Science of the Total Environment 926 (2024) 171672

Contents lists available at ScienceDirect

Science of the Total Environment

journal homepage: www.elsevier.com/locate/scitotenv

Review

Digital technologies to unlock safe and sustainable opportunities for medical device and healthcare sectors with a focus on the combined use of digital twin and extended reality applications: A review

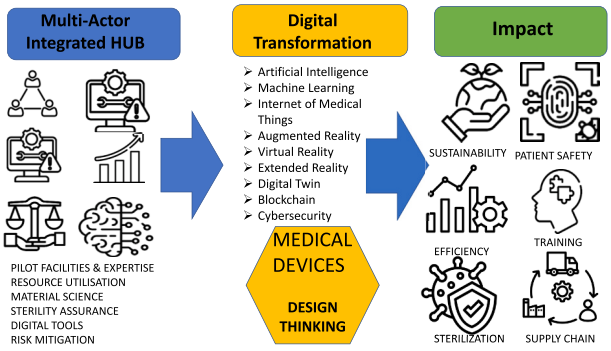
Neil J. Rowan *

Centre for Sustainable Disinfection and Sterilization, Technological University of the Shannon, Midlands Campus, Ireland
CURAM SFI Research Centre for Medical Devices, University of Galway, Ireland

HIGHLIGHTS

- Reusable medical devices have increased complexity for patient risk.
- Improvements in device deign and effective training enabled by digital tools.
- Digital twin and extended reality can help unlock end-to-end cycle opportunities.
- Integrated multi-actor HUB approach to sustainable development of medical devices.

GRAPHICAL ABSTRACT



ARTICLE INFO

Editor: Damià Barceló

Keywords:
Medical devices
Digital transformation
Design thinking
Sterilization
Sustainability
Circularity

ABSTRACT

Medical devices have increased in complexity where there is a pressing need to consider design thinking and specialist training for manufacturers, healthcare and sterilization providers, and regulators. Appropriately addressing this consideration will positively inform end-to-end supply chain and logistics, production, processing, sterilization, safety, regulation, education, sustainability and circularity. There are significant opportunities to innovate and to develop appropriate digital tools to help unlock efficiencies in these important areas. This constitutes the first paper to create an awareness of and to define different digital technologies for informing and enabling medical device production from a holistic end-to-end life cycle perspective. It describes the added-value of using digital innovations to meet emerging opportunities for many disposable and reusable medical devices. It addresses the value of accessing and using integrated multi-actor HUBs that combine academia, industry, healthcare, regulators and society to help meet these opportunities. Such as cost-effective access to specialist pilot facilities and expertise that converges digital innovation, material science, biocompatibility, sterility assurance, business model and sustainability. It highlights the marked gap in academic R&D activities (PRISMA review of best publications conducted between January 2010 and January 2024) and the actual list of U.S. FDA's approved and marketed artificial intelligence/machine learning (AI/ML), and augmented reality/virtual reality (AR/VR) enabled-medical devices for different healthcare applications. Bespoke examples of benefits underlying

* Corresponding author at: Centre for Sustainable Disinfection and Sterilization, Technological University of the Shannon, Midlands Campus, Ireland
E-mail address: neil.rowan@tus.ie.

https://doi.org/10.1016/j.scitotenv.2024.171672
Received 14 February 2024; Received in revised form 9 March 2024; Accepted 10 March 2024
Available online 12 March 2024

future use of digital tools includes potential implementation of machine learning for supporting and enabling parametric release of sterilized products through efficient monitoring of critical process data (complying with ISO 11135:2014) that would benefit stakeholders. This paper also focuses on the transformative potential of combining digital twin with extended reality innovations to inform efficiencies in medical device design thinking, supply chain and training to inform patient safety, circularity and sustainability.

1. Design thinking for improve patient safety

The medical device industry constitutes a multi-billion sector globally that has increased in sophistication to meet the evolving and diverse needs of modern healthcare (Garvey, 2024). Meeting such healthcare needs has underpinned end-to-end supply chains along with the manufacture of new complex reusable and single-use medical devices (Rowan et al., 2023a). However, healthcare acquired infections (HAIs) linked to contaminated use of some medical devices (particularly reusable items) continues to contribute towards patient morbidity and mortality (Garvey, 2024). While single use medical devices can cause HAIs due to cross-contamination issues in healthcare (such as urinary tract infections), there is a greater probability of patient infection arising from using reusable medical equipment such as endoscopes and duodenoscopes (Garvey, 2024). Disposable medical devices undergo effective sterility assurance; however, these can subsequently cause post-operative and other medical-device related infection due to contamination in healthcare environment. For example, surgical site infections (SSIs) due to intra-operative contamination from single use devices have been ascribed to airborne microbial contamination of surgeon's hands and instruments (Chauveaux, 2015). SSIs are surgery-related infections occurring within 30 days of the surgical intervention, or within one year after the introduction of a medical implant (Chua et al., 2022). While terminal modalities effectively sterilize single-use medical devices; prevention from device-related-infections in patients due to subsequent environmental and user-mediated contamination is challenging where those with comorbidities are particularly vulnerable (Chua et al., 2022). Healthcare contaminated devices include central venous access devices, cardiac-implantable electronic devices, Ommaya reservoirs, external ventricular drains, breast implant plus tissue expanders, ureteral and esophageal stents, biliary stents and so forth (Viola et al., 2023).

General recommendations for the prevention of device-related infections include hand washing, infection control and prevention programs, MRSA screening and decolonization, perioperative antisepsis protocols, and perioperative antibacterial prophylaxis (Viola et al., 2023). For example, central venous devices that are used in at least 4 million patients in the U.S. are left in place for several months are essential for patients living with cancer. However, incorporating specific device-related antimicrobial interventions and procedures by infection control team to address such complex infections in patients is challenging (Patal et al., 2023; Whitaker et al., 2023). The introduction of U. S. Food and Drug Administration (FDA) approved antimicrobial-impregnated catheters (AICs) has added protective layer against life-threatening catheter-related bloodstream infections. Use of antimicrobial envelope (such as TYRX, Medtronic) that locally releases a high concentration of minocycline and rifampin has helped patients at high risk of developing cardiac-implantable electronic-device related infections (Blomstrom-Lundqvist et al., 2022). The ability to visualize, model, design simulate, develop, sterilize, test, verify and validate such medical devices from an end-to-end process perspective will remain essential and would substantially benefit from an integrated multi-actor effort that connects clinicians, healthcare professionals, sterilization providers, manufacturers, SMEs/entrepreneurs, patients and regulators. Given this complexity, the application of appropriate digital innovation would help address key needs (many in real-time) including improving efficiencies, resource utilization, safety and security (Table 1).

In 1957, Earle Spaulding introduced a new infection prevention classification based on the need to establish safe guidelines for the use of medical devices (Rowan et al., 2023a). This system describes types of device and instruments as non-critical, semi-critical and critical to reflect how these items will be used on patients (Table 2). This classification system has been adopted by industry into appropriate standards for decades that informs manufacturers' instructions for use (MIFUs) in dialogue with healthcare providers and regulators. However, MIFUs for complex medical devices typically have a substantial number of complicated steps that may not align with healthcare capabilities to efficiently clean and process, such as for duodenoscopes (Rowan et al., 2023a; Kremer et al., 2023a). This is attested by the documented occurrences of device-related infections where there were no documented failures reported in reprocessing by the healthcare provider (Garvey, 2024). Recent research has emphasized the role of effective and appropriate device cleaning with complex design features. Such 'difficult-to-reach' features may be potentially contaminated with recalcitrant biofilms harbouring microbial pathogens (Kremer et al., 2023a). Kremer et al. (2022) noted that cleaning and associated validation requirements are essential for the safe use of reusable devices. However, test methods and associated endpoint for cleaning validations have varied worldwide. Kremer et al. (2022) reiterated the importance of ensuring end-users to keep an awareness of appropriate international standards that have updated the requirements to include cleaning endpoints, and for the use of test soils for demonstrating cleaning efficacy of washer-disinfectors. Medical devices will continue to evolve to support clinicians for better patient outcomes (Kremer et al., 2023d). Moreover, given the complexity and number of MIFUs steps for some medical devices, it is becoming increasing challenging to ensure that we can appropriately mitigate risk to patients of contracting a device-related infection in the healthcare environment (Rowan et al., 2023a).

Different antimicrobial measures are applied to mitigate patient risk of infection arising from use of medical devices that are met by high-level disinfection or sterilization modalities (Fig. 1) (Rowan et al., 2023a; McLaren, 2020). The role of a sterility assurance subject-matter-expert with a full appreciation of the end-to-end device process including supply chain and material science will remain critical (McLaren et al., 2021). However, there is increasing evidence of unwanted infections attributed to the reuse of processed medical devices due to failures in processing and sterilizing expectations. Therefore, despite recent advancements in the development of new international standards by stakeholders, there remains significant technical and logistical challenges to address effective cleaning and processing of complex reusable device devices for safe patient use (Kremer et al., 2023a). Recently, there has been a focus on the suitability for cleaning, reprocessing and sterilization for reusable devices at the initial design thinking stage; however, there is a need to consider this in the context of use and reuse in the end-to-end supply chain and sterility assurance, such as developing, testing and validating alternative sterilization modalities (McLaren, 2020; McLaren et al., 2021; Kremer et al., 2023d). There are many complicated and interrelated factors influencing the safe and effective processing of medical devices that increases the chances of operational and processing errors (McLaren et al., 2021). There are also considerable opportunities to develop sustainable 'green' medical devices that considers use of new biomaterials based on appropriate selection of medical device sterilization modality to ensure effective design for satisfying customer needs, supplier selection, management (scheduling, production, distribution, after sale-customer care) (Rowan et al., 2023a; Kremer et al., 2023c). This also considers a greater spot light on increasing healthcare resuse options given the surge and

Table 1
Digital technologies — definitions and applications in medical device and healthcare sectors.

