EIT Health INNOV+DOCTOR

Start-ups meet Doctors: Neurorehabilitation

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Executive Summary

EIT Health Spain is leading 'INNOV+DOCTOR – a strategic initiative which aims to promote clinical innovation across Europe. During 2020 we have worked hard to introduce new objectives, and to internationalise existing ones, building on the foundations laid down in Spain during 2019. One such objective - 'Start-ups meet Doctors' – saw us deliver two roundtable sessions with healthcare professionals and entrepreneurs, delving into two specific themes. On 27th October our participants focused on neuro-rehabilitation; and on 25th November we explored the field of Artificial Intelligence.

This report captures the key themes from the second session and sets out our conclusions and recommendations towards further innovation in Artificial Intelligence. We also share some examples of good practice towards early dissemination of our findings.

Our vision for this series of roundtables is that we can further promote the latest and emerging clinical innovations in different areas of healthcare; highlight the opportunities for joint working towards delivering truly innovative solutions for patients; and start a European-wide conversation on the benefits of encouraging and supporting thematically focused conversations between healthcare professionals and entrepreneurs towards high value care.

Our sincere thanks to those who participated, and contributed their valuable time and knowledge.

Cristina Bescos

Managing Director, EIT Health Spain

Introduction

Clinicians and doctors are well-placed to identify healthcare needs and innovative solutions; and start-up companies and entrepreneurs are fundamental in developing these solutions. There is a need to further encourage, facilitate and support these partnerships and wider ecosystems towards true innovation in the design and delivery of high value care.

In 2019, EIT Health Spain launched a new initiative called INNOV+DOCTOR to drive and promote clinical innovation in healthcare for the benefit of patients. INNOV+DOCTOR works by:

- Facilitating focused discussions between healthcare professionals and start-up companies to explore some of the key challenges and opportunities in clinical innovation
- Supporting healthcare professionals and entrepreneurs to access the market with their innovative ideas and solutions
- Growing the European community of Clinical Ambassadors to facilitate the sharing of success stories, good practices and innovation pathways, promoting healthcare professionals as innovators and entrepreneurs
- Collaborating with EU medical societies to operationalise their innovation, acceleration and educational activities.

A key activity of INNOV+DOCTOR is to introduce entrepreneurs from start-up companies to leading healthcare professionals, to facilitate discussions around the challenges and potential solutions for clinical innovation in different areas of healthcare. 'Start-ups meet Doctors' launched in October 2020 with the first session focusing on neurorehabilitation.

Objectives:

- Gaining an increased appreciation of how collaboration can benefit patients, start-ups and healthcare professionals
- Understanding the emerging challenge propositions for start-ups in the healthcare system
- Identifying good practice and success stories to help spread the importance of clinical innovation.

Five entrepreneurs and three clinicians were invited to join the discussion, which was hosted and moderated by EIT Health Spain via Zoom on 27th October 2020. It took place against the backdrop of the COVID-19 pandemic - a driver for disruptive innovation in itself - with great emphasis on the need for tele-rehab and digital health, combined approaches, integrated solutions, and reimbursement models.

The current situation: State of the art in artificial intelligence

"Neurorehabilitation is a spiral management process in which a treatment program is initiated and constantly revised and updated, based on therapy-mediated improvements".

– Swaiman[i]

In order to effectually discuss and debate how clinical innovation can benefit patients, start-ups and clinicians, it is necessary to first understand the current situation. A presentation on the 'State of the Art in neurorehabilitation' was delivered by Professor Letizia Leocani from Hospital San Raffaele, Milan. Prof. Leocani shared an overview of today's landscape including examples of current innovative practices, the latest technological developments, emerging initiatives of potential interest, and key challenges such as barriers to adoption and implementation. Both the presentation and the discussion that followed, strongly acknowledged the socioeconomic circumstances against which healthcare is being delivered and developed.

The case for tele-medicine

Healthcare professionals should have continuous access to patients for ongoing treatment, assessment and monitoring. The COVID-19 pandemic called for rapid advancements in health innovation, bringing a refocus on the importance of digital health and tele-medicine as part of home-based follow-up. This is especially true for neurorehabilitation patients.

