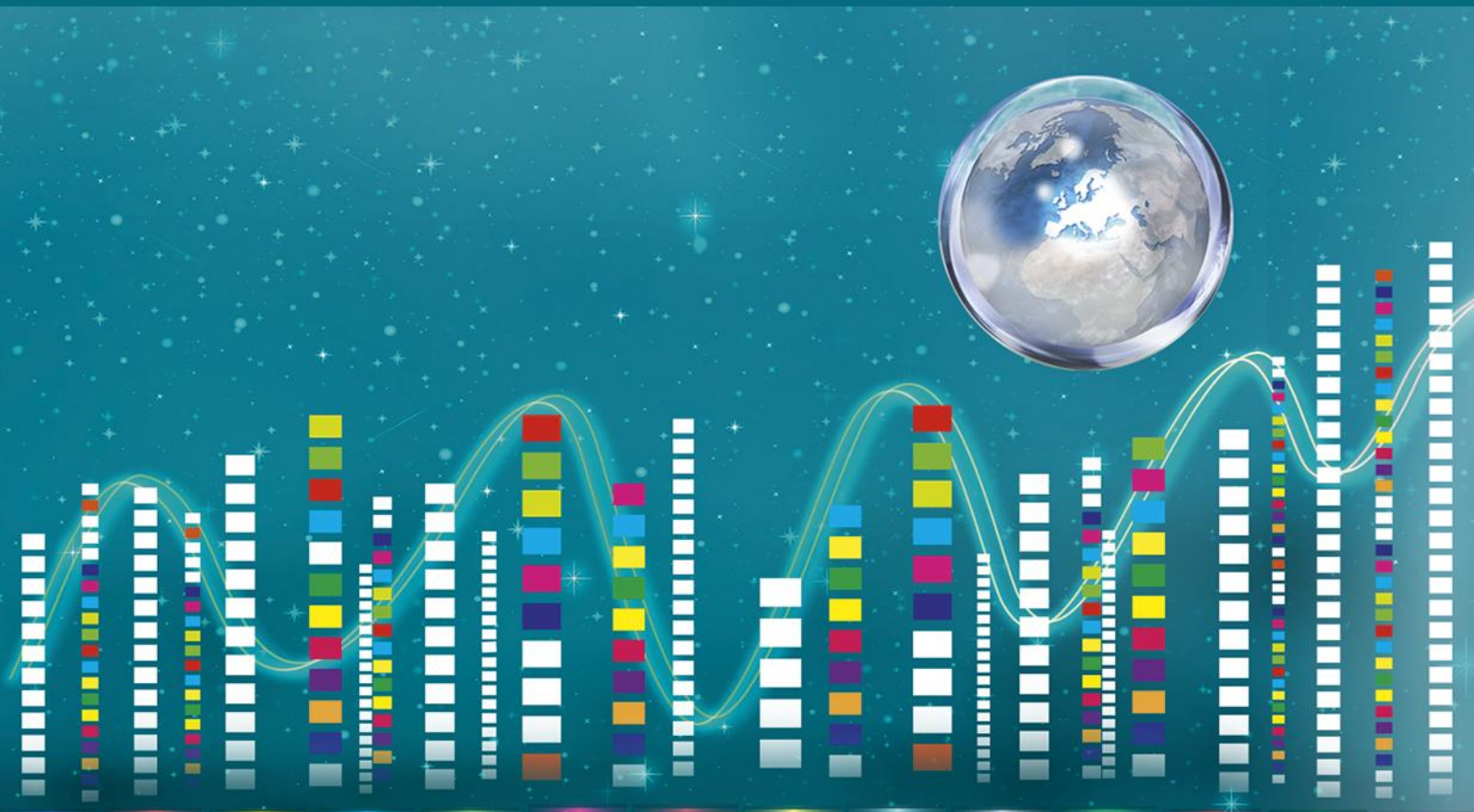
European Commission

Foresight

Precision Medicine

Targeted scenario N°14

Glimpses of the future from the BOHEMIA study



***Precision Medicine* - Targeted scenario N°14**

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Manuscript completed in March 2018

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Luxembourg: Publications Office of the European Union, 2018

PDF ISBN 978-92-79-81191-3 doi: 10.2777/32392 KI-04-18-273-EN-

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EUROPEAN COMMISSION

Precision Medicine
Targeted scenario N°14

Glimpses of the future

from the BOHEMIA study

Directorate-General for Research and Innovation

2018

About BOHEMIA

BOHEMIA is a foresight study (contract N° Contract PP-03021-2015) designed specifically to support the preparation of the next framework programme.

The study put forward policy recommendations for the next framework programme, based on a foresight processes involving scenario development, a Delphi survey and an online consultation.

As part of its recommendations, the study identified 19 likely future scenarios with disruptive implications and associated priority directions for EU research and innovation.

The full range of the results of the study is available at https://ec.europa.eu/research/foresight

Targeted scenario N° 14

Precision Medicine

Summary

It is 2040. Individualized precision medicine combining mass data analyses, genetic engineering, epigenetics, and knowledge about the personal microbiome and the biotic environments helps anticipate and cure illnesses. Human enhancement is an issue of ethical and regulatory concern.

UN Sustainable Development Goals (SDGs) most relevant to this scenario:

The scenario

It is 2040. Precision medicine has taken off. Accounting for individual variability in genes, environment, and lifestyle for each person allows accurate predictions on which treatment and prevention strategies will work best. Precision medicine is not a new idea, but its widespread use and the availability of large amounts of data had been prevented by cost/benefit considerations. Those considerations changed as our understanding of biological processes improved, our data processing capacity grew, and new techniques were developed allowing interventions that were not possible before. Increasingly powerful big data analyses help to identify genetic causes for diseases, and genetic engineering develops focused cures.

