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**When people live with
multiple chronic diseases:**
a collaborative approach to an
emerging global challenge



Escuela Andaluza de Salud Pública
CONSEJERÍA DE SALUD



Words cloud from chapter sections “Why is this topic important?” and “What do we know?”
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The promise of genomics, robotics, informatics and nanotechnologies

This chapter is continuously evolving at www.opimec.org

Vignette: How it could be?

Net-Log

Malaga (Spain), January 10, 2034.

Mixed emotions ravage my soul, if anything is left of it. I now remember almost everything, especially Laura, the most valuable piece of all that was seized from me.

I can no longer continue to evade the truth: I was solely responsible for the accident. I should never have driven in such heavy rain, knowing my own state of health. It is true that up to that point I had never suffered such a severe fainting episode. But on that day, of all days, I should have been more aware than ever of my limitations.

We were on our way to the hospital where I was to receive the Langerhan gene therapy that would finally revert my advanced state of deterioration. A new life, more time to share with her..

And then the emptiness... that inability to remember anything for more than 5 minutes, forcing all those around me constantly to introduce themselves. After the accident I also lost my sight, and they had to amputate a leg. A pacemaker, a hip replacement, hearing aids... I suppose I became a real monster for those around me. But perhaps I did have an inner consolation: my unawareness of what was happening. A living death.

But what am I now, truly? My eyes are nanocameras. My legs made of metal. My body is home to dozens of gadgets which regulate my blood flow. Even my mind is artificial. They call it a neo-hippocampus, and apparently it replaces a part of my brain that was damaged by the haemorrhage caused by the accident, or my illness, it doesn't matter. And what am I now? Man or machine?

Or worse still, what percentage of me is human and how much is not? And my soul? Is that still human?

I suffer now. I suffer the absence of Laura, who was everything. And it may be that my new memory will not help much when I try to stop thinking about her. It would, unfortunately, seem to work very well. On the other hand, though, I must acknowledge that I have been able to meet my grandchildren. With my new eyes and new mind, I can enjoy being with them and then remember every minute together. Maybe I am no longer a burden to others. And maybe those flashes of happiness with my family more than make up for my suffering. I can now help others by recounting my experience in this Biographical Register of Well-being, shared with the whole world. Maybe that is what it means to be human now.

Summary

Have humans reached a turning point in their evolutionary journey? Have they been preparing the way throughout their history for the advances that will enable them to overcome or eliminate previously incurable illnesses this century? Will they reach immortality by the end of the 21st century?

The «scientific» approach to knowledge about the human body began with the observation of its inanimate anatomy on the dissection tables during the Renaissance, moving on to knowledge of the functioning of the organs, then the tissues, the cells and their organelles, finally leading to the decoding of DNA, which then opened the door to an era of promising technologies allowing the manipulation of our bodies at the molecular level. The same process has occurred in other fields, with reality being gradually broken down into its most basic elements. Whether this degree of progressive «unpacking» of our bodies will translate into everlasting health, and even immortality as some prominent scientists suggest, remains to be seen.

Regardless of where the ongoing scientific revolution leads, aggressive efforts are being made to conquer chronic diseases by harnessing the power of genomics, robotics, infonomics and nanotechnology. This technological foursome, also known as GRIN, is driving enthusiastic hordes of innovators to devote their energy and funds to the reverse engineering of existence, working back towards the artificial reconstruction of our very selves. Within this great field of integration, referred to by many as the «grand technological convergence of the 21st century», lie many potentially useful contributions

to the fight against illnesses, in particular those currently considered incurable and chronic. These technologies also promise to re-shape the destiny of our species.

Why is this topic important?

Throughout the final decades of the 20th century, with the decoding of the DNA, the seemingly unstoppable power of computers and the increased ability to manipulate matter at the molecular level, humans began to feel increasingly confident about their ability to eliminate disease and conquer death. At the dawn of the 21st century, however, it is not clear whether this will be possible. At this point, there are more questions than obvious answers, particularly in relation to what seems to be an 'inconvenient' adverse effect of our scientific and technological success since the Enlightenment: the high prevalence of chronic diseases, and the associated wave of poly-pathology.

Humans tend to consider themselves as the pinnacle of evolution, believing everything that has so far occurred has been programmed to result in them. However, it is also possible that humans are mere evolutionary specks moving along a trajectory that leads to a future without them. Given our capacity to create hugely powerful technological extensions to overcome most of our physical (and increasingly, cognitive) limitations, therefore, it is reasonable to ask: Are we simply transitional elements on the pathway towards a «post-human» species?

We have known since Darwin that the genetically best-endowed individuals are those with the greatest probability of surviving and reproducing. We humans have, however, succeeded to a great extent in interfering with the laws of evolution.