In a prospective cohort study FITRiMS (Fitbit Remote monitoring in Multiple Sclerosis (MS)[ii] carried out by the San Francisco Multiple Sclerosis Center at the University of California, 95 individuals with MS were asked to wear accelerometers for one year. They found a correlation between a reduction in the number of steps taken and a worsening of both clinical and patient-reported outcomes, which supports the need for Innovative Medicines Initiatives (IMIs)[iii] such as the Remote Assessment of Disease and Relapse in Central Nervous System (RADAR-CNS)[iv]. This major international research project measures depression, epilepsy and multiple sclerosis using data from patients' wearable devices and smartphones to detect changes in behaviour, sleep or mood. The key goal of the project is to improve patients' quality of life by changing how their symptoms are treated: ultimately predicting and avoiding relapses. Other forms of digital engagement, such as exergaming, have been

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found to promote health in patients whilst encouraging rehabilitation compliance in their own homes.

Soon to be implemented, the Italian project Multiple Sclerosis Fitness Intervention Training with Pilates exercises (MS-FIT) will be delivered by a tool based on the Xbox Kinect, or similar. This two-year study aims to transform Pilates exercises into a virtual reality game as a way to integrate physical activity into daily life; and to promote sensorimotor integration and cognitive stimulation. The MS-FIT tool "does not pursue therapeutic aims as rehabilitation does, but it could have a positive impact on prevention and health in MS", which suggests good candidacy for combined or integrated approaches to neurorehabilitation.

The global telerehabilitation systems market size is poised to grow by USD 329.69 million during 2020-2024, progressing at a Compound Annual Growth Rate (CAGR)[v] of almost 23% throughout the forecast period, according to the latest report by Technavio.

"Emerging technologies are reshaping healthcare in multiple ways—how consumers access it, how and which providers deliver it, and what health outcomes it achieves"
– McKinsey, 2019[vi].

Current technologies and digital health interventions being used in tele-rehabilitation include:

While home-based technology may be viewed by some as less sophisticated than hospital tech, it can be as effective. Furthermore, home therapy can deliver additional benefits to patients from socioeconomic and wellbeing perspectives. For example, there are no waiting times; and studies have shown that by taking on more control and responsibility for their condition patients can improve their psychological health and wellbeing. In turn this may enable a speedier return to normal daily activities and a return to work resulting in additional economic benefits for the patient and for the economy. Patient safety is also

maximised by the avoidance of unnecessary visits to hospitals and clinics, especially during a pandemic.

Latest technological developments and emerging initiatives

Professor Leocani shared some neuro-rehab initiatives to stimulate debate around the table. These are examples only, and not intended as an exhaustive list.

There are some exemplary **digital mobility** initiatives such as **MERLIN**[vii] - an innovation project fun

ded by EIT Health. MERLIN uses a robotic assistant, software games and remote connection to a therapist to allow post-stroke patients with upper-limb impairment to undergo physical rehabilitation at home. The multi-disciplinary team behind this project is interested in how chronic patients respond to the treatment, not only towards their own health improvement, but to inform the kind of improvements and revisions needed to treat those in the more acute phases. Clinical experts participating in the discussion reported that robot-assisted rehabilitation is often preferred by patients to more traditional intensive rehabilitation with a therapist; and is often available at a similar cost.

Body-weight-supported treadmill training (BWSTT) can be used to assist gait rehabilitation, particularly important for patients who are not able to carry their full body weight. The use of a BWS system makes it possible to practice reciprocal stepping at faster speeds with greater safety and less fear of falling compared with overground or treadmill training without BWS. In addition, it reduces the risk for the development of compensatory strategies that could occur when using walking aids during overground walking.

Robots can also be easily disinfected which is obviously a key consideration in current times. More evidence is needed however to demonstrate a clear advantage over conventional physical rehabilitation. In the United States, ongoing research is adding to the field of solutions that address both mobility and cognition in MS patients. At **the Kessler Foundation**, for example, robotic exoskeletons are being studied for their ability to improve learning, memory and walking in people with MS.[viii]

Virtual reality is also playing an important role in neurorehabilitation. **NeurorehabVR**[ix] works with therapists to tailor exercises for individual patients. These customised virtual exercises record physiological and kinematic responses, enabling the therapist to measure the patient's progress over time.