Digital technology definitions*	Examples of benefits and applications
Information and communications technology (ICT) encompasses the capture, storage, retrieval, processing, display, representation, presentation, organization, management, security, transfer, and interchange of data and information.	■ Mobile health (mHealth) – smart devices, apps, and wearables, health information technology, telehealth, personalized medicine; biosensors, ECG monitors; blood pressure monitors and so forth ■ smart hospital management (bed occupancy, device usage, equipment status, operational data.
Internet of medical things (IoMT) – network of smart, interconnected devices and services capable of sensing or listening to requests and perform actions using actuators. IoMT enables network sensors to remote connect, track and manage products and systems.	■ Remote patient monitoring (heart rate, temperature glucose) ■ Robotic surgery ■ Connected inhalers ■ Smart connected contact lens ■ Hand hygiene monitoring
Cloud computing – use of tools and applications (such as data storage, servers, databases, software) based on a network of severs through the internet. It enables user to rent computer resources on demand to store files and applications in a virtualised servers and access all data via the internet.	■ Accelerates clinical analyses and care processes (e.g., electronic health records) ■ Automates data processing & scalability. ■ Increases patient data accessibility ■ Reduces network equipment/staff costs ■ Reduces risks of data loss ■ Integrates physical, digital and data platforms for patient experience ■ Cloud computing for clinical R&D (Azure platform for patient analytics – HoloLens 2 projects holographic images for wearer) ■ Amazon Web Services to create cloud solutions
Artificial Intelligence (AI) defines machines achieving human-like cognitive functions (ex. learning, reasoning, interacting) that comprises different forms of cognition and meaning understanding (such as speech recognition) and human interaction (signal sensing, smart control, simulators) rooted in algorithms and software.	■ Data management ■ Remote surgery and patient monitoring ■ Early detection of patient health issues ■ Diagnostic and procedural assisting ■ Clinical trials ■ Improve device manufacturing efficiency ■ Reduce risk through Machine Learning ■ Advancing wearable technology and medical device — can monitor vital signs and collect patient data in real time ■ Non-destructive sampling (device materials) during design/production
Machine learning (ML) – a subset of AI, use and development of computer systems that learn and adapt without following explicit instructions, by using algorithms and statistical models to analyse and draw inferences from patterns in data. Noting, 10 guiding Good machine learning practices (GMLP) have been identified by U.S. FDA, Health Canada, and UK's Medicines and Healthcare Regulatory Agency (MHRA) for A/ML-driven medical devices. These GMLPs will identify specific areas where International Medical Device Regulators Forum (IMDRF), International Organization for Standardization (ISO) and other collaborative bodies will advance medical device development.	■ 171 AI and ML enabled medical devices marketed in the US added to FDA list and insights (FDA 2023). ■ The devices in this list have met the FDA's applicable premarket requirements, including a focused review of the devices' overall safety and effectiveness, which includes an evaluation of appropriate study diversity based on the device's intended use and technological characteristics. ■ Through the end of July 2023, 79 % of AI/ML-enabled devices authorized (FDA) in 2023 are in Radiology (85), 9 % in Cardiovascular (10), 5 % in Neurology (5), 4 % in Gastroenterology/Urology (4), 2 % in Anesthesiology (2), and 1 % each in Ear, Nose and Throat (1), and Ophthalmic (1)
Big data – continuous increase in data & technologies that needs to be collected, stored, managed and analysed. Complex and multidimensional that impacts processes, technologies. Characterized by Volume (amount of data sets), Velocity (speed of data processing), Variety (types/sources of data), Veracity (quality of data analysed).	■ Better patient care, improved research, smarter treatment plans, reduced costs for patients and health providers ■ Healthcare source of Electronic heath records (EHRs) ■ Apply predictive analytics to create machine learning (ML) models such as likelihood of patient infection ■ Real-time alerts to medical staff by continuously monitoring patient conditions ■ Transforming supply chain logistics ■ Enhancing security of sensitive data (ex insurance claims, design innovation of device)
Blockchain is a shared digital, immutable ledger that facilitates the process of recording transitions and tracking assets in a business network using cryptographic algorithms). Blockchain protocols aggregate, validate, and relay transactions within the blockchain network. The blockchain system records the transactions in sequence. A transaction may contain a value transfer or a smart contract invocation.	■ Traceability ■ Training ■ New business models
Augmented reality – is a real-world augmented experience with overlaying or mixing simulated digital imagery with the real world as seen through a camera or display, such as a smartphone or head-mounted or heads-up display (HUD). Digital imagery may be able to interact with real surroundings (often controlled by users). This is sometimes referred to as mixed or merged reality.	■ Training ■ Visualization of design features/process ■ Overlying medical images onto a patient during an operation to help guide surgery
Virtual Reality – the computer-generated simulation of a 3D image or environment that can be interacted with in a seemingly real or physical way by a person using special electronic equipment, such as helmet with screen inside or gloves fitted with sensors.	■ Bespoke training in safe setting ■ Used to treat post-traumatic stress disorder in army veterans ■ VR rehabilitation therapy – simulates real-life situations to improve physical functions for patients (e.g., physical disability caused by a stroke)
Extended Reality (XR)	■ 3D visual training, spatial audio combining AR, VR and mixed reality (or parts thereof) for monitoring and training (see Tables 3 and 4). ■ Make procedures less invasive (AR/VR) ■ Accelerate diagnosis ■ Allow for self-directed care ■ Possible risks (cybersickness, head and neck strain, cybersecurity risks, privacy risk, distraction in operating room). ■ Future design thinking, visualization, use
Robotics – a branch of technology that deals with the design, construction, operation and application of robots. In multi-robot or swarm robot systems, the robot collaborate to complete predefined tasks.	■ Robot-assisted surgery (precision) such as da Vinci system ■ Robot-assisted radiotherapy (reposition patient without need have anyone in room), reduces procedure time ■ Laboratory automation (reduces human error, expedites processes, removes repetitive tasks, improves staff satisfaction, reduces overall costs, improves safety.

(*continued on next page*)

Table 1 (*continued*)

Digital technology definitions*	Examples of benefits and applications
Cobot, or collaborative robot, is a robot intended for direct human robot interaction with a shared space, or where humans and robots are in proximity.	■ Prosthetics – robotic appendages (grabbing, walking) ■ Rehabilitation and exoskeletons for helping patients recover from surgery, or deal with disability. Can sense electric pulse allowing rebuilding of muscles. ■ Social support – care robots meeting emotional needs of patients (elderly, isolated) ■ Hospital robots – nursing robots can address mundane and repetitive tasks ■ AI training and coaching – see VR. ■ Microbots – help recovery time at cellular level during surgery (Sorimuthu, 2023). ■ Cost savings from staff overtime, extended hospital stays, physical therapy, home care, travel etc. ■ Cleaning and disinfection robots in healthcare facilities (UV-C) ■ Improving cost efficiency, quality, and safety in high production processes ■ Cobots contribute to development and delivery of innovative/reliable devices ■ Addressing labor shortages by optimize limited human resources ■ Cost effective, rapid development such as plug-and-play style to automation ■ Offer flexibility to adjust capacity, throughput avoiding over investment or underutlizaiton of resources ■ Scalability, lower maintenance costs. ■ Flexibility and quick redeployment ■ Efficient use of floorspace/infrastructure ■ High precision (ex assembly applications)
Digital twin – a digital win is a virtual model designed to accurately reflect a physical object.	■ Software for data traceability ■ Real time monitoring ■ Design think and visualization ■ Preventative maintenance ■ Design validation and planning ■ Optimizing operational needs (Table 3)
Edge Cloud/Intelligence – Edge computing is developed as complement to cloud computing, encompassing storage and compute assets located at the edge and interconnected by a scalable, application-aware network that can sense and adapt to changing needs, securely & in real time. The "edge" of network is element of network infrastructure furthest from core.	■ Real-time secure remote monitoring (medical devices or received urgent alert) ■ Patient data/device processed by on site edge compute resources ■ Analysis of patient data (ex. wearables) ■ Detect early signs of illness or disease ■ Smartwatches, fitness trackers ■ Reduce data latency ■ Maintain high availability (via Cloud service) ■ IoT sensors, smart cameras, uCPE equipment, servers and processors
Cybersecurity or information technology (IT) security – is the practice of protecting critical systems and sensitive information from digital attack. It is how individuals and organisations reduce the risk of a cyber attack where cyber security code function protects the devices (smartphones, laptops, tables).	■ Essential component of healthcare and medical devices so as to guarantee systems are secure and shielded from cyber threats. ■ Maintaining precision and dependability of medical equipment and systems ■ Keeping patients secure, protecting financial information, private medical data, confidential patient information.
Cyber-physical systems refer to systems where software and hardware components are seamlessly integrated towards performing well-defined tasks.	Helps safeguard healthcare from malware and ransomware assaults resulting in patient care disruptions, system failure, data breaches

* Adopted in part from Rowan et al. (2023b).

reliance on single-use disposable items (Greene et al., 2022). Consequently, this timely paper provides both an awareness of and describes the use of digital innovation to effectively advance existing medical devices and to unlock opportunities with new design thinking with a lens on sustainability. It also focuses on the potential innovate use of digital tools to help inform and advance reusable and disposable medical devices for existing and future needs including sustainability.

2. Use of an integrated Quintuple helix HUB approach to address appropriate digital solutions

Integration of key actors from different specialist backgrounds, such as manufacturers, academics, industry (including sterilization providers), policy-makers (regulators), healthcare (including Sterile Services Department, clinicians), SMEs/entrepreneurs and patients can help inform opportunities and solutions across the entire production and logistical supply-chain for medical devices from conception to market product launch including supporting regulatory approval (Table 3). The benefits of adopting an integrated multi-disciplinary approach for addressing knowledge and innovation gaps (example, quadruple helix) has been well articulated in the published domain that includes improving efficiencies and cost saving on "testing the tech" before investing by accessing specialist equipment (example, RAMAN Spectroscopy, Flow cytometry, 3D printing, injection moulders, automated washers and pilot sterilization modalities, extended reality suite and so forth) and subject-matter-experts (such as immersive or extend reality technologists, advanced imaging or polymer scientists) (such as highlighted by Rowan and Casey, 2021). The core indicative activities highlighted in Table 3 would be overseen by an experienced HUB manager with appropriate knowledge of underpinning sterility assurance embedded in the academic hosting framework for enabling and accelerating appropriate networking, partnerships with industry, manufacturers, entrepreneurs, regulators and so forth (McLaren et al., 2021). The CURAM SFI Medical Device Research Centre in Ireland represents a typical example of such an effective multi-actor HUB that includes considerable experience in addressing appropriate intellectual property protection and management from data generated for various users. This would also facilitate the testing of new materials with existing or alternative sterilization modalities for optimizing time and costs in alignment with FDA guidance titled "submission and review of sterility information in premarket notification 510(k) – submission for devices labelled as sterile (U.S. FDA, 2024)". For example, the sterilization modalities established in Category A are ethylene oxide (EO), vaporized hydrogen peroxide (VH_2O_2), dry and moist heat, and radiation), established Category B include ozone, hydrogen peroxide, ozone, and flexible bag systems, and novel sterilization modalities include vaporized peracetic acid, microwave radiation, sound waves, low pressure and pulsed UV light (McLaren, 2020). There is also considerable opportunities for introducing non-destructive sampling for medical device development that includes important sterility assurance provision (Table 3) — this includes use of specialist imaging and spectroscopy equipment that can be linked to machine learning models.

