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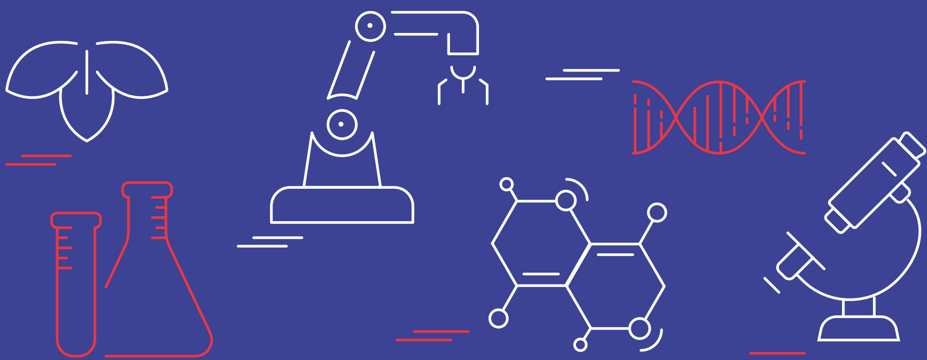

LATVIAN SMART SPECIALISATION STRATEGY (RIS3)

Biomedicine, medical technology, biopharmaceutics and biotechnology

ANALYTICAL REPORT OF THE RESEARCH ECOSYSTEM
(2014–2018)

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representation for research and development of Latvia as part of European Research Area"

Ministry of Education and Science

THE NATIONAL DEVELOPMENT PLAN 2014-2020

EUROPEAN UNION
European Regional Development Fund

INVESTMENT IN YOUR FUTURE

Abbreviations

AMR – antimicrobial resistance

CCUH – Children's Clinical University Hospital

BM – smart specialisation area *Biomedicine, medical technology, biopharmaceutics and biotechnology*

BMC – Latvian Biomedical Research and Study Centre

DU – Daugavpils University

EDCTP – European and Developing Countries Clinical Trials Partnership programme

ERDF – European Regional Development Fund

*ERA-NET – European Research Area Network*s, co-operation platforms in science and research initiated by member states

H2020 – EU framework programme *Horizon 2020*

CF – operational programmes Measure 1.2.1.2. *Support to the development of the technology transfer system* of Specific support objective 1.2.1. *Increasing of private sector investment in R&D*

CVD – cardiovascular diseases

LSPA – Latvian Academy of Sport Education

UL – University of Latvia

UL RMC – Riga Medical College of the University of Latvia

UL SMK – P. Stradiņš Medical College of the University of Latvia

OSI – Latvian Institute of Organic Synthesis

PSCUH – P. Stradins Clinical University Hospital

R1MC – Riga First Medical College

RECUH – Riga East Clinical University Hospital, including the Latvian Centre of Infectious Diseases

RIS3 – Smart Specialisation Strategy *(Research and Innovation Strategy for Smart Specialisation)*

RSU – Rīga Stradiņš University

RSU RCMC – Red Cross Medical College of RSU

RTU – Riga Technical University

TRL – technological readiness level

EDP – entrepreneurial discovery principle

RI – Research institution

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Summary

Latvian Smart Specialisation Strategy prioritises five specialisation areas. One of them is *Biomedicine, medical technology, biopharmaceutics and biotechnology* (abbreviated – BM). The specialisation area is based on traditional research and the industry of Latvia, which has experienced periods of faster, as well as slower development. In the RIS3 of Latvia, the contribution of biology to health is emphasised, while Estonia prioritises the link between information technologies and health and Lithuania – biotechnology, thus reflecting the strong research and commercialisation traditions existing in these countries. In general, in almost all regions of the European Union, the health sector and its sub-sectors are associated with at least one of the specialisation areas.

The report is based on data analysis for the period from 2014 to 2018 and, primarily, on the experience of implementing smart specialisation support tools. A 10-year long period is selected for human resources analysis, since it covers processes of longer duration.

BM is characterised by a growing number of students, which sets it apart from other areas. It is determined by the increase in the number of foreign students; furthermore, higher education in the BM sector shows high export potential. The retaining of the attraction of health-related professions among local students is also an important factor. Although current funding in the health sector is insufficient, it is a sector that is showing a rapid increase in funding amounts, thus it is able to create new jobs. Jobs in the health sector can also be found outside the region of the capital, but research activities demonstrate a significant degree of centralisation. Better geographical integration through new data processing and access methods, is a promising direction for the development of BM in terms of regional specialisation. Good data space management is a prerequisite for participation in global activities, for instance, the Cancer Research Mission.

Research excellence is the factor that characterises the BM specialisation. The impact rates for publications published in collaboration with foreign researchers are generally very high. Obviously, BM is the driving force behind the increase in the attractiveness of the Latvian research system. The analysis also shows the areas, where improvements are required – this is especially true in terms of the reduction of the fragmentation of product development chains and optimal integration into the global value chain system. The report also identifies a number of specific factors required for the functioning of the ecosystem in the area of BM.

New trends should also be noted, for instance, the activities of the European Institute of Innovation and Technology, the launch of the Health Knowledge and Innovation Community in Latvia. The contribution of young scientists and students and the creation of new startups shows the great potential of the contribution of the transformation of the Latvian economy by BM in the development of high value-added products and services.

The challenges of an ageing society, digitalisation, infections and antibiotic resistance are central topics that will attract the attention of the BM in the future. Successful solutions will be the key to economic prosperity and an increase in the number of healthy life years, as set out in medium-term planning documents. Tackling the great challenges will also be a matter for the survival of all humanity through climate change and societal transformation.