> *"The high cost of physical therapy, coupled with the fact that insurance only covers a certain number of therapy sessions makes the idea of using virtual reality for therapy very intriguing. Through various immersive 3D environments, the patient can work on their cognitive as well as physical therapy at the same time".*

A study led by **IDIBAPS** at the Hospital Clinic Barcelona[x] highlights the important protective value that cognitive reserve can have on the brain's network, especially in patients with more severe clinical impairment. The fact that cognition is also influenced by the presence of structural brain damage and aging, highlights the benefits of promoting an intellectually rich lifestyle in people with MS.[xi]

The **Medical University of Graz**, Austria studied patients with MS and found a correlation between thalamic volume and predicted longer-term cognitive decline[xii]. This suggests that medical resonance imaging (MRI) may be able to define different risk groups for people with MS among functions associated with the thalamus (relaying motor and sensory information, memory, alertness, consciousness, and contribution to perception and cognition).

The **Guttman Institute**, attached to the Universidad Autónoma de Barcelona in Spain[xiii] has pioneered neurorehabilitation since 1999. More recent developments include **NeuroPersonalTrainer®**[xiv] - a platform which uses tele-medicine for cognitive improvement with the support of a neuropsychologist. The programmes are designed to assess and monitor memory, attention, language and executive functions in an "**intensive and personalised** manner".

Recent **studies in the USA** sought to evaluate whether Transcranial direct current stimulation (tDCS) can reduce fatigue in individuals with MS[xv]. Two similar studies combining tDCS administration and cognitive training were carried out, and results assessed using the Patient-Reported Outcomes Measurement Information System (PROMIS). The second study showed a statistically significant reduction in fatigue for the active group *vs*. the sham group in a randomised control group, suggesting that **tDCS is a potential treatment for MS-related fatigue**.

Konectom is a smartphone-based digital platform that enables individuals with MS to quantitatively self-assess neurological disability and has potential applications for clinical research and real-world use.[xvi] Digital outcome assessments are processed from the smartphone accelerometer, gyroscope, touch, force touch and GPS sensor information. This is an important development towards predicting the likelihood of a return to employment and will hopefully inform future health and employment strategies in Europe and beyond.

Mobilise-D is another Innovation Medicines Initiative (IMI) European project which views mobility as a "vital sign" in health, based on the thesis that reduced mobility can predict poor medical outcomes regardless of the patient's current state of health. The consortium is developing a tool to measure five different diseases (Chronic Obstructive Pulmonary Disease, Parkinson's Disease, Multiple Sclerosis, Hip Fracture recovery, and Heart Failure); to ascertain whether digital mobility correlates with poor clinical outcomes such as falls, hospitalisation, death, loss of independence and worsening disease status. The researchers hope that digital assessment of mobility can be accepted for use in clinical research and practice in the future.

Tele-rehab and digital health benefits, challenges and limitations

Tele-rehabilitation and digital health solutions are not suitable for all patients. Professional judgemen is required on a case-by-case basis to take into account issues such as sensory or cognitive impairmen usability, comfort and any anticipated stigma. Speaking more generally, there are many benefits to virtual neurorehabilitation, and some key barriers to overcome:

Benefits

- Saves travel time and cost which, in turn, can improve adherence to treatment.
- Patients can be observed at home, where they are usually more comfortable and less anxious.
- Promotes patient empowerment and a more active patient role.
- Daily monitoring can also be done, when needed.
- Patient safety can be protected through a reduction in visits to healthcare settings, especially during pandemics
- Improves utilisation of clinical resources.

Barriers

- Ongoing diagnosis and assessment in virtual settings can present challenges, for example wher clinical tests are required:
    - Clinical tests such as checking muscle strength, reflexes, sensorial response;
    - Tests performed with resource to specific equipment only available in a clincal setting;
    - Motor control assessment.

- Tele-rehab is highly dependent on information and communications technology to connect to remote solutions and therapists.
- There may be training requirements for professionals to better understand the system, and th technology's capabilities and limitations.

