The Comparison Analysis of HTA guideline for Digital Health Technologies (DHTs) in Korea, United Kingdom, France, and Germany

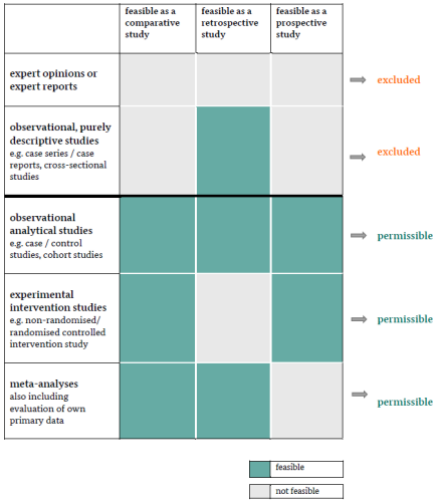
Country	KOR	UK	FRA	GER
Title	**Assessment Guideline for NHI coverage eligibility of Innovative Medical Technology**	**Evidence Standards Framework for Digital Health Technologies**	**Guide to the specific features of clinical evaluation of a connected medical device (CMD) in view of its application for reimbursement**	**The Fast-Track Process for Digital Health Applications (DiGA) according to Section 139e SGB V**
Published date	Dec 2019	March 2019	Jan 2019	Apr 2020
Stakeholders	MOHW (Ministry of Health and Welfare), HIRA (Health Insurance Review & Assessment Service), The Korean Society of Radiology, The Korean Society of 3D Printing in Medicine	NICE (National Institute for Health and Care Excellence), NHS England, Public Health England, MedCity	CNEDiMTS (Commission nationale d'évaluation des dispositifs médicaux et des technologies de santé, Medical device and Health technology Evaluation Committee) of HAS (Haute Autorité de santé)	Federal Institute for Drugs and Medical Devices (Bundesinstitut für Arzneimittel und Medizinprodukte, BfArM), Federal Ministry of Health (Bundesministerium für Gesundheit, BMG)
Scope	Innovative medical technologies: • Currently relevant guideline for AI medical imaging and 3D Printing is only existed • To be updated for other innovative technologies including DHTs	DHTs that are commissioned in the UK health and care system: • Less relevant to DHTs that are downloaded or purchased directly by users (such as through app stores) • Included DHTs that incorporate artificial intelligence(AI) using fixed algorithms but not designed for use with DHTs that incorporate AI using adaptive algorithms	CMDs (Connected Medical Devices) which are: a) intended for use for medical purposes, their end-use implying they are CE-marked b) for individual use (implanted or used by patient themselves) c) the company has submitted an application for reimbursement by national solidarity	DiGA (Digitale Gesundheits anwendungen) is a medical device that has the following properties: • Medical device of the risk class Ⅰ or Ⅱa (according to MDR or MDD as part of the transition regulations) • The main function of the DiGA is based on digital technologies • The DiGA supports the recognition, monitoring, treatment or alleviation of diseases or the recognition, treatment or alleviation or compensation of injuries disabilities • The DiGA is used only by the patient or by the patient and the HCP. This means that apps that are only used by the physician to treat patients (practice equipment) are not a DiGA

