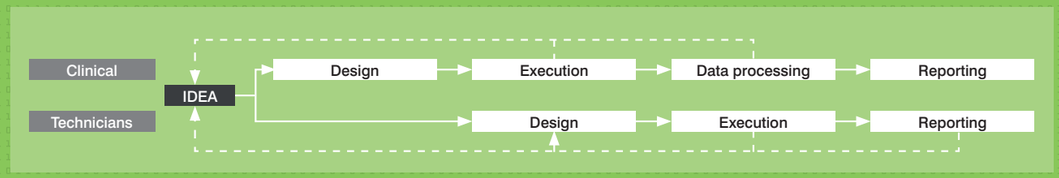


Figure 1. The different pathways of (clinical) research for clinicians and technicians. Alongside the early involvement of technicians in clinical research, we strongly advise technicians and clinicians to meet on a regular basis, both formally and informally. These regular interactions are expected to improve the ease of communication and the sharing of data and knowledge. While these interactions are important for the division of responsibilities and the management of expectations, they could also serve to include technical knowledge in the optimalization of the clinical research workflow or to test technical ideas for their clinical implementation. Last of all, informal meetings might result in new research ideas, as they might help to bridge the gap between technical feasibility and clinical desire.

Frequently mentioned possible barriers in the collaboration between technicians and clinicians are different communication styles (e.g., jargon), various visions and interests, different responsibilities and diverse types of knowledge. When looking at technical innovations, technicians tend to develop complex solutions whereas clinicians desire a more practical solution. Furthermore, there is a lack of awareness among clinicians of what is technically feasible. Due to this knowledge gap, technicians are often not involved in the beginning of a research project. Additionally, clinicians sometimes have a conservative mindset regarding (technical) innovations in clinical care. On the other hand, technicians sometimes come up with solutions that lack clinical insight.

Abovementioned barriers are noticeable in all research stages. The typical pathway of clinical research for a clinician consists of the following components: 1) idea, 2) design, 3) execution, 4) data processing and 5) reporting *(Figure 1)*. The technician's entry point into research typically comes later, as technicians often conduct their research on clinical data. This often results in conflicts during research due to a mismatch in expectations and responsibilities in data collection. For example, technicians are often unaware of the labour intensity and clinical implications of certain procedures. In the most optimal setting, technicians are involved in the first and second stage of a clinical study.

The difference between technical and clinical research is further illuminated by the possibility of adapting or extending research with new ideas. While technicians can easily design new research questions using the collected data, clinicians often need to set up completely new research due to clinical research regulations.

Our recommendations for the advancement of clinical research implementation can be summarized as follows *(Figure 2)*:

+ Communication in each stage of the research project is essential.
+ Technicians and clinicians should learn to speak the same language.
+ Regular (informal) meetings could contribute to overcoming the knowledge differences between clinicians and technicians.
+ Regular (informal) meetings could result in new research ideas.