Precision medicine includes the use of new diagnostics and therapeutics, targeted to the needs of a patient based on his/her own genetic, biomarker, phenotypic, or psychosocial characteristics. In particular, advances such as cell sorting, epigenetics, proteomics, metabolomics, and more are converging with informatics and other technologies, rapidly expanding the scope of this field. For example, advances in DNA synthesis and assembly methods over the past decade have made it possible to alter DNA or RNA and to construct genome-size fragments from oligonucleotides. Change is slow, however, and while epigenetics found their first non-medical applications relatively early, precision medicine targeting individual patient's genetic makeup is still a rare procedure. Predictive Medicine is more and more individualized.

Continuous advances leave little doubt that precision medicine will continue to grow, e.g. through pharmacogenomics. However, to enable applications of precision medicine on a large scale, knowledge of biological phenomena has to be deepened. Understanding and mapping out the interactions between human organisms and their environment is still a huge project, as is the mapping of the human and non-human microbiome. Sensors and apps monitor an ever expanding spectrum of such interactions. Data ownership and privacy regimes incentivize data-sharing and enable projects with greater access to clean, individuated information sets - especially for the combination of precision with prediction medicine. Precision medicine with genetic engineering, alongside the transformation of the individual microbiomes, has opened up new pathways for human enhancement. Some epigenetic and genetic engineering questions raise no ethical concerns (e.g. immunotherapy with own cells) whereas others remain problematic (stem cells).

Relevance for Europe

Health and medicine are key areas of concern for European citizens, rising concerns for people around the world, and an ever-growing part of the world economy. These are industries in which Europe is very competitive. Precision medicine promises the ability to diagnose and cure illnesses on an individual basis, and in a targeted way, without the harmful side-effects of mass medicine. The aspirations of precision medicine give a boost to biology and to biotechnology, which are essential competencies for the medium and long -term future.

Contribution towards the UN Sustainable Development Goals (SDGs)

Precision medicine is primarily relevant to the health SDG 3 "Ensure healthy lives and promote wellbeing for all at all ages". SDG 10 "Reduce inequality within and among countries" is directly relevant as it is important that precision medicine is not only for the rich. Precision medicine and its predictive part are directly related to environmental management, to SDG 11 "Make cities and human settlements inclusive, safe, resilient and sustainable, SDG 6 "Ensure access to water and sanitation for all" and SDG 15 "Sustainably manage forests, combat desertification, halt and reverse land degradation, halt biodiversity loss", and indirectly related to many other SDGs.

Implications for EU policy

The key implications for EU policy lie with medical regulation, research and ethics and organization of health and insurance systems. As the diversity of treatments increases, health insurance systems are challenged by precision medicine and also its sub-discipline predictive medicine. Until now, no regulation for the predictive treatments exist (e.g. amputations in case of the threat of cancer). Economic considerations are in the forefront, but also ethical considerations come to the fore (e.g. who is entitled? in which cases?). Precision medicine approaches are still expensive and rare. But how can there be a clinical trial for individualized treatments? Education of medical personnel is still lacking appropriate courses on how to deal with the "feasibility estimations" in precision and predictive medicine and how to communicate with the patients. Patients' rights are not clear. As in precision medicine, many personal data are generated, related, hosted in databases and retrieved, policies concerning data and their security are as important as the health considerations. Overall many different policies (e.g. health, population policies, economic policies, digitization policies etc.) are related to precision medicine and have to be linked and coordinated.

Future Directions for EU R&I policy recommended by the public consultation

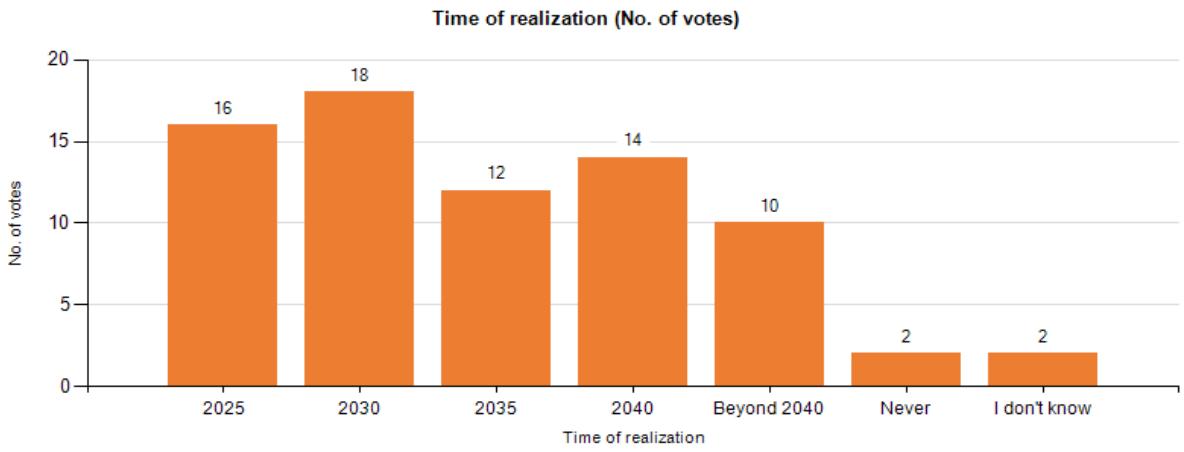
- **Making use of biotechnologies for personalized medicine**
- **Personalised disease prevention for every-day life (including personalised diet and physical activity programmes)**
- **International standards and quality assurance for precision medicine**
- **Strong public health orientation: precision medicine for all, as a part of the way 'towards health for all'**
- **Providing a healthy start to our next generation**
- **Understanding the human microbiome**
- **Understanding epigenetic mechanisms and first applications**

Annex: Relevant Data from the Delphi Survey

The Delphi survey of the BOHEMIA study asked experts about the time of realization of 143 statements about the future, and about the relevance of Research and Innovation for that realization, or about the relevance of the realization for Research and Innovation policy. The experts were asked to justify their judgements with arguments. The whole data set has been published and can be found at: https://ec.europa.eu/research/foresight

