Contrasting evidence requirements for early access schemes for digital health technologies in the UK and Germany: A challenge for multimarket evidence generation planning

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Introduction

Schemes that allow early access to digital health technologies (DHTs), provisional upon further evidence generation, operate in both Germany (Digital health applications [DiGA] Fast-Track Process operated by the BfArM, specific to DHTs) and the UK (NICE Early Value Assessment [EVA] for all medical technologies).

To date, different DHTs have been considered by each scheme. However, as the DHT market grows and matures, developers may seek multimarket launches, or health systems may seek to access innovative DHTs that are available globally. It will therefore be important to understand how evidence generation for DHTs can meet the needs of multiple markets.

- Given the importance of "coverage with evidence development" approaches for DHTs, we focused on the evidence requirements of the two established schemes in Germany and the UK.
- We sought to understand and compare the requirements of each scheme, evidenced by recent experience.

Methods

Assessment and decision documents, and evidence generation plans were identified for:

- Provisional DiGA entries as of June 2024, from the online DiGA Directory, https://diga.bfarm.de/de. Further details of planned trials were identified from the German Clinical Trials Register and clinicaltrials.gov.
- Completed EVAs for DHTs, excluding evaluations of diagnostic technologies as of June 2024, from the NICE website, including guidance and evidence generation plan documents.

Results

In practice, confirmatory evidence to support permanent DiGA registration is through Germany-specific randomized controlled trials (RCTs), focused only on clinical and HRQoL endpoints (Table 1).

- Trial durations were three to six months.
- All studies are in Germany, only one is in a further country.
- Listed endpoints rarely include those evidencing "patient-relevant improvement of structure and processes" (an option specified for demonstration of benefit for DHTs), instead they are focused on medical benefit.

Table 1: Evidence generation plans for DiGA

Disease area	DHT/Indication	Study design		Planned endpoints					
		Initial assessment	Planned	Clinical	HRQoL	Health literacy/ management	Medication adherence	Medication use	Healthcare use
Neurology and pain	Selfapys Online-Kurs/Chronic pain								
	sinCephalea/Migraine								
	levidex/Multiple sclerosis								
Psychiatry and mental health	elona therapy/Depression								
	Mindable/Social phobia								
	MindDoc/Depressive illnesses								
	My7steps App/Psychosocial health/ Depression								
	NeuroNation MED/Mild cognitive disorder								
	HelloBetter Schlafen/Insomnia								
	Novego/Anxiety								
	optimune/Breast cancer (quality of life)								
	SmokeFree/Tobacco dependence								
Metabolic and cardiovascular	actensio/Hypertension								
	mebix								
	glucura/Diabetes								
	ProHerz/Heart failure								
	UNA Health/Diabetes								
	Untire/Breast cancer fatigue								
	Vantis/Heart disease								
Orthopedic	Orthopy/Knee injuries								

Included RCT Other study design

All EVAs recommended observational studies aiming to build a picture of effectiveness, usefulness, and resource impact in the UK National Health Service (NHS) (Table 2).

- Recommended study durations were 6-12 months.
- Commentary and justification for evidence generation recommendations commonly included:
  - Data collection would be needed to allow for future adjustment of observational data for confounding.
  - The impact of the DHT or relevant comparator may differ by service organization at a local level within the NHS, and standard of care may be poorly defined as a comparator.
  - Uptake, use, and effectiveness may vary by patient characteristics.

Table 2: Evidence generation plans for EVA

Disease area	DHT indication	Study design		Recommended endpoints				
		EVA	Recommended future research	Effectiveness	HRQoL	User characteristics	Uptake/accessibility/ engagement	Impact on resource use
Neurology and pain	Non-specific low back pain		Prospective cohort or before-and-after study plus qualitative survey					
Psychiatry and mental health	Manage symptoms of psychosis/prevent relapse		Prospective cohort studies					
	Depression		Parallel cohort study plus qualitative survey					
	Anxiety disorders		Parallel cohort study plus qualitative survey					
	Virtual reality technologies for agoraphobia		Real-world comparative interrupted time series					
	Cognitive behavioral therapy/children and young people/anxiety or low mood		Historical control study with propensity score methods					
Metabolic and cardiovascular	Multidisciplinary weight-management services		Before-and-after or prospective cohort study					
Respiratory	Pulmonary rehabilitation for COPD		Use case survey plus prospective controlled cohort studies					

The identified differences in evidence generation planning reflect the differing perspectives and requirements of the agency decision-makers (Table 3).