				• The DiGA is not a digital application that serves only for the collection of data from a device or for controlling a device. The medical purpose must be achieved through the main digital functions • The DiGA does not serve primary prevention ⇒ DiGA are therefore "digital assistants" in the hands of patients
Functional classification	**1) AI Medical Imaging (following the definition of MFDS)** • Medical Software categorized as medical device a) Software that automatically diagnoses, predicts, monitors or treats the patient's likelihood of disease, condition, etc. using clinical information (e.g., sizes and location of tumor lesions, etc.) obtained by analyzing medical information based on medical big data b) Software that provides clinical information for diagnosis and treatment by analyzing patterns or signals from medical imaging, *in vitro* diagnostic devices, signal acquisition systems (e.g., ECG, brain wave, etc.) based on medical big data • Medical Software that is ***not*** categorized as medical device	Classifying DHTs by function allows them to be stratified into evidence tiers based on the potential risk to users • System service ⇒ **Tier 1** : DHTs with potential system benefits but no direct user benefits • Inform / Simple monitoring / Communicate ⇒ **Tier 2** : DHTs which help users to understand healthy living and illnesses but are unlikely to have measurable user outcomes • Preventative behavior change / Self-manage ⇒ **Tier 3a** : DHTs for preventing and managing diseases. They may be used alongside treatment and will likely have measurable user benefits • Treat / Active monitoring ⇒ **Tier 3b** : DHTs with measurable user benefits, including tools used for treatment and diagnosis, as well as those influencing clinical	**Common features of CMD** * These features can have an incidence on the way in which the CMD is evaluated **1) Rapidity of technological development** • CMDs can be use technologies that are highly scalable • The need for or the possibility of having a remote connection to use them can enable developers to rapidly upgrade their technological solution • The possibility of monitoring the use or performance of CMDs can make it possible to reduce the length of certain development steps related to setting up or to the system test **2) Interaction with other devices/objects/ platforms** • By doing without wired connections, CMDs make multiple	**1) Combination with Hardware** • In principal, a DiGA can be a native app as well as a desktop or browser application • A DiGA can also comprise devices, sensors or other hardware in addition to software, such as wearables, as long as the main function is a predominantly digital one and the hardware is necessary to achieve the purpose of the DiGA **2) Combination with Services** • In principal, the DiGA is a digital medical device. Therefore, the evidence for positive healthcare effect (positive Versorgungseffekte, pVE) must be made without referring to such additional offers like consultation, coaching or services by a private health insurance • The above is not the case when considering services by SHI (statutory health insurance)-accredited physicians, meaning

	a) Software aiding administrative work (wards, inventory management and electronic check-in, etc.) at the medical institutions b) Software for exercise, leisure and daily health care purposes c) Software for education and research purposes d) Software for medical record management, regardless of disease treatment or diagnosis e) Software that provides healthcare providers with tools to manage and track patient health information or help them easily access medical information **2) 3D Printing** • Surgical simulator : Use to determine diagnosis or treatment methods or to use them as surgical measures or non-contacting guides through creating patient customized models using 3D printers to plan surgery and simulate surgery • Surgical guide : To introduce accurate length and angles or surgically remove accurate parts in surgery or treatment • Prosthesis : For the purpose of reconstructing or supplementing defective parts of human body	management through active monitoring or calculation. It is possible DHTs in this tier will qualify as medical devices	interactions between patients, carers, medical staff and machines possible. • By removing the constraints related to distance between users and medical staff, and by offering potentially shared access to the data collected, in real time or more often by conventional monitoring, CMDs can also have an impact on work methods and on interactions between medical staff, patients or their carers **3) Expert data processing systems** • In the conditions provided for by law, data collected can be processed for medical purposes • For data processing, CMDs may use various types of algorithms. The so-called learning algorithms (machine learning) have the ability to evolve over time • Pending new methodologies, the main machine learning methods are said to be supervised or unsupervised	services that the attending, resident physician (or dentist or psychotherapist) renders in connection to the usage of the DiGA. These services are reimbursed by the SHI within the framework of medical remuneration. Therefore, they can or must be included in the evidence of pVE