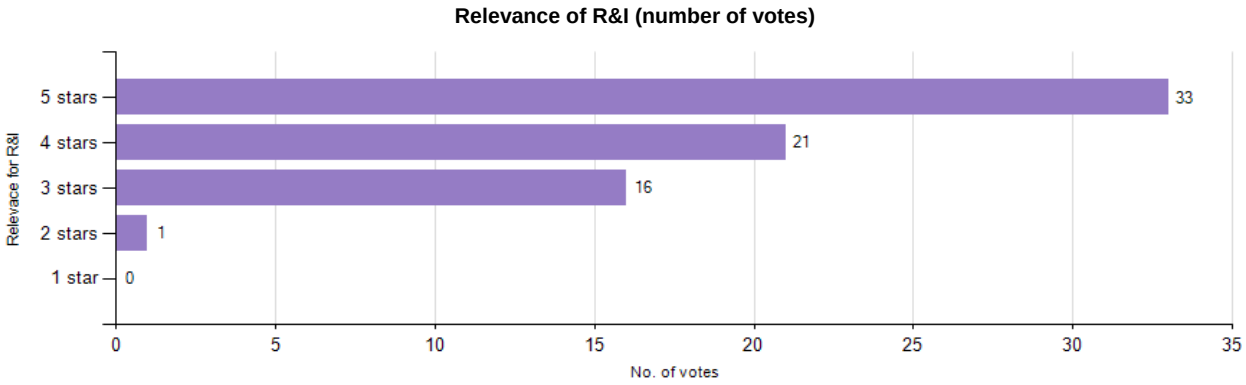
This annex includes the parts of the data set that are relevant to this scenario.

Precision medicines are prescribed in more than 50% of all prescriptions in the EU



Number of respondents : 71

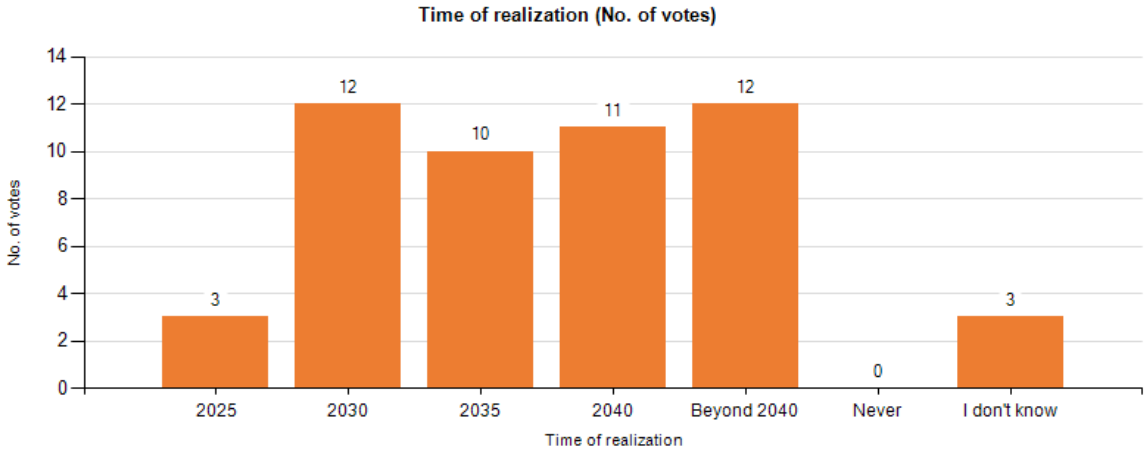
Arguments regarding the time of realization	**No. of votes**
Mobile medicine (use of sensors, apps etc.) will enable much better monitoring of patients and their response to drugs.	57
With the help of big data approaches, individual characteristics of the patients will be taken into account to prescribe the most suitable treatment option.	45
Regulatory measures will take a while to develop and to be adopted consistently across the EU.	35
Rigorously scientific approaches (e.g. biomarkers) are needed to stratify patient groups, draw the right conclusions and then apply or develop appropriate therapies.	28
Pharmaceutical companies are not incentivized to invest in developing drugs that are tailored to a few people.	27
Attention to avoid potential misuse of personal data should be given; maybe the principle of precaution should be applied, ethical frame and regulatory measures are needed.	12
Targeted therapies have already been approved by the FDA.	8
Organ-on-chip technologies will strongly advance the development of precision and personalized medicine.	6
In addition to individual DNA sequencing, for precision medicine to succeed it is likely to require systematic understanding of the microbiome of the individual, which is presently not available.	5
Free access to the clinical trials data, use of AI and a deeper knowledge about causes of diseases will help to develop new strategies of action in precision medicine.	4
Precision medicine requires precise knowledge of the effects of treatments as close to real-time as possible. Patients wanting the benefits will have to agree to provide the data.	3
Precision medicine will help future health outcomes only if it is capable of addressing gaps in access to treatment and health inequalities.	2
Targeted therapies have already been approved by EMA and national authorities.	1
Currently, a lot of funding in the US goes to precision medicine (source: sciencemag).	1