The integrated multi-actor approach avoids the traditional 'silo' approach that focused on use of specific aspect(s) of the device process

Table 2
Examples of applications of the Spaulding Classification system for medical devices encompassing type of decontamination or sterilization modality to mitigate patient risk of acquiring an infection.

Risk category	Description	Type of decontamination or sterilization modality required to address risk
Critical use items	• Where a device enters sterile tissue and must be sterile, defined as being free from viable microorganisms (McDonnell and Hansen, 2020) • Items contaminated with any microorganism (including bacterial spores), or infectious agent (prion) are referred to as high risk to patients. If they are contaminated and enter sterile tissue or vascular system, they have a high potential for causing disease transmission (Rutala and Weber, 2019). Such items should be sterile, such as by using steam sterilization where possible. Examples include surgical instruments • Close attention should be given to the label claims of liquid chemical sterilants as these can vary regionally; they may have the ability to sterilize, depending on their application but may not always be considered practical for routine sterilization.	• Given that many items contain heat-sensitive materials, other appropriate sterilization modalities should be applied including vaporized hydrogen peroxide (VH_2O_2), VH_2O_2 gas plasma, and ethylene oxide gas (EO). • The use of liquid chemical sterilants may also be considered appropriate, such as formulations based on glutaraldehyde (GTA), peracetic acid (PA), hydrogen peroxide (HP), or ortho-phthalaldehyde (OPA).
Semi-critical use items*	• Where a device only comes in contact with intact mucus membranes or nonintact skin, it should also be subjected to sterilization, or if this is not feasible due to sensitive material composition or complex design features, then a high-level disinfection (HLD) process must be deployed at a minimum that would be expected to kill all microorganisms except for bacterial endospores (McDonnell and Burke, 2011). • Examples of semi-critical items including "respiratory therapy, anaesthesia equipment, some endoscopes, laryngoscope blades and handles, esophageal manometry probes, endocavitary probes, nasopharyngoscopes, prostate biopsy probes, infrared coagulation devices, anorectal manometry catheters, cystoscopies, and diaphragm fitting rings" (Rutala and Weber, 2019).	• Depending on regional claim requirements, high level disinfectants should demonstrate broad spectrum antimicrobial activity and typically the ability to eliminate at least 10^6 (or 6-logs) of mycobacterial cells on contaminated surfaces of medical devices. • For the vegetative microorganisms and viruses of concern, mycobacteria are typically deemed to exhibit greater resistance to high level disinfectants; thus, mycobacterial cells are recognised as representative (or bio-indicators) for HLD process efficacy. • Examples of chemical disinfectants authorized in the USA for HLD use include biocides such as glutaraldehyde, HP, OPA, hypochlorite, and PA with HP (Rowan et al., 2023a).**
Non-critical use items	• Where devices contact intact skin (but not mucous membranes), requiring low-level to intermediate-level disinfection. The skin contains intact integumentary layers, and as such, provides a natural barrier to microorganisms. There remains a risk to the skin and as a source of cross-contamination from devices, but this risk is considered low (Rowan et al., 2023a) • These risks can be practically reduced by the combination physical removal and disinfection (McDonnell and Burke, 2011). Examples of non-critical use items include blood pressure cuffs, bed surfaces and rails, patient furniture, bedpans, over-bed tables and so forth (Rutala and Weber, 2019). • Such product labelling support disinfection efficacy against a broad spectrum of microbial pathogens that may include methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant enterococci, yeast (Candida sp.), mycobacteria, and viruses well within typical label claim for US EPA-registered disinfectants.	• Physical removal plays an important role in the removal of pathogens with higher levels of natural resistance to disinfectants such as bacterial spores (as highlighted in studies of surface contamination with clostridia; Thomas et al., 2022).

Modifed in part from information furnished in Rowan et al. (2023a).
** It is important to note that the ability to inactivate microorganisms by a disinfectant/sterilant is only part of an overall safe and effective high level disinfection process, as the disinfectant residuals need to be safely removed and the device correctly maintained prior to patient use.

(McLaren et al., 2021); thus, creating new opportunities to holistically (360°) consider "design thinking" across all key activities over the entire end-to-end lifecycle for complex devices. This approach allows opportunities for introducing transformative beyond-state-of-the-art innovation from adjacent industries, such as digital twin (Table 4)). Yet also ensures that appropriate international standards for development, manufacturing and validation are applied and interpreted correctly. Table 4 also describes key activities and benefits for manufacturers' instructions for use (MIFUs) that will close the innovation gap for meeting client/patient needs. The inclusion of clean room and pilot facilities for cleaning, disinfection and sterilization of new medical devices that connects stakeholders would be beneficial, such as design thinking and sterility assurance informing selection of sterilization modality to meet the safe intended use for patients including functionality, material composition (AAMI TIR17:2017), biocompatibility (ISO 10993), and sustainability (McLaren et al., 2021). An example of appropriate medical device modality selection to meet complexity of medical device design and patient needs is represented in the adapted viewpoint paper of McLaren (2020) (Fig. 1). Such a holistic approach would save on costly manufacturing revisions to medical devices and unlock situations where new-biomaterials in design features can be tested from a development, testing, validation perspective (510k) in dialogue with regulators. Application of approaches that improve efficiencies and data sharing including collaborative partnerships across manufacturing, healthcare, sterility assurance and so forth will impact positively on intended product functionality, shortened timeliness for regulatory approval, efficiencies in resources and risks (McLaren et al., 2021).

This interdisciplinary hub approach is also highly relevant for manufacturers, small companies, entrepreneurs, doctorate research candidates across different disciplines who want to test new ideas using appropriate equipment, methods following appropriate international standards. This would also entail keeping pace with international standards updates. This would also help de-risk for financially viable innovations and investments. It would mitigate against potential unforeseen reputational damage due to possible misinterpretation of appropriate methods for new devices medical devices by inventors as it would have appropriate sterility assurance embedded from commencement of the project for addressing key activities. For example, Smith et al., 2023 (representative of medical device industry), recently expressed concern about the reporting findings from a published study (Deasy et al., 2022), as the test methods and claims in the report were inconsistent with international standards for cleaning and disinfection of reusable devices in washer-disinfectors (WDs) (BS EN ISO 15883-1:2006, 2006; BS EN ISO 15883-2:2009, 2006; BS EN ISO 15883-5:2021, 2022). Deasy et al. (2022) had stated that there are no specific standards for dental head-pieces (DHPs); however, Smith et al. (2023) noted that DHPs, as medical devices, are given as examples of the type of devices in the WD standard series BS EN ISO 15883-2:2009, 2006), and specifically as powdered devices. Smith et al. (2023) also stated that "cleaning and disinfection requirements in these standards therefore apply. For example, cleaning validation using defined test soils and disinfection efficacy requirements described in the standards (BS EN ISO 17664-1:, 2021) are applicable to these reusable medical devices".

3. Digital transformation of the medical device and health care sectors

There is increased interest in the application and development of digital technologies to improve efficiencies and to unlock sustainable opportunities in the medical device and connected sectors (Tables 1 and 4). Definitions of the different types of digital innovation for enabling development of medical devices are articulated in Table 1 in addition to highlighting benefits and applications. Adapting and integrating these digital technologies will help transform supply chain logistics, improve medical device design and production, improve workflows and efficiencies, reduce uncertainties, save costs, reduce resources and errors, improve education and training, reduce waste, improve user satisfaction, improve security, and mitigate for enhanced patient safety. The real-time application of these digital technologies will also enhance knowledge and innovation exchange such as through Open Access shared publishing platforms (Kremer et al., 2023c) that will help stakeholders appreciate the utility of generated data for manufacturing, verification and validation applications, including informing important standards in consultation with regulators. For example, robotics and automation are transforming surgery and radiography through precision and by alleviating fatigue (Table 5). It addresses mundane yet important tasks such as cleaning that can be further aided by applying machine learning. Internet of medical things (IoMT) addresses many key patient needs including digital health (wearables) (Table 1).

The U.S. FDA has acknowledged the role of digital technologies in enabling development of the medical devices sector, for example, 171 artificial intelligence (AI) and machine learning (AI/ML)-enabled medical devices were recently added their list marked in the US hat recognises their ability to create new and important insights from the vast amount of data generated during the delivery of healthcare provision (FDA, 2023a). A central tenet of the FDA's public health mission is to ensure that these potentially transformative devices are "safe and effective which includes an evaluation of the appropriate study diversity based on the device's intended use and technological characteristics. Over the past decade, the FDA has reviewed and authorized an increasing number of devices (marketed via 510(k) clearance, granted De Novo request, or premarket approval) with AI/ML across many different fields of medicine". They FDA noted that no device has been authorized that uses generative AI or artificial general intelligence (AGI) or powered by large language models. Currently the number of AI/ML enabled devices authorized through the end of July 2023 appear in the decreasing sequence radiology (n = 85, 79 %), cardiovascular (n = 10, 9 %), neurology (n = 5, 5 %), gastroenterology/urology (n = 4, 4 %), anaesthesiology (n = 2 %), ear, nose and throat (n = 1, 1 %), ophthalmic (n = 1, 1 %). In general, ML are increasing in complexity including deep learning models that included more hybrid approaches combining different algorithms to achieve safe and effective devices results (e.g., combining use one model to address classification and another model to generate features".