Today, the bearers of defective genes survive and reproduce thanks to scientific advances, allowing for an increase, even in cumulative terms, in the survival rates of specimens that will guarantee the presence of such genes in subsequent generations. Now, the children of diabetics and hemophiliacs may thus be able to live with both diabetes and hemophilia, and yet achieve life expectancy long enough to reproduce and to «gather» even more chronic conditions. Up until less than a century ago, this would have been unthinkable (1, 2).

As we tinker with nature, however, we are not only slowing down the «trimming» aspects of the evolutionary process, but also accelerating the process from an adaptive perspective. Genetic changes that would otherwise require thousands or even millions of years can today be implemented by means of simple techniques of manipulation at the laboratory or research centre of any moderately sized organization. We are now

able to enhance the human body with modifications to an organic function by replacing pieces of DNA or by implanting biomedical devices.

Traditionally we have since childhood been taught that life is made up of four stages: birth, growth, reproduction and death. Given that most adults have their children before the age of 40, it would be easy to understand that with reproduction we fulfill our essential purpose, the survival of our genetic information as a species. From that point onwards, as happens with all other living beings, all we should have left is an alchemical rebalancing with the environment having reached our point of maximum entropy... our death. However, we human have pursued a different path. Thanks to the massive parallel computing power of our brains we have been able to embark on a relentless pursuit for immortality which is bringing us close to the point at which we might be able to surpass many of our most basic limitations (3): carbon-based units of weak bones surrounded by soft tissue, requiring narrow bands of pH and temperature, in the permanent presence of O₂. Some even conceive a not-too-distant future in which our inventions exceed all of our capabilities, blurring the boundaries between human and machine, blending us into a new single entity, known as the Singularity (4).

This chapter deals with the main forces that seem to be driving such unprecedented evolutionary process at this point—genomics, robotics, informatics and nanotechnologies—which are collectively known as GRIN (Genomics, Robotics, Informatics and Nanotechnologies) (5).

What do we know?

Instead of the traditional futuristic archetypes of humanoid robots collecting physiological information from us while using their free time to take care of household chores, technological trends are pointing in the direction of much more complex scenarios on which thousands of interconnected gadgets provide ubiquitous services (6). We are already seeing this through a plethora of projects that promote Ambient Assisted Living (AAL), an area that is receiving considerable attention in those regions of the world that register the longest life expectancy, such as Japan and the European Union (7, 8).

The following is a summary of what is happening in relation to each of the components of the GRIN movement.

The G factor

Today it is already relatively straightforward to change the structure of a section of DNA in a laboratory, use a virus to introduce it into a cell and see if it performs a particular function. This technological feat, however, has not been translated into the spectacular breakthroughs in the management of disease that were expected when the human genome was decoded. Although it would seem that this is just a question of time (9), it is possible that given the myriad elements that explain most of the chronic ailments affecting humans, regenerative medicine and gene therapy will only be successful at curing a handful of minor diseases, failing to produce the expected «silver bullets» that would correct the main sources of morbidity and mortality for single major diseases. The picture is even more dismal in relation to potential gene therapies for multiple chronic diseases.

The R factor

There have also been impressive developments in robotic therapy (10). Nonetheless, the results are still falling short of the expectations of a few decades ago.

In *Metropolis*, the famous film of the 1920s directed by Fritz Lang, a futuristic society was divided into two castes, the thinkers and owners who lived on the surface, and the workers of the underground, laboring ceaselessly to maintain the pace of life of their masters. They ultimately come into conflict. Maria, the leader of the oppressed, is kidnapped by the masters and replaced by an android replica, with the aim of sowing chaos among the rebels. The humanoid image of this robot then became the popular archetype that has ever since inspired hundreds of researchers into artificial intelligence, viewing the replication of the human form as the logical path to the future. However, this descendant vision championed by many has been challenged with compelling arguments.

Many leading experts believe that we should promote the basic conditions required to allow artificial intelligent systems to evolve spontaneously, learning in a self-organized form, in the belief that once they have surpassed a certain threshold of information processing, intelligent behavior would emerge. The aim, then, would be an attempt to emulate what happens, for example, in colonies of termites, which are capable of manifesting the emergent intelligent behavior that allows them to construct sophisticated ventilation and storage systems, in a way that could not be explained by the arithmetic sum of their individual intelligences. In this case, the transfer of simple short-range

chemical messages can generate highly precise coordinated reactions similar to that of neurons interacting through neurotransmission in their synapses.

