinical data required to demonstrate compliance with 2002 UK MDR
FDA Digital Health Center of Excellence fosters innovative regulatory approaches for digital technologies	As of 1st Jan 2021, the MDR applies to Northern Ireland, but not the rest of the UK	Sept-Nov 2021: consultation on reconfiguration of Regulatory framework for digital health technologies

Main evidence needs for regulatory purposes

Evaluation of sufficient and valid scientific evidence from clinical and non clinical studies, to assure that the device is safe and effective for its intended use(s), for high-risk DTx undergoing Premarket approval (PMA)	**Valid clinical association** between the output of the device and the targeted condition, through scientific peer-reviewed literature, existing or de novo clinical performance data	Scientific literature on the safety, performance, design characteristics and intended purpose of the novel device, to demonstrate equivalence to existing device to which the data relates to, or
Clinical data is not needed for most devices cleared by the 510(k) process	**Technical/Analytical Performance** of the device, through verification and validation activities, databases, registries	A critical evaluation of the results of all the clinical investigations made, or
	Clinical performance (clinical safety, effectiveness, performance) to demonstrate clinical benefits	A critical evaluation of the combined data provided from the two bullet points above.



Conclusions

The current regulatory and reimbursement pathways for DTx appear shaped by existing provisions on medical devices. However, some countries (most notably Germany and the UK with NICE) are implementing processes and methods targeted for these technologies. There is a need for Regulators and Payers alike to ensure that their guidance on evidence requirements maintain the pace of the rapid evolution of these technologies.

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FDA=US Food and Drug Administration; EU=European Union; ICER: Institute for Clinical and Economic Review
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References available in separate handout