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The case for an academic discipline of medical device science

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- Medical devices are a very important but largely unrecognized and fragmented component of healthcare.
- The limited regulation of the past and the lack of systematic rigorous evaluation of devices leading to numerous high-profile failures will now be replaced by stricter legal requirements and more transparent evaluation processes.
- This constitutes an unprecedented opportunity, but it also uncovers urgent needs in landscaping, methodology development, and independent comprehensive assessment of device risks and benefits for individual patients and society, especially in the context of increasingly complex devices.
- We argue that an academic discipline of 'medical device science' is well placed to lead and coordinate the efforts necessary to achieve much needed improvement in the medical device sector.
- Orthopaedics and traumatology could contribute and benefit considerably as one of the medical specialties with the highest use of medical devices.

Keywords: implants; medical devices; medical device science

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Medical devices are an important component of healthcare. Implantable devices include cochlear implants, visual prostheses, intraocular lenses, pacemakers, stents, deep brain stimulators, artificial hearts, joint replacements, materials used in trauma surgery, vaginal meshes, breast implants, contraceptives, dental implants and many more. The lifetime risk to patients of receiving implants is high: for example, it ranges from 6% in men in Norway to 23% in women in Finland for knee replacement alone.¹ The development and implementation of medical devices has been questioned for reasons related to widespread clinical use of new devices without evidence

of their safety and performance (e.g. metal-on-metal hip prostheses),² limited adoption and effectiveness of some new technologies,³ and the role of devices in increasing health expenditures.⁴ To reduce patients' and societies' exposure to non-beneficial, costly, and even dangerous medical devices and to enhance the potential of beneficial devices to reach the market, change is needed.

Here, we argue that there is a pressing need for a distinct academic discipline focussed on 'medical device science'. First, we discuss why it is needed. Second, we highlight that now is an appropriate time from the perspective of policy-makers, payers and the public and regarding data availability and direction of device development. Third, we consider potential directions and focus for medical device science. We limit the discussion to medium- and high-risk implantable devices.

The need for medical device science

Currently, medical device expertise at the scientific and public health level is highly fragmented between different surgical and medical disciplines, biomedical engineers, manufacturers, health technology assessment (HTA) specialists, regulators, notified bodies, device data custodians, toxicologists, materiovigilance, and pharmaco-epidemiology specialists, and potentially others. Fragmentation has made it difficult to bridge the gap between pre- and post-market assessment and to identify the extent and importance of treatment with implantable devices in the healthcare sector and the problems associated with it. Fragmentation may thus also be one of the reasons for limited public awareness of the impact of medical devices on patients' lives and the cost of healthcare.

Moreover, a well-recognized problem in Europe is the lack of transparent pre-market testing data, the lack of a systematic obligation for clinical evidence in the post-market period for new medical devices and a weak evidence level.^{2,5} This is in stark contrast to the situation of

treatment with drugs. The evaluation of medicines made significant progress following the thalidomide disaster in 1961. This event triggered major regulatory actions (e.g. the US Kefauver Harris Amendment or ‘Drug efficacy amendment’⁶ signed into law by President John F Kennedy in 1962 ‘to ensure that consumers will not be victims of unsafe and ineffective medications’), and eventually led to the creation of academic centres, the development of the science of drug safety research (pharmaco-epidemiology) and a rigorous drug development and evaluation process including pre- and post-market evaluation. Although high-profile failures of devices⁷ have set the stage for similar changes in the device landscape, few academic centres focussed on medical devices have emerged. Nevertheless, device failures have not gone unnoticed and have resulted in the creation of national registries⁸ – first mainly in orthopaedics and vascular surgery – starting in the seventies in the Scandinavian countries and expanding more rapidly during the late nineties and early 2000s to other countries in Europe and to Australia.^{9,10}

Under-recognized differences in methodology for evaluation of devices compared to drugs may have further hindered progress.² All treatments have benefits and risks associated with the substance/material itself and its interaction with the patient. However, there are differences between medicines and devices. Unlike medicines, which patients can easily swallow, apply externally or receive via minimally invasive intravenous injections, treatment with implantable medical devices such as hip prostheses or coronary stents requires surgery or some other procedure (e.g. catheterization) which carries greater risk. The intervention is dependent on the surgeon’s ability and experience with the device, an important co-determinant of the patient’s outcome, which does not apply to drug treatment. In case of a severe complication, surgery may be needed to remove the device with the second operation carrying generally more risk. Moreover, a medical device often remains in, and may interact with, the patient for the rest of her/his life. As a consequence, exposure to the implant and potential debris is long term, and cumulative effects need to be taken into account (e.g. delayed hypersensitivity type IV reaction to metal debris with pseudo-tumor development many years after hip replacement), thus requiring lifetime monitoring of the patient–implant relationship. The implant’s interaction with the human body depends on the materials used and other aspects of its physical construction as well as on the anatomical site and its specific loading and biochemical environment. Finally, medicines operate by pharmacological, immunological or metabolic means, while medical devices achieve their principal intended action(s) by physical, mechanical or chemical means. Therefore, the methods necessary to test their safety and effectiveness differ. This is true across all medical specialties using surgical or interventional techniques to implant devices.