	• Aids : Application to compress and fixate parts of human body			
Evidence Standards	**1) AI Medical Imaging** • Class A - expert opinion, case series and cohort study(simple), etc. • Class B - cohort study with external validity • Class C - retrospective patient outcome study with confounding adjustment, prospective patient outcome study with confounding adjustment, RCT for patient outcome • Class D - cost-effectiveness research * Common prerequisites: a) Data acquisition process for Machine Learning (Deep Learning) must be ethical b) Target patient groups, imaging devices and image acquisition technology, etc. in study results should be detailed and obvious **2) 3D Printing** • Class A - expert opinion, case report and case series • Class B - retrospective comparative study • Class C - prospective comparative study, retrospective comparative study meta-analysis • Class D - prospective comparative	**Section A: evidence of effectiveness relevant to the intended use of the technology** • For tier 1 DHTs a) Credibility with UK health and social care professionals b) Relevance to current care pathways in the UK health and social care system c) Acceptability with users d) Equalities considerations e) Accurate and reliable measurements (if relevant) f) Accurate and reliable transmission of data • For tier 2 DHTs a) Reliable information content b) Ongoing data collection to show usage of the DHT c) Ongoing data collection to show value of the DHT d) Quality and safeguarding • For tier 3a DHTs a) Demonstrating effectiveness b) Use of appropriate behavior change techniques (if relevant) • For tier 3b DHTs a) Demonstrating effectiveness **Section B: evidence of economic impact relative to the financial risk**	**1) Evidence standards in the process of evaluation by the CNEDiMTS** **a) Individual benefit** • Individual benefit can related to morbidity-mortality criteria or criteria with an impact on morbimortality, but also on criteria relating to the patient's or carers' point of view as reported by them • The challenge is that the clinical development plan has to be in keeping with the CMD's ultimate purpose. In other words, that the endpoint selected is compatible with the company's claim when submitting their reimbursement application • Once the endpoint selected, various tools can be used to measure it. Regardless of the dimension selected, and including for non-clinical criteria, measurement tools must have undergone strict methodological validation • Criteria relating to the patient's or carer's point of view are relevant criteria in their own right **b) Other impacts** • The clinical development plan can include data collection on aspects which reach beyond benefit for the patient alone. In effect, CMDs can have impacts beyond individual	**1) General requirements for studies to prove a Positive Healthcare Effect :** **a) Choice of Methods** Studies that are presented to prove positive healthcare can be clinical or epidemiological studies, but they can also be designed and conducted using methods from other scientific fields such as healthcare research, social research or behavioural research **b) Realisation in Germany** The studies must be conducted in Germany. The limitation to Germany ensures that the study results are sufficiently meaningful. The care situation in which DiGA are used cannot be separated from the question of which positive effects they can have **c) Entry in the Study Registry** The studies must be registered in a public study registry. This ensures the quality and comparability of the data collected **2) Publication of the Complete Study Results** The publication of study results strengthens the confidence of the insured and healthcare providers in the DiGA test procedure. Research

	study meta-analysis, randomized prospective comparative clinical study, cost-effectiveness research * Common prerequisites: a) Data acquisition process must be ethical b) Target patient groups, etc. in study results should be detailed and obvious	• Economic information includes user population size, current and proposed care pathways and parameters for the economic model • Economic analysis level based on type of financial commitment a) Basic for pilot study or local commissioning decision ⇒ Budget impact analysis b) Low financial commitment for local or regional commissioning decision and national commissioning for cost-saving DHTs ⇒ Cost-consequence analysis / Budget Impact analysis c) High financial commitment for national commissioning for cost incurring DHTs ⇒ Cost-utility analysis (if this is not possible, a cost-consequence analysis may be acceptable) / Budget impact analysis • Standards for economic analysis reporting a) Economic perspective b) Time horizon c) Discounting d) Sensitivity analyses e) Equity analyses f) Descriptions of any	benefit which affect the general organization of care from the point of view of the various stakeholders contributing methods of management and participation of the patient in their treatment, treatment production process and professional practices, CMD conditions of use, treatment • It is important that the company identifies these impacts from the point of view of all stakeholders concerned and documents them, via validated methods • Where other impacts arise without superiority in terms of individual benefit compared to the gold standard, the lack of harmful effect from the CMD on the individual should be demonstrated • At least, the non-inferiority in terms of clinical benefit or acceptability by the patient is to be demonstrated • A medical and economic evaluation can also be included on the condition sufficient efficacy data and costs are available **2) CAV claims by data collection based on the design of the planned trial** **a) Situation No.1:** Clinical trials show non-inferiority of the CMD in terms of individual benefit and lack of improvement from the CMD on the other impacts, compared to the gold standard	also benefits from access to the data **3) Application for Provisional Listing** **a) Justification of the Improvement of Healthcare** DiGA manufacturers who apply for provisional listing must plausibly demonstrate that their DiGA can achieve one or more positive healthcare effects. For this purpose, they are required to submit a systematic evaluation of data on the use of the DiGA **b) Evaluation Concept** In addition, the manufacturers shall submit with the application an evaluation concept drawn up in accordance with generally accepted scientific standards, which takes appropriate account of the results of the data evaluation **c) Extension of the Trial Phase** The trial phase of a maximum of 12 months may be extended once for up to further 12 months at the request of the manufacturer. An extension can only be granted once and only upon early application, at least 3 months before the end of the trial phase **4) Specific Requirements for Study Types and Study Designs** • Studies to prove pVE of DiGA