It is important to discern when AI should be applied to safely address a specific societal challenge, particularly in a highly-regulated world of medical devices and healthcare comprising multiple actors. Retursdottir (2024) noted that AI/ML technologies "need to be able to integrate seamlessly into a clinical setting, be easy to use for patients, and have safety critical algorithms that are transparent and explainable to regulator." Moreover, this author noted (1) do AI/ML technologies solve a real problem that is appreciated by stakeholder; (2) do they align with Principle of "Design Thinking" to address feasibility, viability and desirability, and (3) does it use different reputable and reliable state-of-the-art technical research approaches to confirm that AI/ML is the right solution for a problem as opposed to a non-specific technique without purpose. Activities to improve confidence and reliability in AI/ML including avoiding use of bad quality datasets (invalid, missing, non-inclusive or too small) that will affect the reliable performance of ML-model, for example with the development of next generation medical devices such sensitive data can be challenging to obtain for stakeholders (see Table 4 for desirable attributes for enabled devices including training and evaluating machine learning models). For example, in addition to being needed by stakeholders to accurately solve a recognised healthcare problem, AI and ML models need to be explainable as end-users and regulators will need to understand the foundational basis as to how such AI-based medical devices are making specific decisions. Ten guiding principles have been identified by the FDA and MHRA for

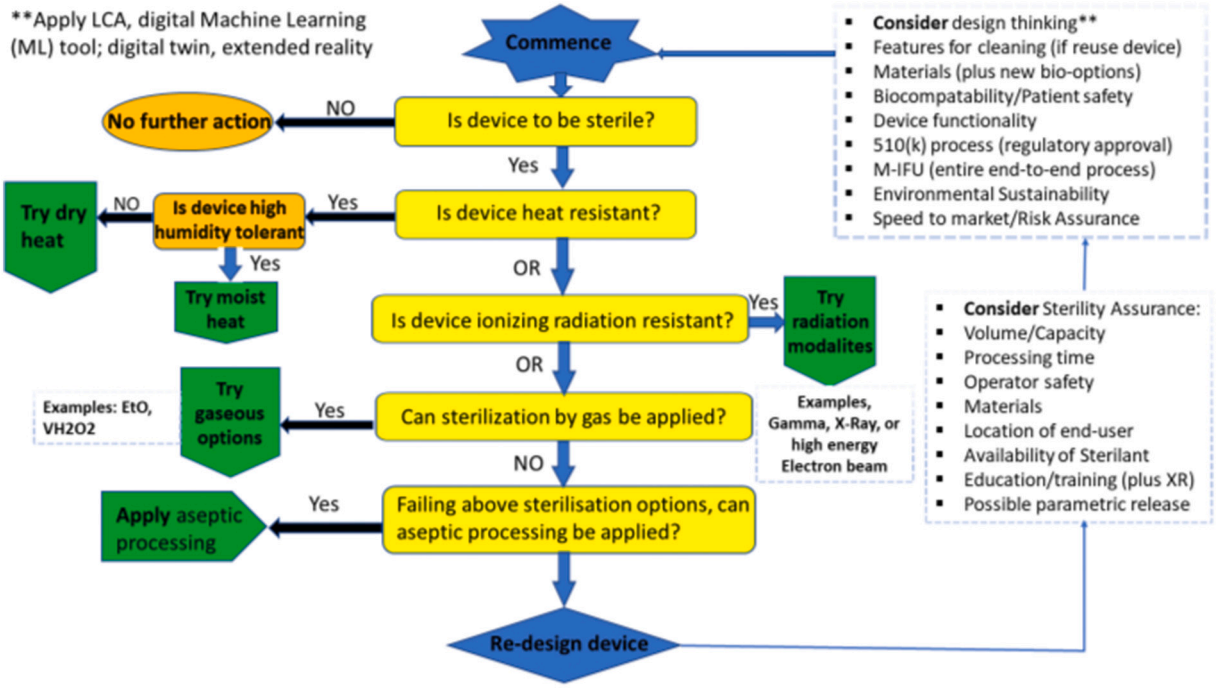
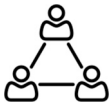


Fig. 1. Flow path of sterilization modality options depending on factors underpinning medical devices design and intended use informed by digital tools. (Adapted from McLaren, 2020).

Table 3
Meeting oppotunities through integrated access and use of multi-actor hub including industry, academics, healthcare, manufacturers, policy (regulators), entrepreneurs, society.

Activity	Description	Benefits
Multi-actor approach	■ Integrated academic, industry, manufacturers, policy (regulators), healthcare, society approach	■ Multi-actor (specialist) inputs
	■ Appoint expert HUB manager	■ End-to-end full cycle (aligned with needs of MIFUs, healthcare)
	■ Step change physical infrastructure & support systems	■ Supporting existing and future Healthcare/industrial sterilization
	■ Modelling, simulations, prediction, verification, validation	■ Networking/conferencing
	■ Education & holistic training programs (End-to-End Cycle)	■ Holistic problem solving
	■ Mentorship opportunities	■ Leverage access to specialist equipment/staffing (cost savings)
	■ Ideation & design thinking to align with TRL, manufacturer needs etc. Appropriate methods/Standards	■ Clustering of resources
		■ De-risking/risk-assessment
		■ Suits small to large operations
Technical	■ Digital transformation	■ Update existing/new medical device design (parts/process)
	■ DT and XR specialist equipment & expert staffing	■ Specialist training (physical to virtual) safe-efficient.
	■ Modelling, simulation, automation	■ Automation, efficiencies, uncouple uncertainties, de-risk
	■ Machine Learning for real time data analysis, prediction and performance	
	Pilot disinfection/sterilization modalities:	■ Pilot testing of new products, (bio-) materials combination with new modalities
	■ Chemical biocides	■ Alternative sterilization products for manufacturers
	■ Steam/dry heat	■ End-to-end design thinking including functionality, biocompatibility
	■ Low temp technology options: such as	
	■ Electron beam	■ Limiting re-testing of devices,
	■ Vaporized hydrogen peroxide (VH_2O_2)	■ Reduction in cost
	■ Testing alternative sterilization modalities (including informing implementation, validation, regulatory requirements)	■ Opportunities for new "Green" (sustainability) testing, verification, validation for products, services
	■ A nexus to commercial large-scale treatments (Gamma, X-ray, EtO etc)	
	3D printing healthcare applications including devices and APIs	■ Medical applications, modelling, simulations, testing, verification
	Advanced (bio-) materials characterization for devices and packaging (pre and post processing/sterilization)	■ Developing methods, products, informing standards (ISO working groups), SWOT, risk mitigation, sustainability (reduced waste)
	Dosimetry (mapping) and software/ future parametric release	Appropriate disinfection, sterilization – group as "family" products for dose
	Automation (washer disinfectors (WD)	Improved efficiencies, reliabilities
	Challenge testing (PCDs) including bioburden using appropriate BIs	Training and innovation on core supporting applied sciences
	Design thinking (devices)	■ Efficiency, reduced risk to patients and environment
		■ Material reuse/eco-efficient process
	Biocompatability (ISO 10993)	In vitro/in vivo (regulatory) including scope for new 3D printing (implants)
	Skills, training and development	End-to-end processing; complex procedures
Regulatory	Advice on existing and updated ISO Standards	■ Appropriate methodology
	Understanding new regulations and rules (example sustainable use of EtO)	■ Reputational integrity
		■ Risk Management
		■ Avoids misinterpretation
		Verification, validation
Business & dissemination	■ Test the tech/test before invest	■ Financial viable product/value proposition (cost structures)
	■ Business model canvas and SWOT	■ Inform certainties on cost and timelines
	■ Integrated ecosystem building	■ Providing key resources
	■ Intellectual property management	■ Providing key activities
	■ Access to finance/investments	■ Networking key partnerships
	■ Appropriate dissemination and communication channels including infographics	■ De-risking and optimized value stream
		■ Market research and needs analysis
	■ Grant and specialist writing supports.	
Sustainability	■ Energy and carbon footprint (LCA)	■ Eco-friendly parts, products, services, processes
	■ Technical, political, societal LCAs	■ Effective waste management
	■ Safe and Sustainable by Design (SSbD) framework approach	■ Educational and training
	■ Waste management (recycling/reuse)	■ Corporate Social Responsibility
	■ Staffing (training)	■ Green product "sustainability testing" to validation
	■ Informing polices, standards	■ Lean six sigma for medical waste
Ethics	■ Artificial Intelligence (AI) trustworthiness	■ Increases productivity
	■ Safeguarding against reputational damage from using incorrect methods, or their misinterpretation	■ Attracts outstanding employees
		■ Employee loyalty
	■ Supporting Regulatory affairs	■ Better reputation
	■ Gender and cultural Inclusiveness	■ Integrity and responsibility
		■ Provides competitive advantage
		■ Attracts more investors
Social Sciences	■ Social marketing	■ Engage with and learn your audience
	■ Social enterprises	■ Promote innovation/customer service
	■ Society engagement and acceptance	■ Understand competition
	■ Outreach activities	■ Build appropriate partnerships
	■ Citizen Science	■ Acquire talent
		■ Impact sales
		■ Keep up with industry trends

(*continued on next page*)

Table 3 (*continued*)

Activity	Description	Benefits
Educational technologies 	■ Specialist healthcare/sterilization training ■ Supports diversity of short courses (micro-credentials) to postgraduate qualification (ex sterility assurance) ■ Wide choice of learner tools ■ Adaptive learning/new skills/new knowledge ■ Prepares learners for future ■ Enhance engagement/satisfaction	■ Training and educational opportunities for experienced staff and newcomers ■ University design by learning (UDL) ■ Enhanced Productivity ■ Boost and improve collaboration ■ Stay current with new technologies ■ Blended with XR/DT innovation
Infection control 	■ Addressing pressing healthcare challenges from holistic multi-actor approach (such as potential microbial MDR and biofilm issues with processed devices ■ Improved device cleaning, processing and sterilization ■ Infection control team kept current ■ Updates on policies and guidelines ■ Offers new suite of preventative solutions to complex microbial challenges where many front-line antibiotics are at crisis point	■ Allows solutions (pivoting) to address key healthcare needs and for unforeseen (ex. Pandemics) ■ Improve healthcare efficiencies ■ Reduces mobidity, mortality ■ Reduces patient risks ■ Improves healthcare savings/spend ■ Reduces patient anxiety and stress ■ Prevents occurrence/spread of HAIs

DT (digital twin); Extended Reality (XR), BIs (Biological Indicators), CIs (Chemical Indicators); Life Cycle Assessment (LCA); EtO (ethylene oxide); AI (Artificial Intelligence); ML (Machine Learning); Manufacturers instructions for use (MIFUs); TRL (technology Readiness level).; Multi-drug resistance (MDR); healthcare acquired infections (HAIs); APIs (Active Pharmaceutical Ingredients).

Table 4
Digital twin and extend reality innovation attributes and benefits for medical device development and testing.