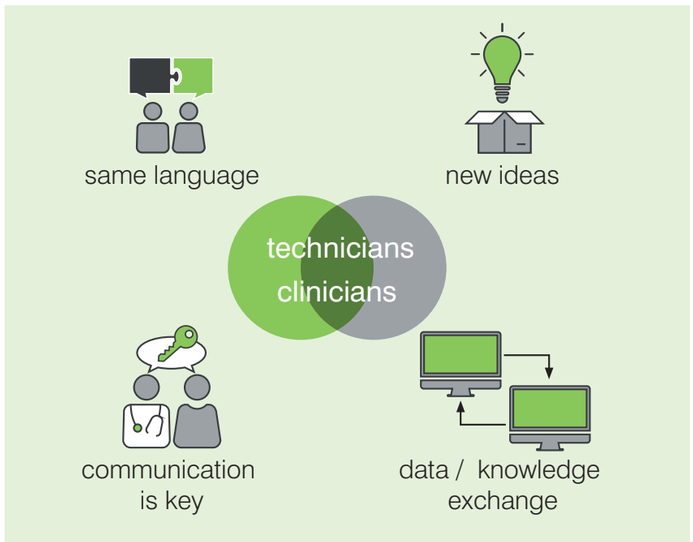
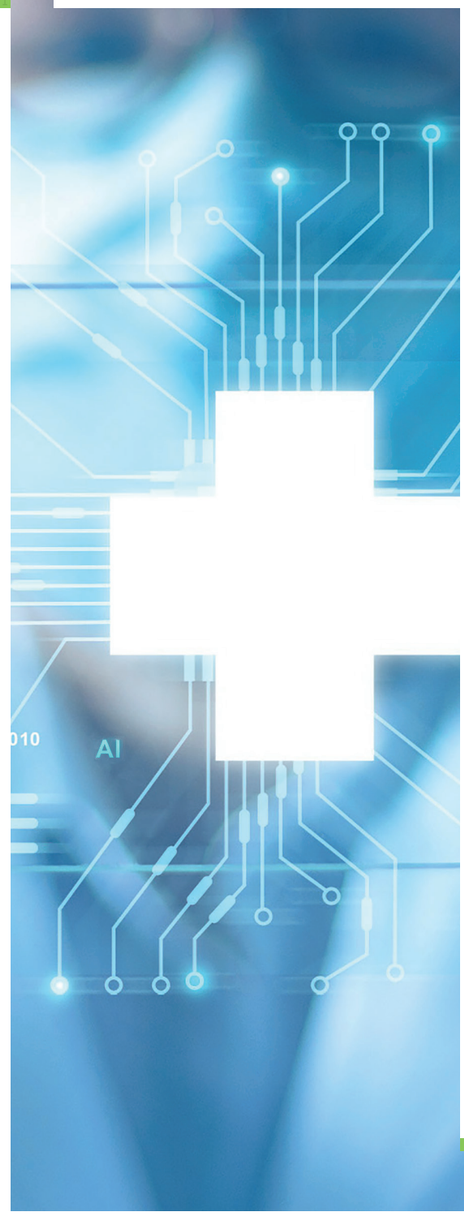


Figure 2. Key features in optimizing teamwork between technicians and clinicians

RAPID ROUTES TO REALITY: ETHICAL DILEMMAS IN FAST-TRACKING CLINICAL DEVICE IMPLEMENTATION

Susan Hommerson, medical/medical device research policy officer, Eindhoven University of Technology



What do you need in the regulatory domain to implement your product in the clinic? The primary requirement is the Medical Device Regulation (MDR). In this session, we will study some of the required technical documents and the logic behind them. Additionally, we will also delve into Artificial Intelligence (AI) ethics, which will soon be legislated by the EU.

The MDR is a regulation, directly applicable in all EU countries. It governs patient safety and compliance with it leads to a CE mark, which is valid throughout Europe. This MDR also applies to clinical studies. The former directive was no longer adequate, a fact that became evident through various scandals, such as the breast implant incident.

Changes in the MDR compared to the previous situation include: more clinical evidence is required, as is increased transparency; there's a greater emphasis on post-surveillance research and a shift in classifications, with many products moving to higher classes. This means there's a quicker need for a notified body. A notified body evaluates the evidence of whether a medical device is safe and meets the CE mark standards. They have the authority to award the CE mark. Every device now carries a Unique Device Identification (UDI) code. Additionally, the EU has set up Eudamed, the European database in which all medical devices are listed and where all ongoing studies are tracked.

The MDR requires a quality management system for manufacturers, the ISO 13485. From this quality management system, documents such as technical documentation necessary for the Investigational Medical Device Dossier (IMDD) for clinical studies are derived.

A Medical Device (MD) is a non-pharmaceutical tool (software, implant, device, reagent, etc.) with the objective of addressing diseases (e.g., diagnosis, monitoring, treatment, etc.). It can also play a role in an injury/impairment or pertain to the investigation, replacement, or modification of anatomy/physiology, or provide information through in-vitro studies or body specimens, such as the coronavirus test.

There is a transition period for MDs to shift from the previous situation to comply with the new MDR. Making adjustments to an existing MD under the old legislation is impactful, as it then needs to meet the new MDR standards. This can be rather cumbersome, leading companies to decide against updating certain MDs and even withdrawing products from the

market. It's not only the manufacturer that is subject to the MDR, but also the supply chain partners. The implications of this can be extensive, to the point where certain MDs might no longer be available for patient care.
Apart from the MDR, there are other laws, standards, and guidance documents that one may encounter, such as the ICH GCP (Good Clinical Practice), the Dutch law on medical scientific research.

EU AI Legislation is currently being developed and is aimed at ecuring fundamental rights and safety. Additionally, it is part of a digital framework including laws on the AI liability framework, safety regulations, the Cybersecurity Act, etc.