Limitations

Its important to remember that a number of factors can affect the choice of technology or intervention. These include security and confidentiality issues; cost and reimbursement considerations; and durability. This roundtable discussion included much deliberation about the benefits of combining and/or integrating different approaches and solutions towards true innovation neurorehabiliation, meaning that interoperability will become a much more important factor when deciding on the most appropriate treatment package**.** Assessment and evaluation of combined and integrated interventions will need to take into account any additive and multiplicative effects of individual treatments and technologies to inform decision making.

Theme 1: Physical *vs.* virtual neurorehabilitation

The 'State of the Art' overview made a very clear argument for more home treatment and monitoring in between the necessary face-to-face interactions. Home therapies are becoming more and more accepted, not least in the face of global pandemics and patient safety.

Virtual solutions need to be appropriate for individual patients' needs, that is: be useable, have the ability to connect to a therapist, be portable where needed and – obviously – have a strong evidence base. If the exercises are fun, interactive and rewarding, there is likely to be more compliance than in doing routine and repetitive tasks. Virtual, digital, and tele-health solutions are not without their challenges. Both therapists and patients need to be capable and comfortable in using the different technologies, whether through an interactive session involving both of them, or using the technology independently of one another. Patients' preferences should be taken into account (for example avoiding certain wearables due to associated stigma); and healthcare professionals need to be confident in their abilities to correctly assess, treat and monitor patients via technology.

Challenges often arise in efforts to roll out and scale up new technologies, be that in a healthcare setting or at home. EIT Health funded project **Neurab**[xvii] is a cognitive rehabilitation application which offers targeted exercises based on traditional pen and paper methods. The neurotablet device allows for remote patient supervision and monitoring for both small and large groups. It also offers networking channels for the patient and family members to communicate with the therapist, who can change the exercises remotely if required. It is inclusive, versatile, easy to use and cognitively stimulating. When the Italian team behind Neurab introduced the device to other European markets however, some clinicians asked for the software to be validated: it was not sufficient to state that it had been designed around the gold standard (pen and paper). Should the team wish to pursue certain other markets, they will need to validate the software as part of a clinical trial once again and in the different countries (markets) they wish to pursue. The result is a lengthy process that can take up to several years, EU alone has 27 countries.

The challenges relating to technology are not confined to tele-rehabilitation. Some hospitals are just not ready to absorb new technologies into their existing clinical setting. Furthermore, hospitals which have the capabilities to do so, are not always ready with clear and robust reimbursement models. One of the biggest barriers to implementing tele-rehab and digital solutions – and innovations more generally - remains to be money. Technology installed in hospitals is paid for by the healthcare system, but it is far from clear who should pay for home-based healthcare and monitoring. The issues relating to funding and reimbursement are discussed later in this report.

Theme 2: Combined approachaes and integrated solutions

> *"A spiral management process in which a treatment PACKAGE is initiated and constantly revised and updated, based on therapy-mediated improvements INCLUDING PROVEN, EFFECTIVE TREATMENT COMBINATIONS"*
>
> – Swaiman / INNOV+DOCTOR

The spiral management process is an iterative approach to identifying and delivering the right treatment(s) at the right time(s). Research has shown that, by combining certain interventions, clinical outcomes can be significantly improved[xviii, xix, xx, xxi]. Combinations may include non-invasive brain stimulation with cognitive behavioural therapy, or non-invasive brain stimulation plus robotic interventions, and/or pharmaceuticals. The main opportunities and benefits for home therapy and rehabilitation therefore lie with the potential to combine and potentially integrate different solutions.

Combination therapies may require regulatory approvals, especially if treatments are to be fully integrated as opposed to two or more being delivered in parallel. Similarly, pre-existing combined approaches may struggle with market access if one component part faces issues around reimbursement as was the case with Restorativeneurotechnologies[xxii], a start-up company combining neuromodulation with exergames. These combined or integrated approaches would be welcome towards true innovation in healthcare delivery and would support an argument for tele-medicine to be harmonised at EU level. Technology companies, start-ups, entrepreneurs and clinical innovators may realise benefits from working together to 're-patent' their solutions, rather than applying for individual new patents.

Naturally, patients would need to be accepting of any new, combined or integrated approaches to treatment and assessment. Benefits for them would include a tailored, truly patient-focused 'package' of treatment, and subsequently a reduction in the number of interventions needed over time. This would also bring benefits to clinicians, technicians and therapists assuming that clinical outcomes can be realised more effectively and over a shorter intervention period.