		additional analytical methods g) Critique of the economic analysis	⇒ No claim in terms of CAV can be made **b) Situation No.2:** After having confirmed the non-inferiority of the CMD in terms of individual benefit, a superiority study shows a benefit from the CMD on other impact(s) compared to the gold standard (especially in terms of accessibility, professional practice and treatment of organization, standard of care and treatment safety) ⇒ A claim to CAV on the other impact(s) can be envisaged **c) Situation No.3:** Clinical trials have shown superiority of the CMD compared to the gold standard and in the use environment, in terms of patient benefit ⇒ A claim to CAV on the individual criteria can be envisaged **d) Situation No.4:** Clinical trials have shown superiority of the CMD compared to the gold standard and in the use environment, in terms of patient benefit, but also in terms of benefit on other impacts (especially in terms of accessibility, professional practice and treatment organization, quality of care and treatment safety) ⇒ A claim to CAV on the individual criteria and the other impact(s) can be envisaged	should, if possible, be based in the reality of healthcare practice and carried out with the help of the collection and processing of data closely related to healthcare. It should be possible to draw on existing data in retrospective studies, where such data are available • Accordingly, an application for listing in the directory requires at least the submission of a retrospective comparative study: case-control studies, retrospective cohort studies or intra-individual comparisons are possible • Irrespective of this, the manufacturer is always free to submit a prospective comparative study <Table. Examples of study design> 

Technical Assessment	The confirmation process of medical technology for new Health Technology Assessment (nHTA): The expert committee of HIRA confirms whether there exist coverage or non-coverage medical technologies with similar target, purpose and method compared with applied medical technology **1) AI Medical Imaging** • Category A : Assist with reading activities such as improving the physician's work process or providing other medical knowledge ⇒ Existing coverage • Category B : AI medical imaging providing minor diagnosis (assisting) information within the general scope of the examination ⇒ Existing coverage • Category C : AI medical imaging providing major diagnosis (assisting) information within the general scope of the examination a) C1 - check the area of suspected lesions and provide a possible diagnosis b) C2* - improvement in accuracy or reduction in errors compared to humans in the same existing procedures ⇒ Existing coverage • Category D : AI medical imaging			In order to be listed in the directory, a DiGA must meet the following requirements (Section 3 to 6 of the DiGAV*) * **DiGAV (**Digitale Gesundheits -anwendungen Verordnung) – Digital Health Applications Ordinance **1) Safety and Suitability for Use** Compliance with the requirements concerning the safety of the device and suitability for use is regarded as proven with a valid certificate of conformity / EG Certificate respectively the declaration of conformity of the manufacturer **2) Data protection** The DiGA specifies and supplements the requirements of the General Data Protection Regulation (GDPR) and other data protection regulations for the manufacturer **3) Information security** **a) Basic Requirements that Apply to All Digital Health Applications:** All requirements under the heading "Basic Requirements" must be fulfilled without exception or must not be applicable to certain types of a DiGA due to their non-applicability **b) Additional Requirements for Digital Health Applications with a Very High Need for Protection:** The requirements need only be