Digital twin (DT)	Extended reality (XR)
Virtual copy of physical entity interconnected via exchange of data in real time	Delivery of 360° visuals, spatial audio – allowing learner active participation using virtual or augment reality scenarios/simulations
■ Real-time monitoring ■ Design + validation of new/existing entity ■ Enables end to end planning for devices ■ Optimizing for solutions in real time ○ DT can foresee defects and faults in advance ○ Accessibility – can be controlled ○ monitored + remotely accessed using DT ○ not restricted by geographical location ○ not limited by remote access ○ Informs preventative maintenance ○ Safer – than physical counterpart if working with hazardous situation thus reduces risk	■ Monitors and reports on frequency of training in real time ■ Training -duration ■ Completion ■ Learner tasks performed ■ Questions answered ■ Deep level of virtual and augmented learning ■ Monitor engagement and cognative levels using wearable sensor technologies ■ Eye gaze ■ Head movements ■ Physiological measurement indicators (Heart rate)
■ Decision making of complex multifactorial scenarios in real time ■ Realistic/holistic measurement of unforeseen and unpredicted scenarios ■ Waste reduction – DT simulates and tests products in virtual environ reducing waste, development costs, time to market	■ Decision-making – level of competencies achieved and potential need for retraining ■ Supporting risk management (ISO 14971:2019) ■ 3D simulation of real experience
■ Optimizing operations – in depth analysis of physical twin ■ Increased multi-user engagements ■ Fusing information and technical innovation ■ Integrated multiscale, multidiscipline, multi-physical simulation of entity (product)/process ■ Bidirectional transfer/sharing of qualitative and quantitative data between physical and DT	■ Strong effects on human perception and behaviour ■ Influences performance, satisfaction, motivation, concentration ■ Informs and advances robotic training ■ Improves training-based outcomes and education including micro-credentials to doctorate provision ■ Reduced anxiety in learning process where there is a complex setting
■ Tracks status of physical twin through life cycle ■ Prediction and optimization of part, product, and process ■ Better understanding by synchronizing data in real time across software applications, database, hard copies	■ Improved design, verification, validation and manufacture of medical devices ■ VR provides low cost, high fidelity training with improved accuracy and task completion ■ VR used to assess, model and implement safety risk assessments/mitigation
■ Reduction in errors, uncertainties, inconsistencies, expenses in product/process ■ Avoids component failures and predicts different stages in life cycle (complex parts, multiple materials).	■ Mimics stress clinical setting for training for enhanced patient safety, reduced errors ■ High fidelity visual/sensory feedback
■ Holistic training – more efficient, safer, illustrative linked to education	■ Address limitation of cognitive overload in trainees due to continuous changes in attention
■ Removes ‘silos’ in process ■ Expediting prototyping, product re-design ■ Close knowledge gap between experienced staff and newcomers (across departments)	■ AR headset remotely train clinicians ■ Develop manufacturers IFUs ■ Improvements in evaluation/assessment in simulated training

good machine learning practices (GMLP) that underlie development of AI/ML based medical devices (Gampa, 2023). Retursdottir (2024) reported that of the 343 medical devices with AI/ML capabilities on the FDA list, 95 % were marked between 2015 and 2021 with majority addressing diagnostic medical imaging needs. FDA approved AI/ML enabled devices involved “locked” algorithms, intimating that given the same input, the model will always give the same output. However, the future of AI/ML innovation must also embrace evolving these models to meet increasing needs of patients and healthcare professionals. Retursdottir (2024) stated that there are “no harmonized standards that regulate use of ML in medical applications and devices where companies are not required to classify their technology as AI/ML based”.

Artificial intelligence and ML will be used to help understand risk assessment and mitigation in device manufacture from an end-to-end perspective. Combined use of digital twin (DT) and extended reality (XR) innovations can help understand and meet the need to safely use

and embrace rapid AI and ML-driven devices in terms of aligning with patients' needs and stringent regulatory requirements (Gampa, 2023). Combining use of immersive and educational technologies will also help maintain a critical focus on devices' quality, security, and safety aspects from end to end device production and supply chain perspective. Gampa (2023) noted that failure to meet these requirements will lead to device recalls and hefty fines from regulatory agencies. Thus, physical to virtual enabling innovations that includes simulating real-world devices using replicated avatars can help device manufacturers incorporate AI/ML into innovations will ultimately comply with market entry by adhering to relevant government laws, regulations, and GMLP.

The accelerated interest in AI/ML as rising and promising medical devices will require marked shift in regulatory approach in addition to consideration of risks and potential consequences of inaccurate models (Retursdottir, 2024), particularly addressing continuously learning AI algorithms for healthcare. AI technology has developed leaps and bounds since first coined at the Dartmouth Summer project in 1956, where it can now interpret medical images 10,000 times faster than the average radiologist and can improve patient diagnostics and care by augmenting digital pathologies (Retursdottir, 2024). However, despite enormous potential, AI technology has a considerable journey remaining to grapple with human health and all its complexities. Moreover, Gampa (2023) reported that "the complexity of regulatory requirements for AI/ML-integrated medical devices has skyrocketed and has, in turn, posed significant challenges for manufacturers in terms of data security, patient safety, and device quality, hindering their access to global markets". The U.S. FDA, Health Canada (HC), and the U.K.'s Medicines and Healthcare Regulatory Agency (MHRA) have united to identify 10 guiding principles with a converging aim of developing good machine learning practices (GMLP) addressing the unique nature of AI/ML-driven devices. This coming together of key regulatory actors adopts or tailors for good practices from other adjacent sectors, or it creates new practices specific for the medical technology or healthcare sectors that also identifies areas where International Medical Device Regulatory Forum (IMDRF), International Organization for Standardization (ISO), and other collaborative bodies can advance GMLP for medical devices development (see Table 5). Clark et al. (2023) conducted a systematic review of 119 public 510(k) application summaries and corresponding marketing materials, where devices with significant software components similar to devices flagged in FDA's published AI and ML-enabled devices where 12.6 %, 6.7 % and 80.6 % were considered discrepant, contentious and consistent respectively between marketing and FDA 510(k) clearance summaries (Table 6). The authors noted that the aim of the study was not to intimate designers or developers were creating or marketing unsafe or untrustworthy devices, but to highlight the need for more harmonized guidelines addressing marketing of such AI/ML devices. The role of end-user perception and understanding of such digital health innovation would also be beneficial (Byrne et al., 2023).

While this is a fascinating topic in the context of all potential digital tools, this paper will mainly focus on the role of combining digital twin with immersive technologies to visualize and unlock the complexities of medical device design including transforming training for healthcare staff for improved patient safety. The application of digital twin and immersive technologies can also help manufacturers introduce more

Table 5
Examples of relevant digital tools informing medical device research, innovation and applications appearing in PubMed database (2010 to 2024).

Combination	Description and relevance	References
VR + AR + MR	Applications in spinal surgery	Sakai et al. (2020)
	Objective performance measurement and subjective evaluation in manual assembly tasks	Daling and Schlittmeier (2024)
XR + MD	Head-mounted devices for medical education	Barteit et al. (2021)
	Medical device safety training using quick XR based technology	Saurio et al. (2019)
	Develop software management app for medical devices that supports XR including neurosurgery	Sugimoto and Sueyoshi (2023)
	Accurate mixed reality surgical guidance	Brown et al. (2023)
	3D printed devices for patient specific applications	Moreta-Martinez et al. (2018)
	Immersive and educational training for healthcare applications including rehabilitation	Bryant et al. (2024)
DT + MD	Regulatory oversight and ethical concerns surrounding software as medical devices and DT technology interface and interpretation	Lal et al. (2022)
	Design of digital twin – human-machine interface server with intelligent finger gesture recognition	Mo et al. (2023)
	Parameter personalization for implantable cardiac defribillation	Lai et al. (2022)
	Visualization of use of DTs to inform medical device development from in silico clinical trial perspective	Bordukova et al. (2024)
	Computational modelling for active implantable medical devices	Nguyen et al. (2023)
	Visualize, develop and validate kinematically accurate upper-limb exoskeleton including Stroke rehabilitation	Grimm et al. (2021)
	Automated creation of individual computations and applications in CT organ dosimetry	Fu et al. (2021)
	Modelling and visual design for miniaturizing medical implants including materials	Kazarinov et al. (2022)
VR + MD + AR	AR in vascular and endocascular surgery informed by device	Eves et al. (2022)
	Applying AR technologies to medical images and models	Sutherland et al. (2019)
	Design and evaluation of AR to medical devices	Escalada-Hernandez et al. (2019)
SUS + MD + XR	Educational tools combined with immersive technologies for specialist medical device training on cleaning and processing	Murray et al. (2019)
		Kremer et al. (2023a)
		Kremer et al. (2023b)
DT + XR	Metaverse wearables for immersive digital healthcare applications	Kim et al. (2023)
	Intelligent radiotherapy applications including dosimetry	Chen et al. (2022)
		Chaudhuri et al. (2023)
	Work-based occupational learning from errors in safe environment	Goppold et al. (2022)
AI + MD	FDA-cleared AI and ML-based medical devices and their 510(k) predicate network	Muehlematter et al. (2023)
	AI and Internet of Medical Things assisted biomedical systems in intelligent healthcare to make devices intelligent and efficient for performing tasks	Manickam et al. (2022)
	Are clinical studies on AI-based medical devices comprehensive enough supporting full health technology assessment	Farah et al. (2023)
	AI software to for advancing medical devices – focus on laparscopic cholecystectomy surgical phase recognition	Shinozuka et al. (2022)
	FDA-approved AI and ML enabled devices an update on status	Joshi et al. (2024)
	Marketing of US FDA cleared AI and ML-enabled software as medical devices – 119 devices reviewed highlighting a degree of variance between marketing and FDA 510(k) summary details	Clark et al. (2023a)

Noting that extent and scope of publications in PubMed particularly address research, development and applications, but this underestimates the level (amount) of actual commercial innovation as reflected by FDA List of approved and marketed AG/VR enabled medical devices (FDA, 2023a; FDA, 2023b).

sustainable materials both in terms of reusable and single-use devices.

4. Selection and application of potential digital solutions for medical devices

A PRISMA approach was adopted to review papers published in PubMed database over the period January 2010 to Jan 2024 using key words medical device (MD, 786,727), sustainability (SUS, 402,083), artificial intelligence (AI, 187,208), digital twin (DT, 1649), augmented reality (AR, 5266), virtual reality (VR, 19,032), mixed reality (MR, 6884), extended reality (XR, 1726), sterilization (STER, 114,448), DT + XR (10), DT + MD (135), XR + MD (124); SUS + MD (19,571), AI + MD (12,267), SUS + MD + STER (221), and VR + MD + STER (11). Publications dismissed due to lack of alignment with specific theme described home monitoring (asthma), visualization museum specimens, precision public health, self-balancing low limb exoskeleton, tooth preparation, hormone delivery, sterile bag use, sterile wash flow, digital brain technology, cardiac electrophysiology, stroke and tele-rehabilitation, finite element modelling, haemodialysis, modelling of healthcare buildings, predictive oncology, infrastructure disaster prevention/reconstruction, historical document reconstruction, bioreactor contamination, organ-on-a-chip devices, bioink exopolysaccharides, gynaecological sterilization technologies, membrane reactors and waste water, laser to clean healthcare furnishings, pain and anxiety during vasectomy, 3D surgical instrument supply chain tracking, toilet flushing, plasma approaches for wound healing, visualising hydraulic systems, sustained activities and therapies for COVID-19.