Table 3: Evidence generation requirements of early access schemes and their implications

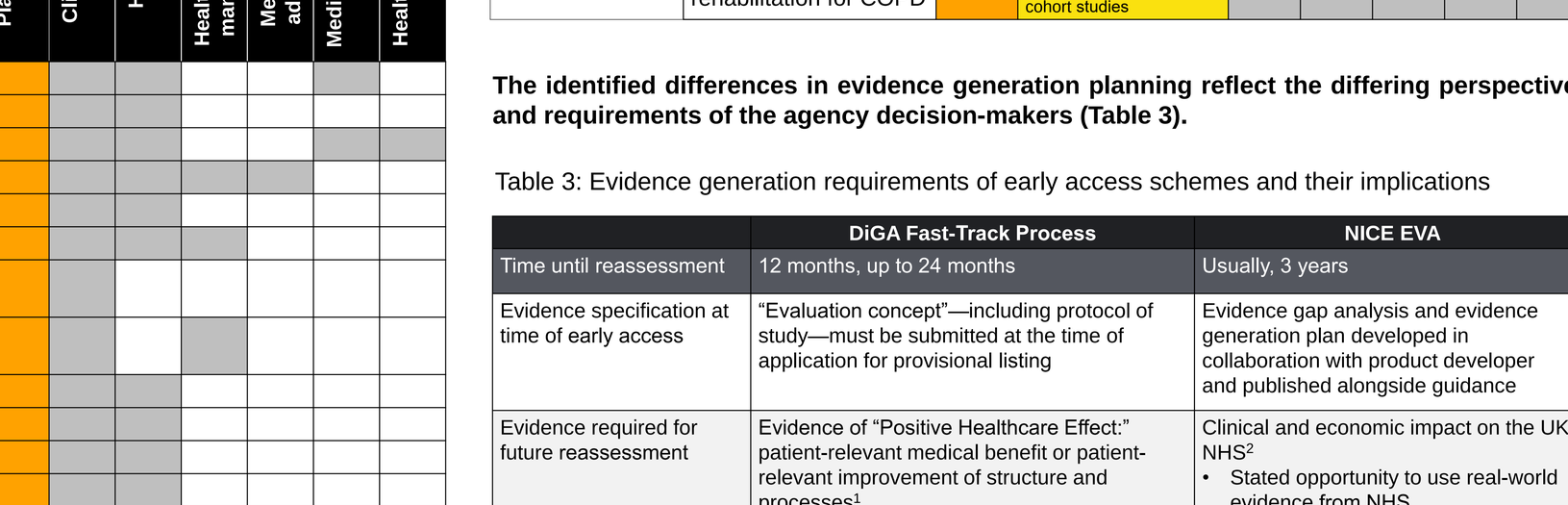
	DiGA Fast-Track Process	NICE EVA
Time until reassessment	12 months, up to 24 months	Usually, 3 years
Evidence specification at time of early access	"Evaluation concept"—including protocol of study—must be submitted at the time of application for provisional listing	Evidence gap analysis and evidence generation plan developed in collaboration with product developer and published alongside guidance
Evidence required for future reassessment	Evidence of "Positive Healthcare Effect:" patient-relevant medical benefit or patient-relevant improvement of structure and processes[1] • Minimum: retrospective comparative study conducted in Germany • Importance of data "based on the reality of healthcare practice" recognized • Economic impact not considered	Clinical and economic impact on the UK NHS[2] • Stated opportunity to use real-world evidence from NHS • Future role for cost-effectiveness analysis
Implication for evidence generation plans	• In practice, Germany-specific RCTs (even if only single center) considered feasible and more certain for future acceptance • No need for data collection for outcomes around health system impact	• Many identified evidence gaps only addressed through real-world data • Data collection and statistical approaches accepted to address confounding

1. DiGA-Leitfaden version 3.5. https://www.bfarm.de/EN/Medical-devices/Tasks/DiGA-and-DiPA/Digital-Health-Applications/_node.html; 2023
2. NICE. Early value assessment interim statement: NICE process and methods [PMG39]. https://www.nice.org.uk/process/pmg39/chapter/introduction; 2022

Conclusions

The identified differences in evidence generation requirements lead to challenges in the developing situation of multimarket DHT launches, and a need for alignment and collaboration between payer agencies and DHT developers (Figure 1).

Figure 1: Historic vs emerging situation for DHT evidence generation



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