Now is the time for medical device science

There are several reasons why now is an appropriate time for an academic discipline of medical device science. First, there is increasing recognition by policy-makers and regulators of the importance of devices in terms of good and bad health outcomes and economic influence. European regulations have become stricter, and US regulatory approaches have been reformed.¹¹ The new EU medical device regulation, adopted in 2017, will be fully in force in May 2021. This will require substantial reorganization and documentation efforts from manufacturers, care providers, researchers and regulators.⁵ Requirements for clinical evidence throughout the device life cycle will increase, and with this there may be opportunities to develop and improve methodologies to generate that clinical evidence. Though the US FDA has a large staff dedicated to medical devices, including in regulatory science research, and collaborates in public–private partnerships (MDEpiNet¹²) to advance the use of real-world evidence and related research methodologies, the European Commission is much more limited in resources for medical devices and there is no centralized agency for medical device evaluation, equivalent to the European Medicines Agency (EMA) for drugs. Dedicated, independent researchers working in this area would therefore be valuable.

Second, public awareness of the importance and harms of medical devices has much increased following the publication of the ‘Implant files’ investigations in 2018 on faulty medical devices and their effects on patients’ health.¹³ Their release has been followed by rapid political reactions. In France, for instance, the National Assembly mandated a report presented in 2019 ‘to make a clear diagnosis of the most salient weaknesses in the framework surrounding medical devices and to outline, just as clearly, serious avenues for improvement’.¹⁴ The German parliament decided in 2019 to create a national implant registry in 2020 with mandatory participation of patients, hospitals, manufacturers and insurance companies.¹⁵

Third, the amount of available data on medical devices is increasing rapidly. There is already long-standing experience with monitoring of devices from large established population-based registries – however, these are mostly for cardiac/vascular implants and joint replacements.¹⁶ International networks of registries have emerged encouraging data harmonization (e.g. outcomes and risk adjustment factors), and multi-registry studies, among others.^{10,17} Major steps in harmonization have also been achieved through the introduction of a unique device identifier (UDI) and the work of the International Medical Device Regulators Forum (IMDRF), which aims at medical device regulatory harmonization.¹⁸ The reform of the European Medical Device Database (EUDAMED) should increase transparency of the pre-clinical and clinical evaluation process in Europe. In addition, progress in

information technology and data handling capabilities has facilitated access to, and linkage of, established and new large population-based registries to other datasets such as electronic healthcare records or clinical databases. This may lead to opportunities for better monitoring of device performance and use across the life cycle.

Finally, devices are becoming more complex: combinations of biomaterials, drugs, cells or molecules and devices are increasingly frequent. For example, tissue engineering combines scaffolds, cells, and biologically active molecules into functional tissues, and neuroprosthetics (e.g. cochlear implants) combine knowledge from neuroscience and biomedical engineering. We may be in a period of significant change for medical devices.

Directions for a medical device science

The need for responsible innovation in the medical device sector requires improvements to testing in the pre-clinical phase but must also include efficient high-quality clinical evaluation of safety and effectiveness. Moreover, consolidation of the fragmented knowledge on medical devices is required, along with better understanding of the current situation and of knowledge gaps. Moving towards a cross-disciplinary full-cycle framework specific to medical devices while integrating previous work^{19–21} would be valuable.

Little is publicly known about the number of devices on the market, the evidence available for them, or reasons for failure and recall, particularly outside of the US. In Europe, for example, there is currently little transparency in the clinical evidence available for devices.^{5,22} Landscaping work and collaboration with regulators, public health organizations (e.g. HTA), and manufacturers may therefore be important. The implant files,¹³ which provided information on the failure and risks of devices, was unable to locate information on the total number of devices used, for example. Without this information, it is impossible to conduct a meaningful assessment of the safety of marketed devices because we do not know how frequent safety issues are and how these compare to other medicinal products.

Much of device evaluation, at the level of individual devices, nationally, and globally, has been focussed on safety (or lack thereof). However, considerably less is known about the benefits that devices provide. Without this information, it is very difficult to make conclusions about the value of marketed devices, which is related to the benefit–risk ratio, not just the risk. Work to improve the assessment of effectiveness of devices (Does it work?) will therefore be valuable. And more data about benefits of devices will allow better assessment of cost-effectiveness (Is it worth it?).

Improvements in risk prediction, benefit–risk evaluation, and risk management are needed. Computer-based modelling and simulation may allow for more precise

risk prediction while potentially reducing the number of patients exposed to a new device.²³ Better benefit–risk evaluation may be achieved through e.g. comprehensive and collaborative pre-market assessment,²⁴ full-cycle failure analyses, and systematic integration of imaging in early clinical implant surveillance. Studying the causes of why and how implants succeed or fail – in a cross-disciplinary way – would provide greater insight into human–device interaction. Advanced clinical research design and analyses methods from device and pharmaco-epidemiology, statistics and HTA need to be systematically applied to speed up and improve clinical evaluation and the quality of the evidence (e.g. registry-nested clinical trials). Better risk management strategies should include efforts in knowledge implementation among all stakeholders.

There is little capacity amongst regulatory bodies to do such work, particularly given the regulatory structure in Europe, and incentives for industry may not be aligned with maximizing patient benefit. In addition, where methods are available, there is great need for informing stakeholders (e.g. industry, clinicians, public) on how to apply them and/or how to interpret the results. Academia is well placed to lead and coordinate these efforts. The future academic divisions of medical device science will require researchers from biomedical engineering, surgery, epidemiology, health data science, toxicology, health economics, IT, implementation science and other areas working interactively and across medical disciplines.

Conclusions

In order to respond to the challenges surrounding medical devices and to responsibly enhance their potential to improve public health, we believe that the establishment of an academic discipline ‘medical device science’ is needed. We have discussed why now is an appropriate time for this development, and highlighted areas where the discipline might initially focus. Medical device science should be informed, but not dictated by, experiences with medications, and should integrate contributions from all stakeholders.

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ICMJE CONFLICT OF INTEREST STATEMENT

AL declares no conflict of interest relevant to this work.

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