4.1. Digital twin use in medical devices and healthcare

Digital twin (DT) is seen as the virtual copy or model of any physical entity (digital twin) where both are interconnected through the exchange of data (Singh et al., 2021a). From a medical device evolution perspective, it enables design, planning, predictive maintenance, training, decision-making, risk analysis, in depth data analysis, safety, reliability, multi-actor accessibility, waste reduction and cost efficiency by the bidirectional sharing of quantitative and qualitative data between the physical counterpart (medical device) and its digital twin (Table 4). It provides a safe remote virtual environment to develop and track status of new medical device from design, materials, processing through its full life time. Thus, enabling the visualization, production and testing of parts, product or process for intended purpose that limits or avoids component or process failures that includes provision for preventive maintenance and improved performance. Digital twin (DT) was born out of the Industry 4.0 era from the aerospace industry where its' global market size is projected to reach USD 16.44 billion in 2024 (Businesswire, 2024).

Table 4 highlights key performance benefits and opportunities from applying DT to meet needs in the medical device sector. It is envisaged that these will inform future key performance indicators for the industry that will help regulators understand its applicability for shaping future medical devices that will potentially lead to updating existing and generating new ISO standards with stakeholders. However, appropriate device communication and data collection/sharing standards that define its quality requires standardization for uniformity to make it accessible to regulators to approve process without compromising security (Wagner et al., 2019). Additionally, future challenges for developing DT to unlock opportunities for medical device applications relates to confidentiality, privacy, transparency and ownership of unique data that will be influenced by company policies (Singh et al., 2018). Table 4 provides examples as to how DT has specifically informed the development of medical devices. Singh et al. (2021b) have highlighted the real versus virtual costs of device prototyping that clearly intimates positivity developers and investors. DT sought-after characteristics include high fidelity (a near-identical copy of its physical counterpart), dynamic (changes with respect to time and needs), self-evolving with its counter physical twin over life span, uniquely identifiable based on its physical twin and vice versa over the full life cycle, multiscale, multidisciplinary and multiphysical and hierarchical. The latter relates to the integrated nature of parts or sub-models of the DT that make up the final product or process. Despite its apparent benefits, DT is still an emerging innovation that requires buy-in from stakeholders to meet its potential. DT is initially an expense investment as the end-to-end process requires significant investment in ultra-high-fidelity computer models to create DT that is specialist labour intensive and time consuming.

4.2. Extended reality use in medical device and healthcare sector

Extended reality (XR) innovation is an overarching term that combines virtual reality (VR), augmented reality (VR) and mixed reality (MR) that have the potential to transform medical device and healthcare sectors (for example, Tables 4 and 5 provide definitions and examples of applications). The FDA has noted that these approaches deliver new types of treatments, and diagnostics that can change how and where care is delivered. These holistic 360° virtually visual innovations have the ability to "deliver standard and radically new types of technical content in highly immersive and realistic ways, remotely, and specifically tailored" to meet pressing healthcare and clinical needs for different end-users (industry, policy-makers, physicians, patients, caregivers and so forth). Table 4 provides a summary of key benefits and activities for existing and future applications in medical device and healthcare sectors that contrast markedly from DT innovation. However, when considered together, DT and XR innovations can provide powerful training tools for complex medical device design processes delivered in a safe and reliable virtual environment. Kremer et al. (2023c) highlighted the benefits of applying immersive and education technologies to unlock opportunities particularly in training and smart of next generation reusable medical devices through the lens of entire end-to-end process. However, the use and interpretation of XR is highly subject matter (expert) driven where effective blending of these real-world augmented and virtual-world experiences would likely to be met by specific digital companies engaging with medtech industry and healthcare end-users. This can be also be enabled by collaborating through multi-actor innovation HUBs that will reduce costs along with providing a considerable number of other benefits (Table 3). For example, learner experiences can be monitored by evaluating physiological parameters (eye gaze, heart rate, etc.) that will inform efficacy of training undertaken, and potentially the need for retraining, or additional training delivered in a safe remote environment.

Real-world examples highlighted by the FDA for XR applications that are already being used to treat patients include AR system that overlays medical images onto a patient during an operation to help guide surgery, VR rehabilitation therapy simulating real-life situations to improve physical functions for patients who have experienced disability associated with stroke or other medical conditions (FDA, 2023b) (Table 4). Moreover, the FDA noted the increasing number of treatment domains used to treat and help patients including pediatric diagnostics and treatments, pain management, mental health, neurological disorders, surgery planning, intraoperative procedures, ophthalmic diagnostics, telemedicine, virtual care, post-operative and other rehabilitation therapies. Table 4 highlights experienced and potential benefits of XR applications. Different examples of XR innovations both reviewed and approved by the FDA for marketing of devices through 510(k) clearance, granted De Novo request, or Premarket approval across different fields of medicine and healthcare is found at FDA, 2023b, where it expects this trend to continue.

4.3. Digital tools to help inform device design for improved cleaning, processing and patient risk

Application of machine learning will help the real-time evaluation of complex device features for effective cleaning of complex reusable

Table 6
Ten good guiding machine learning practices (GMLP) for AI/ML based devices in context of design/training (as framed by FDA, HC, MHRA).

GMLP no.	Description	Relevance to AI/ML based device design and training
1	Leverage multidisciplinary expertise throughout the product life cycle	■ Important to have sterility assurance along with in depth knowledge and understanding of AI/ML for device development for design, clinical workflow, benefits, potential risk for patients ■ DT/XR training will also help stakeholders understand knowledge gap including regulatory requirements that can inform safe and effective clinical meaningful needs over full life cycle. ■ This ensures compliance with QMS, consensus standards, applicable regulatory requirements
2	Implement good software and engineering practices for AI/ML-based medical devices	■ Data security, integrity, and privacy over product life cycle of AI/ML enabled devices and for AI/ML software including good software engineering practices, data quality assurance, data management, robust cybersecurity practices that should address methodological risk management and design processes including ensuring data authenticity and integrity.
3	Represent the intended patient population through clinical study participants and data sets	■ In clinical study, training, and test data sets, manufacturers mush appropriately represent relevant characteristics of intended patient population, use, and measurement inputs in a sample of adequate size including managing bias, assess usability, and identify circumstances where model may underperform (list of potential biases are highlighted in Gampa, 2023)
4	Maintain training data sets as independent from test data sets	■ Selecting and maintaining training and test data such that they are independent of one another (role of digital training, educational technologies (Kremer et al., 2023c). ■ Consider all potential sources of dependence, data acquisition, site factors – test data for ML model accuracy. ■ Manufacturers should validate that test and training data meet specified criteria encompassing descriptive statistics and addressing label leakage (use of DT/XR to visualize full process to help understanding independence of data sets and for maintaining related training).
5	Use the best available methods for selected reference data sets	■ Use of DT/XT training to represent well-characterized and clinically relevant data for medical device and use that can help inform and develop specific use of AI/ML software including evaluation and testing that will promote model robustness and for intended use.
6	Tailor the model design to the available data and ensure that it reflects the device's intended use	■ Potential use of digital tools to visualize and inform mitigation of known risks, such as overfitting, performance degradation, and security risks that helps model design to suit available data. ■ The real time holistic perspective offered by digital tools can be tailored to reflect greater or thorough understanding of clinical benefits and risks related to the device where model can derive clinically meaningful performance goals and testing. ■ Potential use of integrated multi-mode XR connectivity of end-users can help inform global and local performance of the device, uncertainty or variability in device's impacts and outputs, intended patient populations, and clinical use conditions.
7	Focus on the performance of the human–AI team	■ Potential greater involvement of model in "human in the loop" that embraces human factors and human interpretability of models' outputs. ■ XR innovation also helps mitigate against just the performance of ML model in isolation. ■ Other digital visualization technologies can help manufacturers identify risk related to usability of the device and evaluate safety-relevant use scenarios.
8	Use testing to demonstrate the device's performance during clinically relevant conditions	■ DT and XR innovations can help potentially help inform accuracy of AI model selection that includes evaluation metrics, optimizing parameters and testing where such performance activities play central rol in obtaining adequate and compliant data required to gain regulatory approvals.
9	Provide users with clear, essential information	■ DT and XR can help establish and provide clear and contextually relevant information will help users (healthcare providers and patients ○ Products intended use and indications of use ○ Performance of model for appropriate subgroups ○ Characteristics of data used to train and test the model ○ Acceptable inputs ○ Known limitations ○ User interface interpretation ○ Clinical workflow integration of the model ■ In addition to enabling device modifications and for updating from real-world performance monitoring that adds to deep learning models that also provides feedback loop for developer to improve and address concerns.
10	Monitor deployed models for performance and manage re-training risks	■ Deploying of monitored AI/ML models can help with accuracy of safety and performance based on real world use that can also inform models used by human-AI team for periodic and continually training purposes such as post-market surveillance plan, incident response plan, configuration controls, over-fitting, unintended use, or data set drift (degradation). ■ Combined use of DT/XR innovation can help visualize and test design changes for managers based on regulatory requirements before implementing them.

Adoption based on responding to details of Gampa (2023) reflecting GMLP content based on FDA, HC and MHRA expert inputs.

devices from end-to-end process that represents a more conservative approach compared with the alternative compendial method for testing the entirety of the device (Kremer et al., 2023a). Rowan et al. (2023a) reported that the Spaulding's classification approach is sub-optimal for informing appropriate patient risks using some complex devicees as it fails to appreciate the role of device features in effective cleaning that can affect overall sterility assurance and patient safety (Table 2). Kremer et al. (2023a) evaluated a total of 56,000 flushes of the device features (n23) highlighting both the rigor and the enormity of big data generated from studies encompassing several analysed factors where machine learning would help with simultaneous data modelling, simulations and evaluations for informing validation. The complexity of device features is a central issue to consider for designers and manufacturers in their instructions for use (MIFU). Thus, this features categorization approach will help address the existing patient gap at this important interface between device manufacturers and healthcare facilities for effective cleaning, and reliable processing of reusable medical device devices. Digital technologies can be used to evaluate critical data for addressing key cleaning steps in processes including device conditioning, soil formulation, soil volume, soiling location, soil application, device articulation, and soil conditioning/drying. Manufacturers cleaning IFUs also provide a range of processing parameters for validation including detergent preparation, flushing, soaking, volume, temperature for validation. Future application of robots and automation will help with

addressing precision and mundane tasks associated with device cleaning.

Use of Internet of medical things (IoMT) will also potentially transform supply chain logistics where reusable devices are queued and staked in healthcare prior to cleaning, and processing that will help mitigate against device drying. Kremer et al. (2023d) proposed the grouping of device features in families representing different designated bands reflecting accessibility to soiling on a device surface and effectiveness of cleaning regime to mitigate risks. Again, this would be informed by an automated learning processing for precision (such as ML). Michels et al. (2013) also categorized cleaning processes based on groups of complex features based on analysing residual protein levels, namely instruments with joints, instruments without joints (lumens and cavities), sliding-shaft instruments, tubular instruments, microsurgical instruments, and complex instruments. Use of digital tools to facilitate data generation and sharing on this important topic will help inform ANSI/AAMI/ISO 17664-1:2022, AAMI RIT12:2020 and other future ISO standards on device cleaning that focuses on resuable device features and risk mitigation. There is increased interest in determining the efficacy of manual and automated cleaning of complex device features including addressing recalcitrant biofilm removal (de Melo Costa et al., 2022b). de Melo Costa et al. (2022b) advocated that for sterilizing service units, with no access to automated cleaning equipment, it is important to brush the inner hinge during manual cleaning.