Average: 4.21 **Dispersion:** 0.71

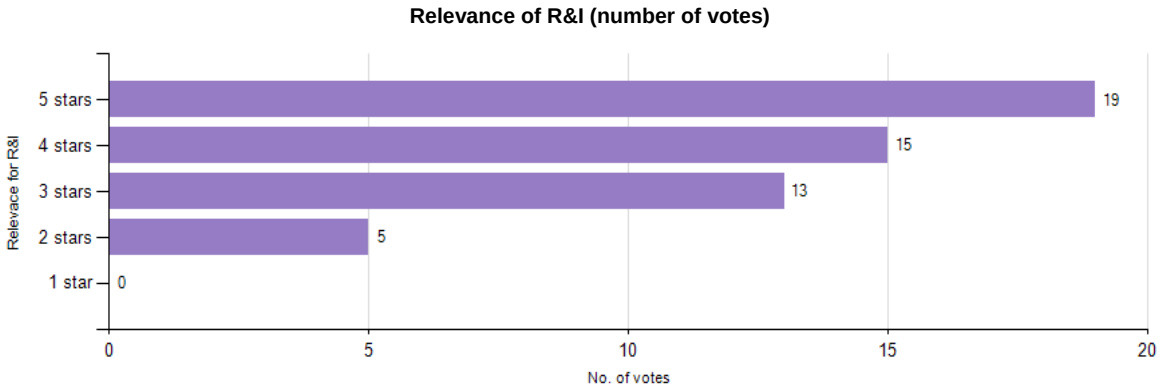
Arguments regarding the relevance of R&I	**No. of votes**
More complex patient profiles that better match individuals will need to be established to enhance predictability of response to treatment.	62
Need for new experimental research for tailored drugs.	32
The current system for classifying diseases will have to be substantially modified in the future.	29
The pharmaceutical industry needs to get research incentives outside the traditional patent system for conditions and diseases that affect few people, and people in poor markets.	24
Improved method for measuring biochemistries in vivo and in real time are required to support better targeting of drugs and improved management of health.	16
Combination of drugs, behavioral changes, digital assistants etc. will personalize health care, with emphasis on prevented, health maintaining part. More responsibilities fall to people themselves.	13
The traditional patent system will need to evolve and adapt to new developments. Pharmaceutical companies will need to find a new business model, public incentives are the solution.	9
Our knowledge of individual patient response & reaction to a given therapy, the impact of lifestyle management and continuous monitoring is too limited. More clinical research is needed.	5
Systematic understanding of the microbiomes of individuals and interaction of same with bodily functions and impact on disease is needed.	4
R&I efforts should consider as early as possible challenges concerning the market access and the healthcare implementation of innovative approaches.	3
Improvement in real time monitoring of precision medication is essential combined with management of the knowledge asset across all individuals with similar diagnosis for continual process improvement	3
Not on individual level - but precision medicine on group level. Big data used for identifying groups of risks	3

Epigenetic-based technologies are used in the first non-medical human applications (for example to stay slim, lifestyle)



Number of respondents : 51

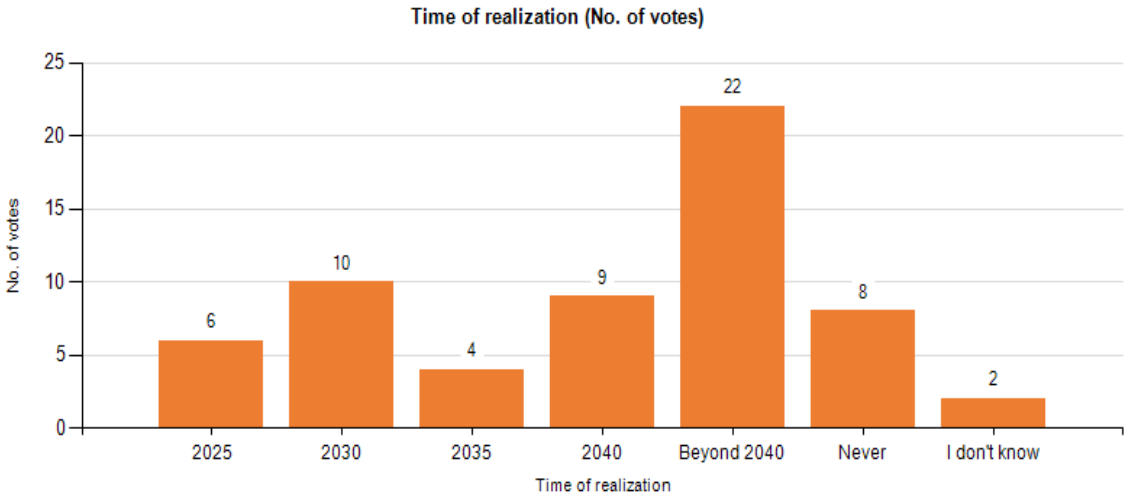
Arguments regarding the time of realization	**No. of votes**
It takes time to turn current knowledge into applications. Research is currently only starting to understand the complex regulatory networks in the human body (genetics in general, DNA, RNA, signals etc.). A lot of basic research is still needed.	41
Epigenetics-based technologies are already tested in first medical cases, especially the treatment of cancer (USA), but not yet in non-medical human applications. It is likely that these will follow with some years of delay.	24
Tight regulation of research and innovation is likely, given the possibility to imagine extreme, even terrifying applications.	12
The tools for gene editing are improving rapidly and first applications are being tested. Furthermore, experimentation with gene editing produces knowledge about other functions of the regulatory network of the human body.	11
Public debate must be organised to allow citizens to become informed on something as important as their own health.	7
The public debate about the pros and cons of interfering with the human body's regulatory networks will be fierce and difficult.	7
There will be significant demand for non-medical applications from the time the first trials are positive.	3
Epigenetics-based diagnostics will probably be used for e.g. lifestyle advice in the near future.	1