As these two currently opposing strands evolve, an intermediate pathway represented by advances in so-called «human-machine interfaces» is evolving; the very same approach that has guided the development of tools capable of overcoming our limitations (e.g., pulleys, cars, planes, computers). Today, the boundary between biological and artificial is becoming blurred. Advanced surgical techniques are now beginning to be used to incorporate cybernetic creations as extensions to our own biological structures, bordering in many cases on what some still view as science fiction. Chronic conditions associated with the loss of limbs following accidents, in particular in traffic incidents and the workplace, are being managed with highly sophisticated controllable myoelectric prosthetics and re-nervation techniques [11] which may soon incorporate haptic interfaces capable of providing a sense of touch. Cognitive robotic innovations are also being spurred on by advances in functional magnetic resonance imaging, which allows careful observation of neurological activity in areas affected by neurodegenerative conditions or by strokes.

The I factor

Information and communications technologies represent more than simply another piece in the jigsaw being outlined here. They are essentially the glue that binds together the GRIN complex and underpins its potential.

The power of online social networks has been expressed clearly during natural disasters [12]. As official information management systems were rendered ineffective by Hurricane Katrina, members of the public were able to generate, in a matter of hours, an online repository of resources and database of victims, allowing thousands of people to locate their relatives swiftly [13].

Similarly, many patients who were previously left to endure in solitude the daily consequences associated with chronic diseases are now beginning to join forces, supporting each other as «prosumers» [14, 15] or as e-patients [16].

In addition to the growing level of patient emancipation afforded by social networks, another powerful shift in the way in which humans create and manage knowledge is being brought about by hybrid webs or «mash-ups» [17]. In essence, this involves something like «a pinch of this and a dash of that» in order to extract and blend different functional

elements of disparate applications into a new set. As a result, it is now possible to blend electronic health records, large databases of demographic data, online maps and powerful statistical tools to create dynamic spatial representations of the distribution of diseases in a population, and their associated risk factors (18).

Another wave of change is being nurtured by the unprecedented wave of technological convergence that is ushering in the age of mHealth (mobile health), heralded by mobile telecommunication devices connected to the Web. This is leading to the emergence of powerful telehealth solutions designed to improve the quality of life of people living with chronic diseases and to optimize the use of limited resources (19).

Unfortunately, little is known about the value of this veritable renaissance in reducing suffering for people living with multiple chronic diseases.

The N factor

Nanotechnologies, which allow the manipulation of matter at its smallest scale, are giving birth to an area already known as «Nanomedicine», a hybrid of the physical and biological sciences that promotes the interaction between the human body and different materials, structures or devices which operate on a nanometric scale.

The most important aspect of nanotechnologies lies not only in the manipulation of matter itself, but the potential derived from the radical change undergone by the physical and chemical properties of matter when working at such a scale (20): electrical conductivity, color, resistance or elasticity (21).

At present, the application of nanomedicine focuses on three major transversal strands, irrespective of the pathology being targeted (22):

- *Nanodiagnosis*, comprising the development of analysis and imaging systems designed to detect illnesses at the earliest possible moment, both in vivo and in vitro. A promising area of work focuses on nanobiosensors (21), minute tools that combine **biological receptors** (a cell, a fragment of DNA or protein) capable of detecting the presence of a substance, with **sensors or transducers** capable of measuring any related reactions.
- *Nanotherapy*, the controlled release of drugs, through systems able to deliver drugs exclusively to the affected areas or cells in the body, in the hope of achieving maximum therapeutic effects with minimal or no adverse events. Exciting work is

being conducted on innocuous biodegradable nanoparticles (23) which can carry drugs and then be effectively eliminated by the kidneys once they have performed their task (24).

- *Nanoregeneration*, the purpose of which is to repair or replace damaged organs or tissues. Carbon nanotubes (25), for instance, are being created to build replacement limbs with levels of performance that exceed those of their natural counterparts.

Unfortunately, the knowledge available on the role that nanotechnologies play in the management of multiple chronic diseases is scant.

What do we need to know?

Some of the key questions requiring careful consideration (although they may be unanswerable) are:

- Are multiple chronic diseases the inevitable price that we must pay for our greater longevity?
- Does the level of complexity associated with most multiple chronic diseases exceed the capacity of GRIN technologies to offer tangible solutions?
- Even if we could eliminate chronic diseases through GRIN technologies in the mid to long term, will we be able to use innovations to mitigate their impact in the short term?