5. Digital practices in medical device sterilization

5.1. Applications in sterility assurance

Sterilization is defined as conducting a validated safe monitored process to render a product free of viable microorganisms, which is a critical function underpinning device safety and for considering new innovations such as material science, biocompatibility, functionality and potential parametric release (McEvoy et al., 2023a; Rowan et al., 2023a). Achieving desired sterility assurance level (SAL) is the probability of a single viable microorganism occurring on an item post sterilization (Rowan et al., 2023a; Garvey, 2024). Moreover, SAL is seen as the probability of one viable microorganism surviving on the challenge device surface in a microbial population of million treated bacteria (6 D reduction). Determination of appropriate sterilant dose reflects decontamination efficacy or bioburden (organic material and artificially-inoculated recalcitrant biological indicators or BIs) in test devices where correction factors are applied. However, SAL is conventionally determined post microbial growth responses using lengthy incubation of treated biological indicator (BI, such as *B. atrophaeus*, or *G. stearothermophilus*) from sampled challenge devices in tandem with monitoring dosimetry readings (Rowan et al., 2023a). Chemical and physical indicators are also used to confirm the appropriate sterilant is applied within tolerances over treatment time for validation of processes. Developing new device innovation is challenging given the complexities of meeting scalability for volume of device throughput (industrial providers or healthcare end-users) using appropriate sterilization modalities that could be informed by using pilot facilities with stakeholders, such as for new design innovations according to appropriate ISO standards. Recent important studies have shown that vaporized hydrogen peroxide (VHP, also represented by VH_2O_2) sterilization modality exhibits log -linear inactivation kinetic data supporting the standing statistical probability that the applied gaseous sterilant kills treated biological indicators in a uniform manner (McEvoy et al., 2023b). McEvoy et al. (2023c) have also recently reported that the dose produced by X-ray, electron beam and gamma-irradiation can be interchangeably considered for to treating medical devices for appropriate microbial reduction. This supports the important concept of sustainable sterilization where selection of the type of modality can be made to meet the design features, material composition and functionality, which must also satisfy regulatory approval (Karimi Estahbanati, 2023).

5.2. Future potent in parametric release of sterilized products

McEvoy et al. (2023a) noted that this approach can be potentially adopted to accelerate product (or parametric) release that relies on use of process data, and to potentially reduce sterilant dose based on linked bioburden studies. Parametric release (according to ISO 11139: 2018) reflects appropriate records demonstrating a product is sterile based on sterilization processes delivered within specified tolerances. Adoption of parametric release by the sterilization industry has been thus far slow where integrated use of digital innovation could contribute to expediting this process, such as through modelling, simulations, and machine learning for real-time analysis of data. For example, potential real-time use of digital innovation with parametric release based on analysis of monitored and calculated data offers advantages including (1) eliminates the time, risks, and costs associated with BI, sterility testing and dosimetry analysis, (2) reduces the amount of unreleased inventory, and (3) allows for continuous demonstration of process control (McEvoy et al., 2023a). It is still a current requirement in ISO 11135:2014 to directly monitor EO concentration. McEvoy et al. (2023a) recently highlighted how data provided during sterilization of devices (described through examples for ethylene oxide (EO), VH_2O_2 (or VHP) and radiation may be better used to inform parametric release implementation. The authors noted that “EO and VHP demonstrated the ability to the sterilization equipment to deliver validated parameters repeatedly after load presented was validated”. This study also highlighted benefits of this approach that considers variability that has not been addressed in performance qualification (PQ). A key tenet underpinning device validation and potential use of the ‘calculated’ parametric release approach is the generation of sufficient appropriate data that demonstrates repeatability of the validated process; moreover, the more quality data generated the better digital tools such as machine learning algorithms and models can precisely inform this complex process. McEvoy et al. (2023a) also noted that radiation processes are also on a trajectory for implementing parametric release, however use of current photon delivery is not appropriate for measuring all critical parameters for this purpose. McEvoy et al. (2021) also separately reported on the potential use of real time enumeration technologies such as using flow cytometry for assessing efficacy of VHP on treated BIs where such initiatives have the future potential to inform automation.

This integrated approach will also serve to reduce ethylene oxide dose for a more sustainable process where EO produces toxicological end-points that requires abatement before product release (Garvey, 2024). For example, EO is broadly applicable for the sterilization of medical devices having a variety of complex materials, whereas use of VH_2O_2 is sensitive to cellulose (McEvoy and Rowan, 2019). The use of new cleaning classification system (Kremer et al., 2023d) with sustainable sterilization modalities will inform future applications in reusable medical devices in healthcare. It will also inform automation and in situ decontamination of 3D printed devices, such as for surgery or for organ printing to offset current need for use of animals in biocompatibility testing of implantable devices (Table 3). However, heathcare budget needs to reflect upon the need to pivot for enhanced reuse and in situ decontamination and innovation. International standards, such as TIR17 addressing materials will require frequent updating, such as for the alternative use of more sustainable biomaterials combined with using appropriate sterilization modalities in order to unlock our next-generation of green medical devices and circularity. A critical understanding of material science is important for applying appropriate sterilization modality underpinning a validated process for medical device products (Murray et al., 2013; Murray et al., 2014; Murray et al., 2018). The application of advanced imaging and spectroscopy may also inform non-destructive sampling (NDS) of materials in the use of medical devices including opportunities for machine learning to rapidly evaluate and inform efficiencies and applications (Manley, 2014; Yan

et al., 2022).

5.3. Digital modelling of data for simulations and to inform innovations

Development and application of appropriate digital tools that permits the simultaneous modelling, simulation and monitoring of holistic data can inform the appropriateness of new medical device design and functionality, including addressing key areas to enable sustainability (Table 3). The role of design thinking and specialist training will help unlock challenges in medical device design, processing, supply chain and for patient safety (Rowan et al., 2023a; Kremer et al., 2023d). Addressing such opportunities, including the potential for automation, can be met by precisely and safely replicating physical data for the intended new medical device design in a virtual environment (digital twin), such as for 3D printable devices, which also dually includes provision for undertaking immersive virtual training (or re-training) to achieve desirable learner competency (Murray et al., 2019; Kremer et al., 2023d).

Recent advances in our understanding of molecular and cellular mechanistic responses of *Bacillus atrophaeus* spores to H_2O_2 revealed that the formation of reactive oxygen species from this sterilant is the rate limiting factor in oxidative spore death. Bertz et al. (2024) used non-destructive optical sensing with trapping Raman spectroscopy in real-time to show that H_2O_2 mediated spore death to occur in two phases: (a) initial fast release of dipicolinic acid (DPA), a major spore bioindicator indicating irreversible rupture of spore's core, and (b) the oxidation of remaining spore material leading to fragmentation of the spore's coat. These finding was corroborated using optical microscopy. Hydrogen peroxide is effective in gas and liquid phases, with low temperature vaporized hydrogen peroxide (VH_2O_2) recently been approved for terminal sterilization of medical devices as Cat A process that offers more sustainable environmental benefits compared to the long-standing use of ethylene oxide gas. The future use of machine learning models to potentially monitor simultaneous damage caused by VH_2O_2 for treated bioindicators spores will also inform trajectory towards parametric release of treated devices. Such studies would require validation using appropriate challenge devices, bioburden testing and so forth; however, future deployment of Raman spectroscopy does provide exciting opportunities given that use of existing laboratory-based microbial culture responses for bioburden testing/validation require lengthy incubation periods to determine VH_2O_2-mediated spore death. Additionally, sensor-based approaches that monitor spore viability/damage by H_2O_2 in the gas or liquid phase (such as piezoelectric and impedimetric sensors, potentometric chemosensors) "all suffer from the fact that they have response times of a least several to tens of minutes (which precludes real-time validation of spore degradation) or are incompatible with in situ experiments, such as gaseous conditions (Bertz et al., 2024)". The non-destructive trapped Raman spectroscopy approach hurdles this technical limitation. Additionally, H_2O_2 is a strong oxidising agent that decomposes into reactive species such as hydroxyl/hydroperoxyl radicals that non-selectively oxidizes spore material. However, microbial catalase and superoxide dismutase that counteract these oxygenated free radicals may be damaged where use of standard nutritious agar and aerobic incubation may promote microbial autolytic suicide at sub-lethal treatment doses — thus, the real-time use of Raman spectroscopy with ML modelling combined with conventional biorburden/SAL culture-based testing will potentially reliably confirm irreversible spore lethality over the entire end-to-end sterilization process in addition to informing parametric release for families of different devices geometries/design shown to be reliably killed over particular treatments sterilant doses for appropriate SALs. Thus highlighting the role of advancing imaging, spectroscopy and machine learning in advancing conventional sterilization microbiology for treated medical devices including testing for new design thinking and introducing new biomaterials (such as packaging). Desirable to progress towards sustainable sterilization practices including selection of materials and dosage particularly to address new innovation in material science and polymers – beyond steam and dry heat sterilization modalities there is suite low temperature physical and gaseous options for designers and end-users to embrace (Fig. 1).

There is a growing interest in the potential use of spectroscopy and digital imagery as non-destructive testing (NDT) approaches for reliable inspection of small-scale material defects (such as targeting dimensions below 100 μm), which is crucial for structural safety of critical components in high-value applications (Ines Silva et al., 2023). These NDT can also be considered in end-to-end design thinking for next generation devices that encompasses sterilization modality. Robust and reliable NDT can reduce safety concerns and preventative maintenance costs for equipment over whole lifecycle (Wang et al., 2020). Early defects are often possible to repair, contributing for the circular economy and sustainability by allowing extended life and reuse of components. Ines Silva et al. (2023) noted that "distinguishable high detection accuracy and resolution is provided by computed tomography paired with computer laminography, scanning thermal microscopy paired with Raman spectroscopy, and NDT techniques paired with machine learning and advanced post-processing signal algorithms". Yan et al. (2022) highlighted opportunities for use of machine learning (explainable AI and Gaussian mixture models) in microplastic identification using Attenuated Total Reflection Fourier Transform Infrared Spectroscopy (ATR-FTIR) enabling real-time monitoring using spectral data augmentation approaches. Other promising NDTs are near-infrared (NIR) spectroscopy (Manley, 2014), time-of-flight diffraction, thermoreflectance thermal imaging, advanced eddy currents probes, micro magnetic bridge probe used in magnetic flux leakage, driven-bacterial cells, Quantum dots and hydrogen-as-a-probe. Wang et al. (2020) reported that the role of intelligence and automated inspection systems with high accuracy and efficient data processing capabilities will help shape future innovations. Interestingly, Cebi et al. (2023) described combined use of FTIR, NIR and Raman spectroscopy for rapid non-destructive metabolomic fingerprinting in adjacent field of food screening.