	providing new information beyond the general scope of the examination ⇒ nHTA target Category E: AI medical imaging replacing existing costly medical practices ⇒ nHTA target * In case of C2, it could be considered as nHTA target if it is necessary to have additional in-depth assessment about improvement or reclassify the existing coverage **2) 3D Printing** • Category A : Simply changing the manufacturing method or the difference of medical technology innovation is smaller than that of existing technologies ⇒ Existing coverage • Category B : Significant change in value such as treatment outcomes and cost effectiveness ⇒ Existing coverage(re-categorization considered) • Category C : Targets, objectives and methods are not same or similar, differed safety and effectiveness with existing technologies due to changes in target, objective and method ⇒ nHTA target			considered if a very high protection need has been identified for the DiGA due to the type of date processed, the addressed care scenarios and / or the context of use * The specifications in the DiGA for information security are based on the relevant publications and recommendations of the Federal Office for Information Security (BSI) **4) Interoperability** DiGA should prospectively communicate with each other and interact with other services and applications on the national e-health infrastructure, so that real added value for healthcare can be achieved. **5) Further quality requirements** • Robustness • Consumer Protection • Ease of Use • Support for Healthcare Providers • Quality of Medical Content • Patient Safety
The Criteria of Reimbursement	**1) AI Medical Imaging** • Level 1: Technology that can derive		**1) Evaluation of actual clinical benefit (ACB)** **a) Benefit of the medical device:**	The BfArM assesses the manufacturer's statements about the examination of the evidence of

Assessment	additional profit or indirect cost-saving effects for medical institution by increased efficiency of care practice ⇒ Not applicable for separate reward • Level 2: Technology that demonstrates a similar level of diagnostic ability to existing procedures/significant improvements in some part of existing procedures but show similar level of existing procedures overall ⇒ Not applicable for separate reward • Level 3: Technology that has significant improvement in diagnostic abilities compared to existing procedures/create new diagnostic value and treatment effectiveness ⇒ Considerable for separate reward • Level 4: Technology that demonstrates cost-effectiveness in addition to Level 3 ⇒ Considerable for separate reward **2) 3D Printing** • Level 1 : Technology that can derive additional profit or indirect cost-saving effects for medical institution by increased efficiency of clinical operation such as treatment and surgery		• its therapeutic, diagnostic or disability compensation effect • its role in the therapeutic, diagnostic or disability compensation strategy • given other therapies or other diagnostic or compensation methods available **b) Public health benefit:** • the impact of MD on the improvement of the state of health of a population, in terms of mortality, morbidity and quality of life • response to an unmet or insufficiently met therapeutic or diagnostic or disability compensation need • its impact on public health policies and programs ⇒ <u>If the ACB is sufficient</u>, the opinion issued by the CNEDiMTS is favorable to inclusion on the MD on the LPPR (List of products and services qualifying for reimbursement) **2) Evaluation of clinical added value (CAV)** Where ACB is sufficient to justify registration for reimbursement, the CNEDiMTS must also issue an opinion on "the evaluation of CAV with respect to a specifically	positive healthcare effect (pVE) of the DiGA provided by the manufacturer with the product qualities (from data protection to user friendliness) **Positive healthcare effects:** **a) Medical Benefit (medizinishcer Nutzen, mN)** The medical benefit is defined in the DiGAV as patient-relevant effects, particularly regarding - the improvement of the state of health - the reduction of the duration of a disease - the prolongation of survival or - an improvement in the quality of life ⇒ Those who claim a medical benefit for a DiGA must show that patient-relevant endpoints, in particular morbidity or quality of life, are positively influenced **b) Patient-relevant improvement of structure and processes (patientenrelevante Struktur- und Verfahrensverbesserungen, pSVV)** The concept of pSVV is based on the fact that DiGA offer good and new possibilities for improving care, especially with regard to process in the patient pSVV are - seen as part of the detection,