Average: 3.92 **Dispersion:** 1.02

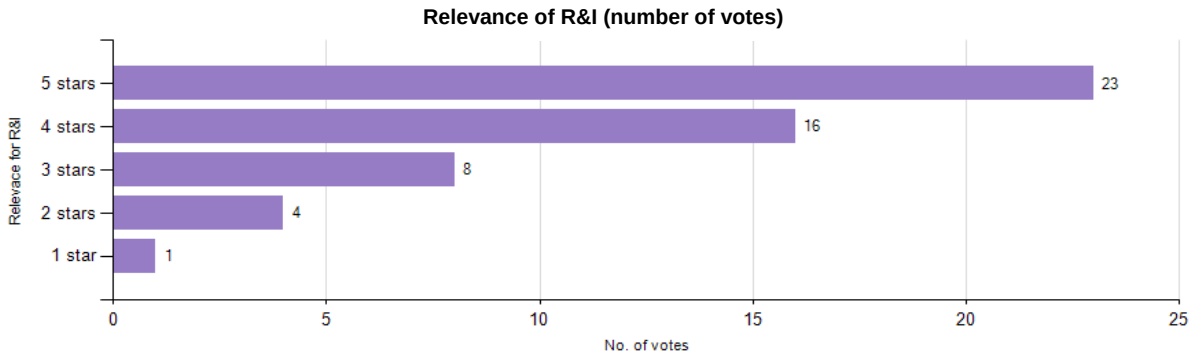
Arguments regarding the relevance of R&I	**No. of votes**
The complex regulatory network of genes is not yet understood. This is necessary not only for developing applications but also for the related risk assessments and for resolving ethical debates. A lot of basic research is still needed.	49
An International Summit on Human Gene Editing: A Global Discussion (Olson 2016) sums up that Gene Editing is only a part of the R&I picture. Epigenetic questions have to be understood and examined if gene editing is to be applied in the right way.	15
Proponents argue that, if somatic therapies are developed, in theory nearly every disease can be cured. These claims need to be monitored and investigated carefully. The public debate needs to be supported with scientific data.	14
Most importantly is life style prevention. Healthy living, active aging and more actuate tools for early diagnostic with the implementation of biomarkers (finding the hormone and blockers)	5
As in DNA sequencing, commercial applications will be offered long before we will have a sufficient understanding to provide solid advice e.g. regarding lifestyle.	1

Precision medicine and customized healthcare that targets a patient's specific genetic makeup (adaptation of DNA and RNA according to specific wishes) is offered in European healthcare systems



Number of respondents : 59

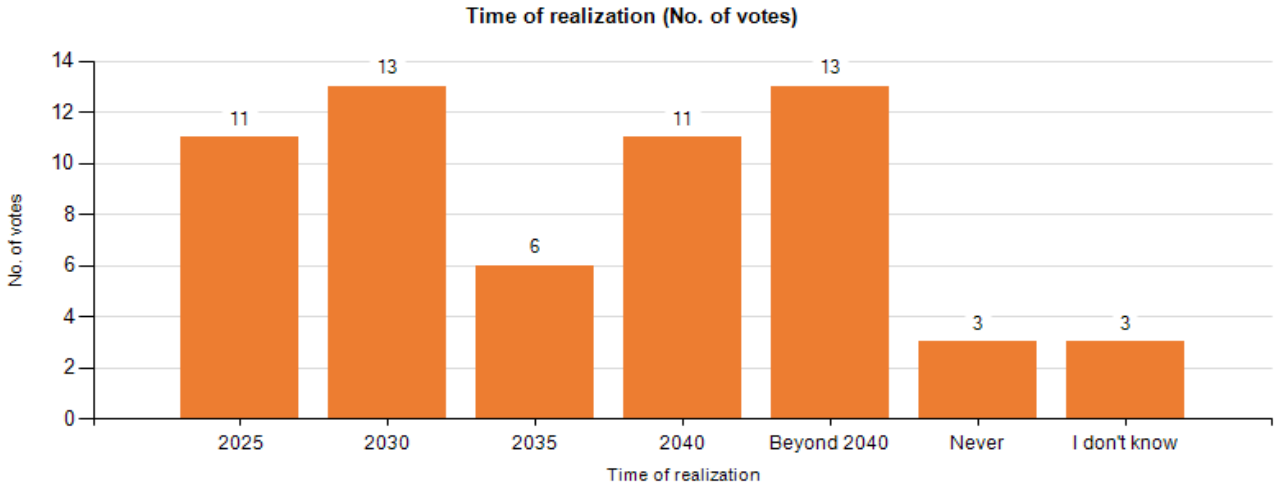
Arguments regarding the time of realization	**No. of votes**
The genetic make-up of an individual is not the only factor influencing the manifestation of a disease, therefore adaptation of DNA and RNA will not be offered by healthcare systems.	40
Sensors and apps will soon be widely used in medicine, making it possible to monitor patients under patient-specific medicine.	27
Needs more research and more cost-cutting.	17
We are more than genes. Genetic make-up has to come together with a deeper understanding of DNA and cellular self-organization on a concrete environment.	11
European public opinion will be generally reticent with respect to drugs targeting an individual's genetic makeup.	10
Manifestation of disease is a function of how genes are expressed which can vary due to multiple factors, including the microbiome, all of which needs to be understood for effective precision medicine.	7
Organ-on-chip technologies will enable the development of precision medicines in an efficient and cost-effective way.	5
As mentalities evolve, medicine will have carried out a paradigm shift that will encompass the targeting of specific genetic makeup and human enhancement in general.	4
The US Food and Drug Administration has recently approved targeted drugs.	3
Precision medicine will not be individual but based on identifying high risk groups using Big Data.	1