Theme 3: Research

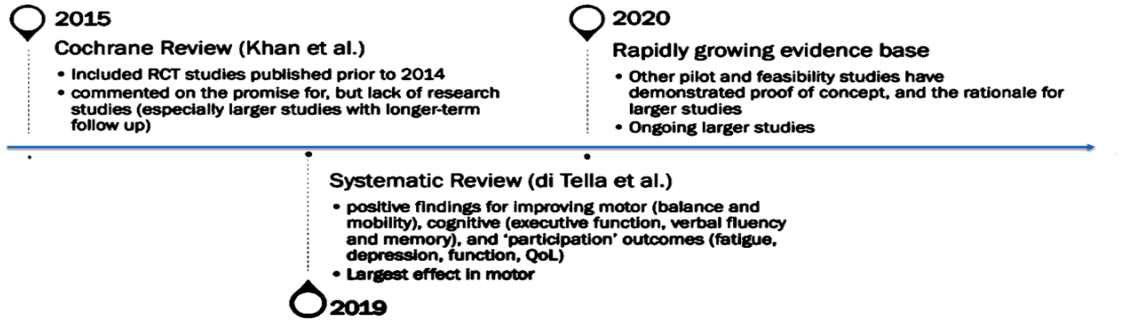
The discussion covered in some detail the need for more research and larger clinical trials, especially in light of COVID19.

Digital health and tele-health solutions for neurorehabilitation are many across Europe, yet each solution, device or intervention goes on its own validation journey. Combining smaller studies with multicentric studies would allow testing on larger cohorts. In addition, there may be benefits from pre-defining criteria among a number of smaller studies, this could accelerate simultaneous CE approval in different countries. Of course, the burden will always be on the ancient principle "*first do no harm*" and so proving benefit will always have to balance with legal and regulatory strategies, e.g.: "who owns the patent?".

Clinical trials for neurorehabilitation will need to be redesigned regardless of their size, if they are to include combined and integrated approaches. This is especially likely to be the case for combinations which include neuromodulation - an area which is extremely active, and which continues to receive increased investments[xxiii].

The roundtable participants all agreed that EU investment into research coordination centres would be very welcome. Data from larger studies can help researchers and their partners to better articulate patients' needs, prove efficacy of treatments and solutions to address these needs and – ultimately – develop a case for public institutions (national health systems, Governments, local authorities and municipalities) to consider funding and reimbursement for these solutions.

Telerehabilitation efficacy over the last five years



Theme 4: Funding and reimbursement

As a general rule across Europe, state or public hospitals tend to be better funded than community health initiatives. While a strong case has been made for more tele-rehab and digital health solutions in neurorehabilitation, it is not always clear who should pay for interventions delivered outside the hospital. The technologies are available, but often expensive and not within financial reach of every patient. Furthermore, it could be expensive to charge patients for (continued) healthcare simply because of the setting in which it is delivered, assessed, or monitored. But who should pay? National health systems, local authorities or municipalities, insurers?

Most current reimbursement models are based on single visits and single interventions or technologies. Combined or integrated treatment packages - done well – can improve the level of care that patients need and deserve. This should be a driver for healthcare managers to develop systems which encourage the reimbursement of packaged rather than individual treatments. Approaches like these would support progression towards more personalised medicine, designed and delivered by multi-disciplinary teams who also need consider the health economic aspects. Value based healthcare provides a framework for this: the creation of more efficient and sustainable healthcare systems, focused on outcomes that make the biggest difference to patients. Evolution by providers towards this value-based concept should, in turn, strengthen the case to payers when negotiating reimbursement terms.

The previous theme in this report - Research – touched on the need for more multicentric studies and proposed a focus on shared component parts of different technologies. This combined research approach would generate larger data sets, and have the ability to prove higher clinical efficacy, hopefully increasing the chances of securing further funding and reimbursement for neurorehabilitation.

Other areas which warrant further discussion include

- The need for solutions to be CE marked in different countries, bringing thoughts around the benefits of a centralised approval system
- The delays associated with requests for medical device codes – where they don't exist in different EU healthcare systems
- The role of insurance companies in reimbursement
- How smaller technology companies can compete and/or collaborate with corporate giants such as Apple and Google.