For AI, a risk classification has been established with four levels. Within this framework, risk is firstly defined across multiple high-risk domains: social, infrastructure, economic, and so forth. Secondly, an AI system is considered to be high risk if it is a safety component of products such as medical devices. .

This doesn't necessarily mean that certain activities or applications are prohibited, but that there are heightened requirements in terms of transparency. Ten standards are going to be established for AI systems:

HIGH-RISK SYSTEM STANDARDS

1. Risk management systems
2. Governance and quality of datasets used to build AI systems
3. Record keeping through logging capabilities by AI systems
4. Transparency and information provisions to the users
5. Human oversight of AI systems
6. Accuracy specifications for AI systems
7. Robustness specifications for AI systems
8. Cybersecurity specifications for AI systems
9. **Quality management system for providers of AI systems, including postmarket monitoring process**
10. **Conformity assessment for AI systems**

There is also an ethical standard comprising seven ethical principles, often used in research. It adopts a lifecycle approach, meaning that these items must be continually reviewed and addressed.

ETHICAL STANDARDS IN AI
THE ALTAI PRINCIPLES DISCUSSION

1. **Human agency and oversight**
2. Technical robustness and safety
3. Privacy and data governance
4. Transparency
5. **Diversity, non-discrimination and fairness**
6. **Environmental and societal well-being**
7. Accountability

Probably also: human rights assessment, democratic values and rule of law

For example: No. 1 addresses the role of the human being, e.g., the one who bears responsibility. No. 5 pertains to data collection, emphasizing the importance of avoiding bias, but also regarding discrimination and tackling the complexity of acting on AI's predictions.

While these principles are set, implementing them requires collaboration from all disciplines to make the right decisions, not just ethicists, for example.

5

IMPLEMENTATION SCIENCE: A BEACON OF HOPE FOR LOW/MIDDLE INCOME COUNTRIES' HEALTHCARE?

Anne van Tetering MD, Ella de Vries MD and Kirsten Thijssen MD, PhD students of Máxima Medical Center and Eindhoven University of Technology

Low/middle income countries with concurrent low health status of the population stand to benefit more from implementation science in healthcare than high-income countries, given the triad of high need, high potential, and low existing capacity. Nonetheless, studies about implementation science have shown that a technology (or a training course, a protocol, etc.) which works in one setting under certain conditions may not be appropriate in other circumstances. One important aspect to consider is a difference in cultures between the place where a technology was developed and where the technology is intended to be implemented. To understand differences in cultures between countries, the theory of 'the Culture Map' by Meyer can be used. In this theory, national cultures have been mapped on eight scales (Fig 1.). We will highlight three of these scales and give examples of how these differences can lead to challenges, drawing from past experiences in the Netherlands, China and Uganda.

Communicating

Meyer differentiates low-context communication from high-context communication. In countries with low-context communication, messages are expressed and understood at face value. Good communication means it is precise, simple and clear, and repetition is appreciated. In contrast, in countries with high-context communication, messages are spoken and read between the lines. They are implied but not plainly expressed and good communication is sophisticated, nuanced, and layered. As a result, people from the Netherlands, a country where low-context communication is appreciated, will often misunderstand people from Uganda or China, countries with high-context communication. For example, when attempting to get ethical clearance for research in Uganda, it was very unclear to the Dutch people on our team what steps had to be taken, even after asking repeatedly. Therefore, walking into a room and having to present our whole study to the board of the medical ethical committee without previous notice came as a great surprise to the Dutch. It is highly likely the Ugandan counterparts had implied this, but the message was missed by the Dutch. Another example is the tendency of people in low-context communication societies to send emails after a meeting, summarizing the discussion, recording agreements and highlighting tasks that have been assigned. In high-context communication styles, this can be seen as offensive and distrusting. It is also interesting to note that counter-intuitively, the highest chance of miscommunication lies between one high-context person and another high-context person from another culture, as the messages that are conveyed between the lines are completely different.

Evaluating

In Meyer's theory, countries can range from a direct negative feedback style to an indirect one. The direct style means that feedback is provided frankly, bluntly and honestly. Negative messages are not softened by positive ones, absolute descriptors are used e.g., totally inappropriate, completely unprofessional) and criticism may be given to an individual in front of a group. On the other end of the scale,