	⇒ Not applicable for separate reward • Level 2 : A key role in determining the treatment/surgery method to minimize the physical or cost burden of a patient(improved efficiency such as shortened treatment/surgery time and operation easiness) ⇒ Not applicable for separate reward • Level 3 : Clinically significant improvement in treatment outcomes(improved safety and accuracy of surgery to demonstrate reduction of complications, re-procedures, side-effects and hospitalization period, increased patient satisfaction) ⇒ Considerable for separate reward • Level 4 : Cost-effectiveness is clinically and significantly demonstrated in addition to Level 3 ⇒ Considerable for separate reward		designated, comparable product, procedure or service or comparable set of procedures, products or services, considered to be a gold standard according to the current state of knowledge of science, whether accepted or not for reimbursement. This evaluation concludes on the CAV as • **Major (I)** • **Important (II)** • **Moderate (III)** • **Minor (IV)** • **No improvement (V)** CAV has an impact on the MD tariff, negotiated by the French Healthcare Products Pricing Committee (CEPS) with the company * The CNEDiMTS evaluation criteria are regulatory criteria which apply regardless of the type of MD, connected or not	monitoring, treatment or alleviation of disease - the detection, treatment, alleviation or compensation of injury or disability - aimed at supporting the health behavior of patients or integrating the processes between patients and healthcare providers - include in particular the areas of 1. coordination of treatment procedures 2. alignment of treatment with guidelines and recognized standards 3. adherence 4. facilitating access to care 5. patient safety 6. health literacy 7. patient autonomy 8. coping with illness-related difficulties in everyday life 9. reduction of therapy-related efforts and strains for patients and their relatives
Reward Scheme	**1) 3D Printing** • Existing medical devices in reimbursement and non-reimbursement list : a) If the cost, effect, or function is equal or similar to that of the product previously listed, 90% of the reimbursement price of the technologies is determined b) Despite a), if there is no need to make a difference in the			**1) Provisional Listing in the DiGA** • For DiGA which has not yet been conducted a suitable study to prove positive healthcare effect • In this case, the DiGA must already meet all requirements in accordance with security, functional capability, quality, data protection and information security (Section 3 to 6 DiGAV) at the time of application

	reimbursement price, the reimbursement price will be same c) If the applied medical technology is improved through proven data such as clinical usefulness, cost effectiveness, and technology innovation, etc. compared to the technologies already listed, the technology is assessed in accordance with the "Value Appraisal Standard Table" • Patient customized : In principle, provide selective benefit (patient copayment with 80-90%), and in case of cosmetic purpose or a significant decrease in cost-effectiveness, it is non-reimbursed • Separate assessment : The technologies which other products with same purpose is not listed			• Only the study to prove the positive healthcare effect can be conducted retrospectively within the framework of a trial phase lasting up to 12 months • If no study results are submitted or if the application is refused at the end of trial phase, the DiGA is delisted from the directory by the BfArM **2) Final Listing in the DiGA Directory** Manufacturers who have already conducted a comparative study with their DiGA that is suitable for demonstrating a positive healthcare effect can apply for final listing If the notification is positive, be included in the DiGA directory no later than 3 months after the complete application has been submitted and the BfArM has issued a positive decision
Source	http://www.mohw.go.kr/react/jb/sjb0301vw.jsp	https://www.nice.org.uk/Media/Default/About/what-we-do/our-programmes/evidence-standards-framework/digital-evidence-standards-framework.pdf	https://www.has-sante.fr/upload/docs/application/pdf/2019-04/guide_to_the_specific_feactures_of_clinical_evaluation_of_connected_medical_device_cmd_in_viewof_its_application_for_reimbur.pdf	https://www.bfarm.de/EN/MedicalDevices/DiGA/_node.html

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