Average: 4.08 **Dispersion:** 1.05

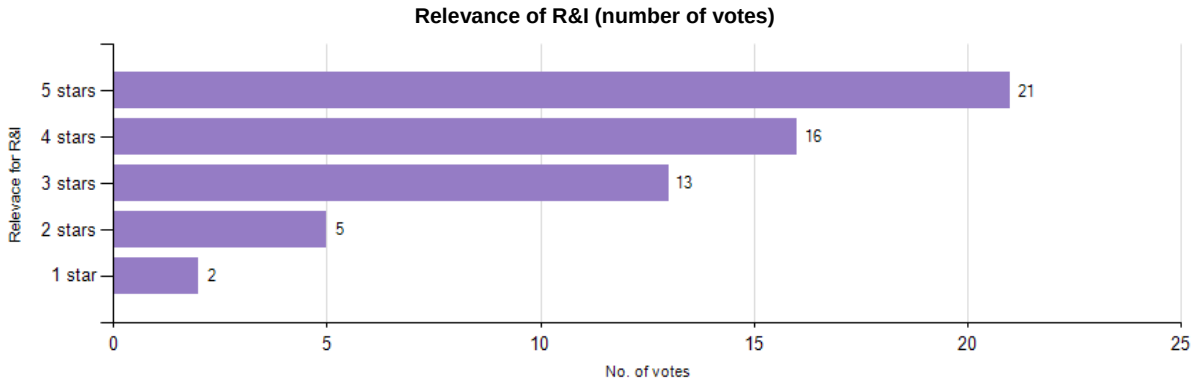
Arguments regarding the relevance of R&I	**No. of votes**
New experimental research procedures for precision medicine have to be developed and adopted widely.	43
Programs will have to be developed and then scaled up to train clinicians in individualized medicine.	27
Drugs targeting an individual's genetic makeup could be a Pandorra box. Hence very strict framework of applications should be available and tightly controlled.	21
Close monitoring of all patients that participate in personalized medicine will be required creating massive data flows, security, privacy and related ethical concerns.	7
Medicine continues to be practiced rather than being a science. Huge research is needed at the cellular level, tissue, systems and epidemiologically for precision medicine to come into common use.	5
Better understanding of the human microbiome is important to understand its effect on (and possible utilization for) personalized medicine,	3
Personalized medicine is likely to require greater patient involvement in treatment including technologies for self-monitoring and related patient education.	3

Data on interactions between patients and their personal environment (including abiotic and biotic factors) are routinely and systematically collected for diagnosis and the creation of personalized therapy plans



Number of respondents : 59

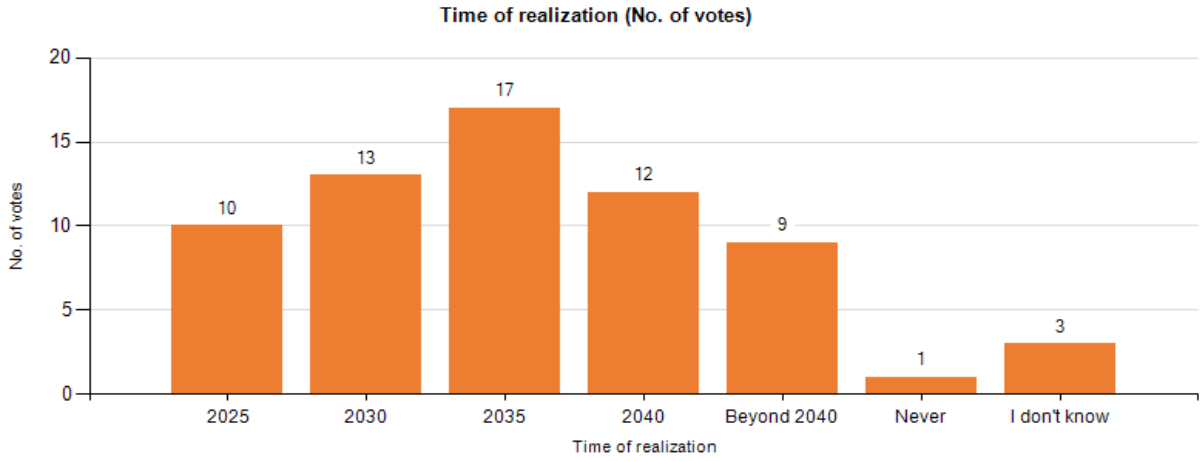
Arguments regarding the time of realization	**No. of votes**
Combining structured data (genotype, phenotype, genomics) with semi- or unstructured data (lifestyle, environmental, health economics data) still poses multiple challenges.	48
There is a huge step between the identification and collection of data, on the one hand, and the creation of therapy plans as a common practice, on the other.	40
This asks for a holistic human perspective that is much broader than the medical perspective on health.	13
Deep learning will help in the analysis of the data, structured data and unstructured data are quite helpful, if pattern can be found.	9
This is inevitable provided the ethical use of data can be properly managed.	8
The combination of structured and unstructured data will be extremely useful in the quest for patterns by means of AI strategies.	7
The US government's Precision Medicine Initiative (PMI) supports research looking beyond genetics and biology, at behavioral and environmental factors.	5
A clear legal and ethical framework is needed to prevent misuse and misinterpretation of such complex data sets, including IT security measures.	5
Just because data collection is uninformative does not mean it will not be done.	3



Average: 3.86 **Dispersion:** 1.24

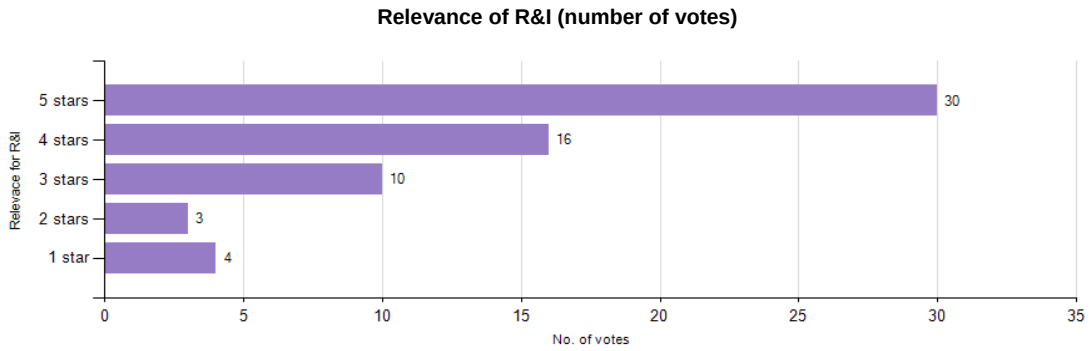
Arguments regarding the relevance of R&I	**No. of votes**
The correlations between the different factors still have to be identified and analyzed on a scientific basis.	49
Scientific databases have to be build up and filled with data.	33
The EU needs something analogous to the U.S. Precision Medicine Initiative involving 1 million volunteers providing genetic, environmental and other data to succeed.	12
Self-learning systems such as IBM Watson will drive this development.	10
Sharing of data between countries is difficult and a barrier for innovation in this field. Data on register level and easier collaboration between EU countries id needed and discussed ethically.	8