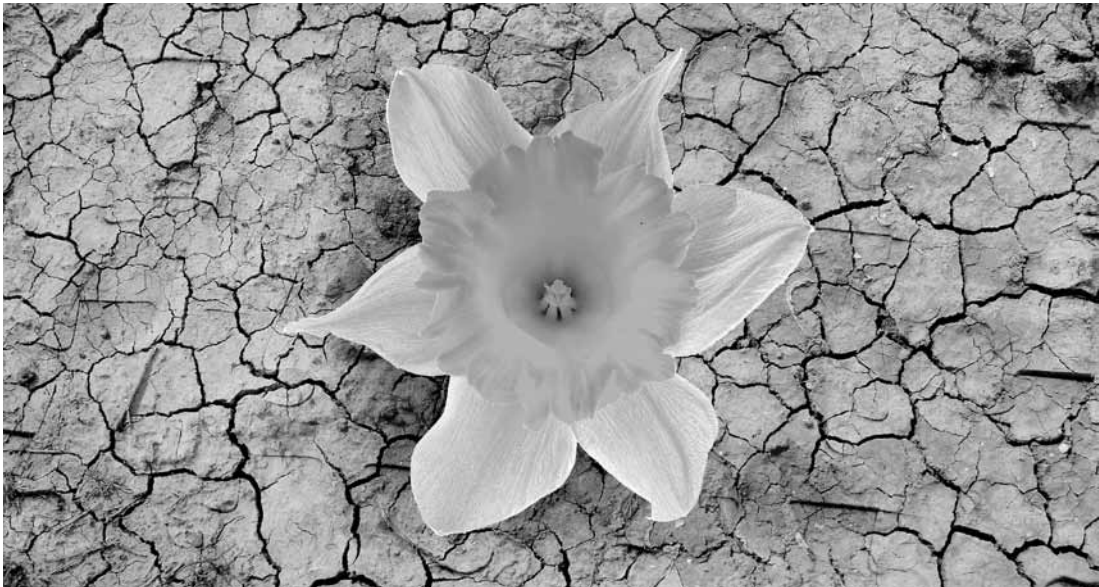
What innovative strategies could fill the gaps?

Harnessing the power of emerging GRIN technologies will require a careful balance between the inevitable super-specialization inherent in them and the need to create system-wide responses to the challenges associated with multiple chronic diseases. It will as a result be necessary to nurture truly inter-disciplinary skills among clinicians, policymakers and managers.

It will also be essential to develop «bridge technologies» and powerful incentives to promote the efficient flow of knowledge across the boundaries of each of the technological domains. Knowledge management tools and managers will thus act as the central pillar of the sustainable reuse of information, the average lifespan of which will continue to shorten.

New methodologies will also be essential to enable clinicians, managers, policymakers and the public to make informed decisions at a speed that can match the pace of technological innovation (26).

For GRIN technology theorists, humans will soon be able to gain more than a year of life expectancy in each chronological year, thus bringing immortality within reach before the end of the 21st century. Others believe that the same technological prowess that gave birth to GRIN technologies has given us the capacity to destroy our very sources of survival, thus turning us into a suicidal species unlikely to survive to see the end of this same century (27, 28). As the future is impossible to predict, all we can do at this point is hope for the best, while being as receptive as possible to innovations that could help relieve the pain, anxiety, fear, sadness and despair caused by multiple chronic diseases. As for the remainder... we shall see.



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Abbreviations

AAL: Ambient Assisted Living

BMJ: British Medical Journal

CAM: Complementary And Alternative Medicine

CCD: Complex Chronic Disease

CCM: Chronic Care Model

CIRS: Chronic Illness Resources Survey

CMPs: Case Management Programs

CVD: Cardiovascular Disease

DMPs: Disease Management Programs

EASP: *Escuela Andaluza de Salud Pública*

EPP CIC: Expert Patients Programme Community Interest Company

GRIN: Genomics, Robotics, Informatics and Nanotechnologies

ICCC: Innovative Care for Chronic Conditions

ICD: International Classification of Diseases

ICED: Index of Coexisting Disease

IDS: Individual Disease Severity

MCCs: Multiple Chronic Conditions

MD team: Medical Doctor

MeSH: Medicines Medical Subject Headings

MI: Motivational interviewing

MPOWER: Monitor (tobacco use and prevention policies), Protect (people from tobacco smoke), Offer (help to quit tobacco use), Warn (about the dangers of tobacco), Enforce (bans on tobacco advertising, promotion and sponsorship), Raise (taxes on tobacco)

NHIS: National Health Interview Survey

NHS: National Health Service

OECD: Organization for Economic Co-operation and Development

OPIMEC: *Observatorio de Prácticas Innovadoras en el Manejo de Enfermedades Crónicas Complejas*

PACE: Program of All-inclusive Care

QALY: Quality-Adjusted Life Year

QRISK: Cardiovascular disease risk score

RE-AIM: Reach, Effectiveness, Adoption, Implementation and Maintenance

SNOMED CT: Systematized Nomenclature of Medicine-Clinical Terms

SSPA: *Sistema Sanitario Público de Andalucía*

TCAM: Traditional Complementary And Alternative Medicine

TPE: Therapeutic patient education

VHA: Veterans Health Administration

WHO: World Health Organization

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When people live with multiple chronic diseases: a collaborative approach to an emerging global challenge

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