6. Digital tools to inform sustainability in medical device — quo vadis?

Digital innovation will help advance established and transform future medical devices from end-to-end design thinking to supply chain logistics including addressing enhanced patient safety, effectiveness and sustainability subject to satisfying regulatory review and approval requirements. The application of AI and ML will add significant value to future LCA studies informing important quantitative assessments for sustainability across the medical device sector. Romeiko et al. (2024) reviewed forty published studies from across adjacent fields that reported on quantitative assessments using combinations of LCA and ML including addressing life cycle inventories, computing characterization factors, estimating life cycle impacts, and supporting life cycle interpretation. The authors noted the value of continuous collection of big data to improve reliable ML modelling, prediction accuracy, pattern discovery and computational efficiency and pattern discovery; such as, potential future ML use of data generated by Kremer et al. (2023d) on use of 56,000 flushes from different device features to determine effective new cleaning classification for reusable families of medical devices with nexus to informing and improving patient risk. Future sustainability research using combined ML and LCAs should clearly report on selection criteria for ML models to match device intended use and to also report on ML model uncertainty analysis (Romeiko et al., 2024). These authors also noted that the increasing "complexity of environmental challenges demands adoption of interdisciplinary collaborative research to achieve deep integration of ML into LCA to support sustainability development" as exemplified by use of quintuple helix hub approach for stakeholders. Friedericy et al. (2022) reported on the reduced environmental impact of sterilization packaging for surgical instruments in the operating room where comparative LCA of rigid

sterilization containers were far more environmentally friendly than disposable polypropylene packaging (blue wrap) in terms of carbon footprint and eco-costs.

The healthcare sector has become increasing reliant on using disposables where meeting supply chain frequently dominates budget spend with significant consequences for medicine's carbon footprint and our fragile environment (Greene et al., 2022). Modern medicine enterprises are distinctively wasteful where enhanced use for many disposable items have been born out of convenience and efficiency with minimal evidence to support the superiority of some disposable supplies over thoroughly sterilized reusable ones (Greene et al., 2022). This is particularly relevant for general non-critical use items. These authors noted that "discarded material that are disposable rather than reusable comprise 85% of medical waste. Moreover, enormous volumes of plastic packaging, single use-tools, and diagnostic devices produce greenhouse gases when incinerated or while decomposing in landfills and oceans". Pickler et al. (2019) reported that the healthcare sector is a major environmental polluter where it represents ca. 5.5 % of the total national carbon footprint of countries. It is estimated that blue wrapping for sterilization of surgical equipment results in staggering environmental pollution with 115 million kg of plastic waste on an annual basis in the U.S. (Kagoma et al., 2012).

The application of suite of digital technologies intimated in Tables 4 and 5 will potentially help improve the implementation of European Medical Device Regulation (MDR) where Deirdre Clune MEP raised concerns about lack of progress in approval of new devices. In addition, efforts to a establish a more robust and transparent European MDR framework needs to unlock more timely pathways for accessing new medical devices prioritizing safety, health and innovation that will also impede sustainability. "The current European MDR lacks predictability and efficiency, and fails to keep pace with the required innovation to develop medical device innovation resulting in increased cost affecting SMEs that alarming implications for patients due to lack of availability of medical devices" (Deirdre Clune, MEP, 2024). There are over 700 digital innovation hubs in Europe that presents future opportunity for consolidation, convergence and pivoting to address sustainable needs for supporting and enabling innovation across the medical device and healthcare sectors (Rowan et al., 2023b).

Combining use of DT and XR innovation from a holistic end-to-end design thinking and training perspective offers significant potential for saving on resources, energy and time including opportunities for introducing appropriate new sustainable biomaterials. Pilot device testing, development and validation would typically require appropriate use of sterilization modality, where access to a subject-matter sterility assurance expert, such as hub manager and/or terminal sterilization industry expert, would help designers and manufactures address an effective process (McLaren et al., 2021). This would also de-risk for decision making and investments; for example, device cleaning and sterilization are appropriately built into the new design thinking from creation (TRL1) to market deployment (TRL9) avoiding situations where the material composition of new devices are non-sterilisable, or non-functional or appropriate for intended use or where more sustainable or alterative modalities (such as aseptic approaches) may be applied for production and packaging of devices including supply chain logistics (Fig. 1). Researchers have also highlighted the potential of implementing educational and immersive technologies to inform bespoke training for end-to-end medical device production including addressing key bottleneck areas such as cleaning for improved patient safety and sustainability (Murray et al., 2019; Kremer et al., 2023d).

Ibn-Mohammed et al. (2023) reported despite the fact that functional materials and devices (FM&Ds) have critically important roles in different devices and products improving patient safety and quality of life, these also place a significant environmental burden on our fragile natural ecosystems prompting enhanced use of LCA from a more quantified value chain perspective. These authors highlighted that bottom-up LCA framework models for informing medical device sustainability are frequently limited in scope that are typically static or retrospective. As volume of FM&Ds that are manufactured increase this is likely to present situations that proxy values will be used to fill data gaps; thus limiting their appropriateness in terms of relevance, accuracy and quality of results. These shortcomings across all phases in the environmental sustainability LCA model can be addressed by using computationally guided parameterized models enabled by AI/ML. "Smart materials constitute non-living stimuli-responsive material systems endowed with sensing, actuation, logic, and control functions to respond adaptively to environment to which they are exposed, in a manner that is usually repetitive and beneficial" (Strock, 1996). The role of AI/ML in each phase of bottom up LCA can be applied for determining the environmental burden of devices covers inventory analysis, characterization, normalization, impact assessment and interpretation.

Efficient real-time deployment of digital technologies will also help company compliance with future EU Corporate Sustainability Reporting Directive from a business model perspective such as use of blockchain. In addition to addressing sustainable R&D activities for medical devices, collaborative use of an interdisciplinary integrated HUB approach will also facilitate an awareness of key ISO standards (and updates), and strategic policies/directives for stakeholders including manufacturers and end-users. Lean six sigma (LSS) strategy for boosting efficiencies in medical waste stream that can also help cut costs through measured performance and analysis of root causes that will inform sustainable improvements and establish appropriate controls (McDermott et al., 2022). McGrane et al. (2022) adopted LLS framework to address potential barriers and bottlenecks for regulatory environment for informing effective project management, continuous improvement, and engineering changes in medical device manufacturing industry. Skalli et al. (2023) described positive environmental, social and economic impacts of interlinking LSS, the circular bioeconomy with Industry 4.0 technologies on sustainable organizational performance within manufacturing firms.

McGain and McAlister (2023) noted that several published LCA studies (McGain et al., 2017; Donahue et al., 2020; Rizan and Bhutta, 2022) revealed that disposable items have a greater impact from raw material extraction and manufacturing compared to reusable medical devices. The authors also highlighted that in terms of carbon footprint and material sustainability, reusable medical devices offer 300 times more desirable outcomes for our environment. Brenner et al. (2023) highlighted the challenges of identifying and achieving broad stakeholder recognition of key performance indicators (KPIs) including end-user acceptance of digital health technologies as attested by only five of 2192 reviewed publications either mentioning or considering harmonized KPIs. The critical role of end-user (patients, clinicians) experience and acceptance of digital health technology will also inform applications and future sustainability practices (Byrne et al., 2023). Alt et al. (2022) also highlighted the potential safe use of VH_2O_2 for decontaminating single-use medical devices contaminated with SARS-CoV2 from a sustainable waste management perspective.

7. Summary

The potential for digital technologies to enable and to advance expectations and opportunities in real-time for medical devices and healthcare sectors is enormous, which will potentially transform safety, precision and efficiencies across the entire end-to-end process. Reusable medical devices will benefit from new design innovations for improved patient safety and sustainability that will be informed by digital transformation of processes and approaches with stakeholders, such as blending new Kremer cleaning classification with Spaulding's sterilization system for next generation devices. Moreover, the combined role of using digital twin and extended reality innovation will advance training, diagnostics and interventions in real-time that will be enabled through access to and use of integrated multi-actor HUB facilities for testing new technologies with subject matter experts, such as sterility assurance. A

PRISMA review of best-published journal papers revealed a marked disparity and underappreciation as to the extent of new digital health technologies when compared to current lists shared by the FDA that reviewed and approved these innovations for marketing at 510(k) clearance, granted De Novo requests, or Premarket approval. Bespoke examples of benefits underlying future use of digital tools includes potential use of machine learning for supporting and enabling real-time parametric release of complex sterilization monitored and calculated data with correct processes that would benefit manufacturers, sterilization providers and patients. This paper also highlights an awareness and knowledge gap for stakeholders (particularly academics) on the actual range and variety of different digital innovations used in real-world situations in terms of validated, marketed and applied digital technologies for patient use in medicine and healthcare. Similarly, there appears to be a lack of appreciation by academic/researcher communities as to the central importance of using appropriate and up-to-date ISO standards that presents potential scenarios where appropriate methods may not be correctly applied or that methods may be misinterpreted, particularly from a 'silo' academic R&D perspective. This further emphasises the importance of adopting a multi-actor approach encompassing beneficiaries and end-users such as industry, healthcare, policy-makers, academics and society for effectively addressing solutions across the medical device and healthcare sectors. Such a holistic integrated HUB proposition will also facilitate engagements by experts in informing future sustainability needs such as performing appropriate LCAs using different materials, sterilization modalities and so forth for effective waste mitigation and reuse/recycling. The knowledge shared by leading actors such as terminal sterilization industry is extremely valuable and will continue to drive new developments The future is very promising for digital health technologies as attested by the public health mission of the FDA recognizing that "these innovations are playing an increasingly significant central role in many facets of our health and daily lives – ensuring that these innovative devices are safe and effective, and that they can reach the full potential to help people".

CRediT authorship contribution statement

Neil J. Rowan: Writing – review & editing, Writing – original draft, Visualization, Resources, Methodology, Formal analysis, Conceptualization.

Declaration of competing interest

The author declares no conflict of interest.

Data availability

Data will be made available on request.

Acknowledgement

The author acknowledges Irelands' CÚRAM SFI Medical Devices Research Centre.

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