Conclusions and recommendations for further clinical innovation and collaboration in neurorehabilitation

The body of evidence collected during this roundtable demonstrated a number of areas which need to be addressed in order for innovative neurorehabilitation solutions to be successful in the long term. Conclusions and recommendations include:

Key message

1. Tele-rehab has a large part to play in neurorehabilitation, both for treatment and for monitoring. Remote monitoring – as part of telemedicine - is essential for ongoing assessment.

Systems and drivers

2. Value based healthcare is an important driver for improved patient outcomes and more cost-effective healthcare delivery and should be central to the (re)design and development of innovative solutions.
3. System leaders and innovators should consider lobbying for centralised (European) approaches to common issues such as regulatory approval and coding for medical devices.
4. The role of insurance companies in reimbursement needs to be better understood.

Market opportunity and socioeconomic outcomes

5. The current market is fragmented with several players occupying the market share. The year-on-year growth rate for tele-rehabilitation in the COVID-19 era is estimated at 17% based on a high patient influx. This would suggest there is room in the market for additional home-based treatment and monitoring solutions and/or new combinations.
6. Certain technological solutions with the abilities to predict wider socioeconomic outcomes (for example, early return to work) have potential to inform future health and employment strategies in Europe and beyond.
7. Digital assessment of mobility may correlate with poor clinical outcomes and could be considered for use in clinical research and practice in the future.

Combined and integrated approaches

8. Opportunities and benefits for home therapy and rehabilitation lie with the potential to combine and potentially integrate different solutions.
9. Innovators and developers should consider the individual component parts of their technological solutions, in the interests of marketability in different countries.
10. More evidence, larger studies, combined and integrated approaches and solutions have the potential to create stronger cases for public sector funding and reimbursement.
11. Combined approaches e.g. neuromodulation and exergames would demonstrate true innovation in healthcare delivery; and possibly support an argument for tele-medicine to be harmonised at EU level.

Health improvement

12. Lack of exercise contributes to deterioration in people with MS. This strongly supports the case for home-based neurorehabilitation.
13. The fact that cognition is also influenced by the presence of structural brain damage and aging, highlights the benefits of promoting an intellectually rich lifestyle in people with MS.

Choice and preference

14. Robot-assisted rehabilitation has been found preferential to patients over intensive rehabilitation with a therapist and is often available at a similar cost. Yet more evidence is needed to demonstrate a clear advantage of the use of robotics over conventional physical rehabilitation.
15. A number of factors affect the choice of technology or intervention: these need to be considered when assessing the additive and multiplicative effects of individual technologies and interventions – both for the patient and for the clinician/therapist.
16. Patient preferences should be taken into account when offering different technical solutions, for the avoidance of any stigma and towards treatment adherence.

APPENDIX 1

Participants

Medical Doctors and Clinicians

- Pablo Casado Adam, Specialist in Physical Medicine and Rehabilitation (PMR) at Universitary Reina Sofia Hospital, Córdoba, Spain
- Jakub Kaźmierski, Head of the Department of Old Age Psychiatry and Psychotic Disorders at Medical University of Lodz, Poland
- Letizia Leocani, Group leader, Experimental Neurophysiology and Associate Professor at Università Vita - Salute San Raffaele, Milan, Italy

Start-ups and Entrepreneurs

- IJsbrand De Lange, CEO at STIL B.V.
- Agnese Di Garbo, Co-founder, Clinical Manager and Psychologist at Restorative Neurotechnologies Srl
- Beatrice Festini, Partner, PR and Communication at Neurab
- Dave Hurhangee, CEO and CTO at Sentinel Biosensor
- Alison Liddy, Co-founder and CEO at Relevium Medical
- Guillermo Pérez del Pulgar, CTO and Project Manager at Foren Project

EIT Health Staff and Collaborators

- Cristina Bescós, Managing Director at EIT Health Spain
- Irene Sánchez, Business Creation Manager at EIT Health Spain
- Joan Guanyabens, Medical Officer at EIT Health Spain
- Daniela Dias-Santos, Startups Meet Doctors moderator
- Kirstie Crowther, Startups Meet Doctors rapporteur
- Mara Belluco, Events and Engagement Officer at EIT Health Spain

APPENDIX 2

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