Nano-rods (polymeric nanoparticles) are routinely used to deliver medicine on a cell-specific scale



Number of respondents: 64

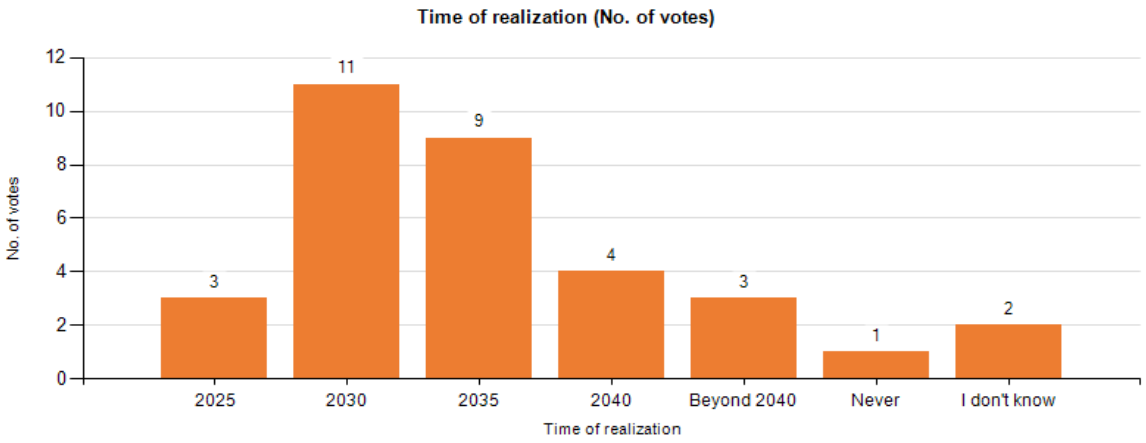
Arguments regarding the time of realization	**No. of votes**
There are a lot of tests necessary before nano-rods can be used in medical applications. This takes time.	49
Gold nanorods (GNRs) already work as delivery vehicles for some diseases (e.g., mycobacterium tuberculosis) and hold a lot of promise for many others.	24
Clinical trials should be conducted within research projects to finally assess this.	23
With a wide range of nanoparticles available, specific nanoparticles should be selected for different applications based on safe-by-design approach.	10
Hyperthermia is a possibility.	5
Cancer, neurodegenerative disorders, and cardiovascular diseases are fields impacted by NP technologies that push scientific boundaries to the leading edge of transformative advances for nanomedicine.	4
I find it wrong if not outrageous that such specialized and marketing-laden topics (e.g., nanosciences, nanorods) have fared so far-up in EU's scientific institutional priorities.	4
Targeted delivery should not be categorized on a specific technology, but rather on its efficacy.	1



Average: 4.03 **Dispersion:** 1.41

Arguments regarding the relevance of R&I	**No. of votes**
A lot of time is needed to move from research scale to clinical applications	33
research on ligands is still an issue for cell level selective delivery	31
Swinburne University researchers have reported that gold nanorods can be used to inhibit cancer cell growth in cervical cancer.	12
A new pulsed-magnetic method which uses nanorods to deliver drugs deeply in the body can offer new pathways for research.	7
Focus on functionality of technologies, don't label it as "nano" for the sake of being a buzz word	6
Utilizations of polymeric NPs include drug delivery techniques such as conjugation and entrapment of drugs, prodrugs, stimuli-responsive systems, imaging modalities, and theranostics.	5
Polymer-based nanoparticles (not exclusively nanorods) are the more promising approaches for nanomedicine applications.	5
For more effective and distinctly targeted delivery of therapeutic applications, particle size, morphology, material choice, and processing techniques are all research areas of interest.	5

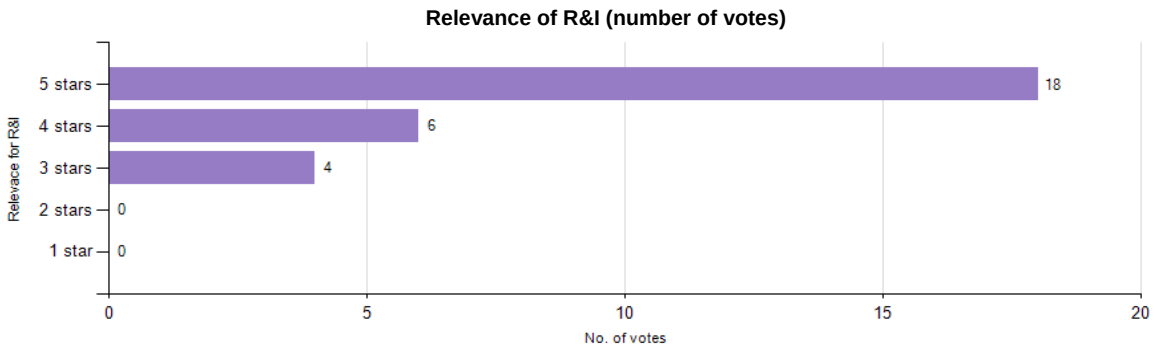
Nanobots for diagnosing health problems are licensed for use by medical doctors in the EU



29

Number of respondents:

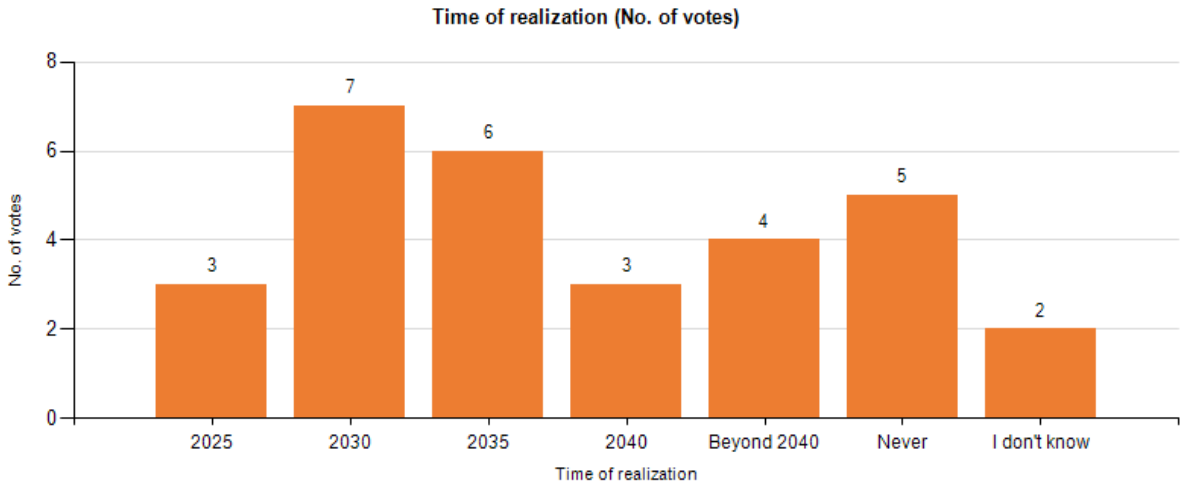
Arguments regarding the time of realization	No. of votes
Many diseases, including HIV can already be detected by low-cost DNA nanobots.	15
Relevant regulation will play an essential role and a general agreement on the subject is not straightforward.	11
Israel's Bar-Ilan University began the human trials of their quest to utilize nanobots in cancer treatment.	10
Personalized healthcare demands knowledge of individual DNA, microbiome makeup, medical and dietary history, and other factors demand AI. Research will drive the widening of the role of AI.	7
Again, this is an old dream but currently it seems unlikely to be fulfilled in the near future.	5
Nanobots are likely to be a footnote in personalized medicine. There are more promising ways to improve health outcomes.	4
Ethical issues might hinder uptake: what if the data are getting in hands of other people than the patient and the treating doctor?	3
The international and inter-university nano-research centre IMEC (Leuven, Belgium) already has a prototype for very early detection of cancer in blood samples via nano: about 100% correct diagnosis.	3
Scaling up may be a problem.	2



Average: 4.5 **Dispersion:** 0.54

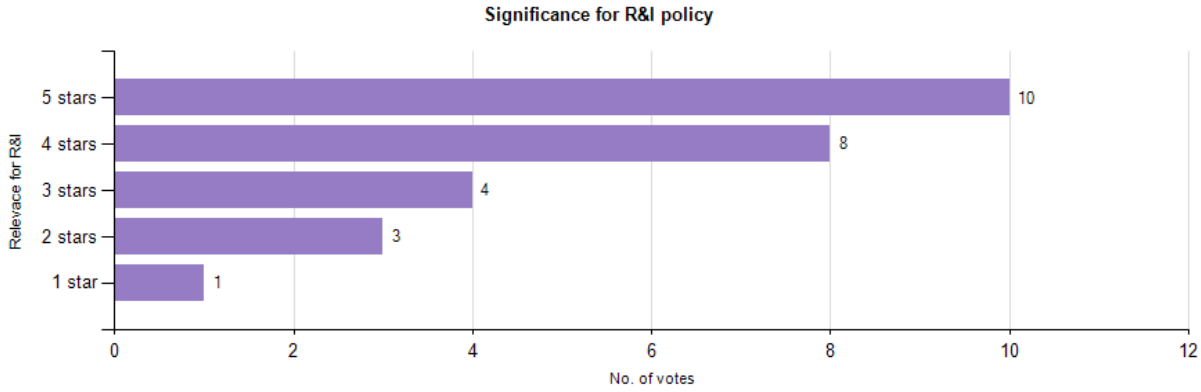
Arguments regarding the relevance of R&I	**No. of votes**
This is an emerging technology and it is important for the EU to be a player.	19
The safety of using nanobots needs further exploration.	18
Diagnostic and sensor systems need to be integrated with nanobots to assure patient safety and effective treatment. Such systems largely do not exist.	11
It's essential to consider the ethical issues related and to integrate ethics within R&I processes	6
It's essential to consider equal accessibility of this technology for the inclusive society.	2

Agreeing to a quantified-self scheme (measuring and transmitting personal health data in real-time) is mandatory for participation in the health insurance system



Number of respondents: 29

Arguments for time of realization	**No. of votes**
This would be a big step into the age of post-privacy and would violate various (current) EU rights.	19
People will get used to it. And big data capacities will allow real time transmitting and evaluating of data.	14
Insurance authorized devices such as CPAP included automated reporting. If you want the care you accept to give data.	5
People will own their data and decide who gets access to it.	4
60% of US adults are currently tracking their weight, diet and exercise routine.	4



Average: 3.88 **Dispersion:** 1.37

Arguments regarding the significance for R&I policy	**No. of votes**
The EU needs to strengthen citizens' rights, giving them better control of their data and ensuring that their privacy continues to be protected in the digital age.	20
The challenge for policy makers is to balance personal rights with the pending changes of the digital revolution.	15
How is legal ownership determined when a dataset is created and curated by the user himself/ by the employer?	6
Personalized medicine to be effective has to be measured real time. Those that want the benefits will need to agree to provide the data.	6
real time availability of data in exchanges between different health care providers is essential	5

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It is 2040. Individualized precision medicine combining mass data analyses, genetic engineering, epigenetics, and knowledge about the personal microbiome and the biotic environments helps anticipate and cure illnesses. Human enhancement is an issue of ethical and regulatory concern

Studies and reports