1 General characterisation of the specialisation area

In the smart specialisation area *Biomedicine, medical technology, biopharmaceutics and biotechnology*, fundamental and applied research is concentrated at four main institutions:

- Latvian Institute of Organic Synthesis (OSI)
- Latvian Biomedical Research and Study Centre (BMC);
- Rīga Stradiņš University (RSU)
- University of Latvia (UL)

Clinical trials and approbation occur at the following clinical university hospitals:

- P. Stradins Clinical University Hospital (PSCUH);
- Riga East Clinical University Hospital (RECUH), including the Latvian Centre of Infectious Diseases;
- Children's Clinical University Hospital (CCUH).

Along with the aforementioned institutions, there are also a number of institutions operating at the interface of sciences, for instance, Riga Technical University – in the research of biomaterials, BIOR – on the interface of biomedicine and bioeconomics, operations of UL Institute of Mathematics and Informatics integrates medicine and informatics; furthermore, specialised hospitals (in traumatology and orthopaedics, mental health, National Rehabilitation Centre *Vaivari*, etc.) are also important players in the area.

In the area of BM, we can talk about strong research traditions and traditional sectors of the economy – pharmaceuticals, biotechnology, medical equipment. Information technologies have entered the industry early, further developing bioinformatics and expert systems in medicine.

2 Link to global trends

There are several megatrends in the BM sector. The first megatrend is the ageing of society, which requires diagnostics, treatments and methods to make it accessible to elderly people. The second megatrend is mobile and personalised medicine, which provides new opportunities for both treatment and monitoring. The third megatrend could be a biological challenge – antibiotic resistance, which could lead to a complete overhaul of the entire system of medical services and defining the limits of medical services utilisation in a few years, as well as the threat of new infections.

Megatrends determine the fact that the health sector is accounting for a growing share of GDP in all countries of the world and is one of the most important sectors for the future. Efficient saving of public expenditure is increasingly gaining weight as a criterion of health technology assessment in the health sector, leaving the creation of always new commercial products behind, since the translation of extremely expensive treatments into clinical practice requires new approach to assessing effectiveness of health technologies.

3 Investment in specialisation area

Total investment in the area of BM specialisation in the reporting period of 2014–2018 amounted to EUR 45.9 million. They are broken down by funding instrument as follows:

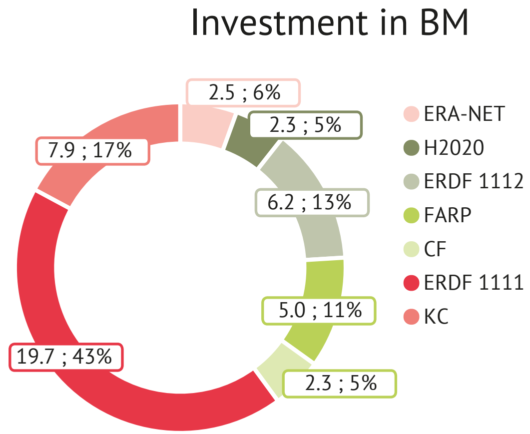


Figure 1. Investment structure in BM

Meanwhile, the breakdown by niches (sub-sectors) on the basis of health priority themes of *Horizon 2020* is as follows:

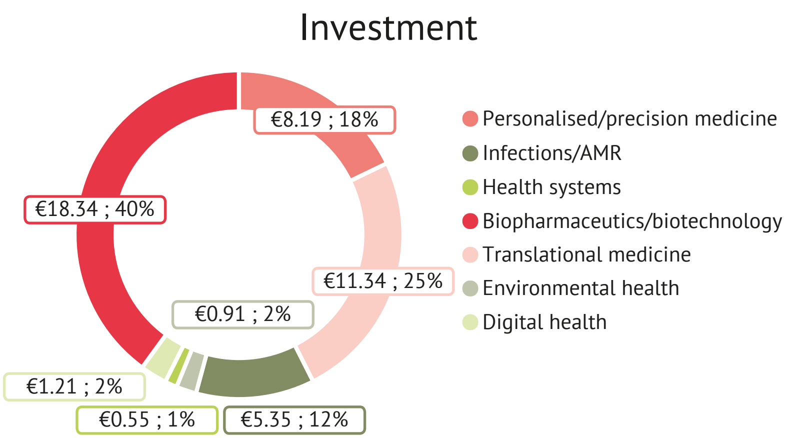


Figure 2. Distribution of investments by BM thematic niches

Of the total investment, 36 million came from RIS3 instruments (80%). Consequently, the specialisation condition is generally met. A certain disproportion is observed in the ratio between post-doctoral and applied research, which is partially determined by the essential differences in the starting time of these activities (the applied research support programme was commenced with a large call, which absorbed more than half of the funding available for the activity). This will certainly affect the opportunities of postdoctoral students to continue their work at RI, by applying the new skills and knowledge in applied research.

The flow of new knowledge (*ERA-NET, H2020*, FARP) accounts for 22% of funding and thus coincides with the *OECD* average for all sectors.[1] However, given the high scientific intensity of the area, future risks may arise here due to the lack of basic research required for the effective diffusion of knowledge in the innovation system. That is even more indicative, given the importance of critical mass and externalities in this area, which results in concentration of funding for scientific excellence in Europe in large centres and, in case of Latvia, there are few research activities outside the region of the capital Riga.

From a cross-sectoral perspective:

The overall thematic structure of the investment is not surprising. Strong new industries dominate, such as personalised/precision medicine, and traditional – translational medicine and biopharmaceutics. Substantial support is needed to deliver critical mass in digital and environmental health, since these are sectors with great future potential, as well as in health systems research, which includes a social science component, thus ensuring the absorption and sustainability of technological innovation. To this end, Latvia must participate in the Horizon Europe partnerships planned by the European Commission, which cover precisely this part of the research. Research on infectious disease as global threat receives significant support.

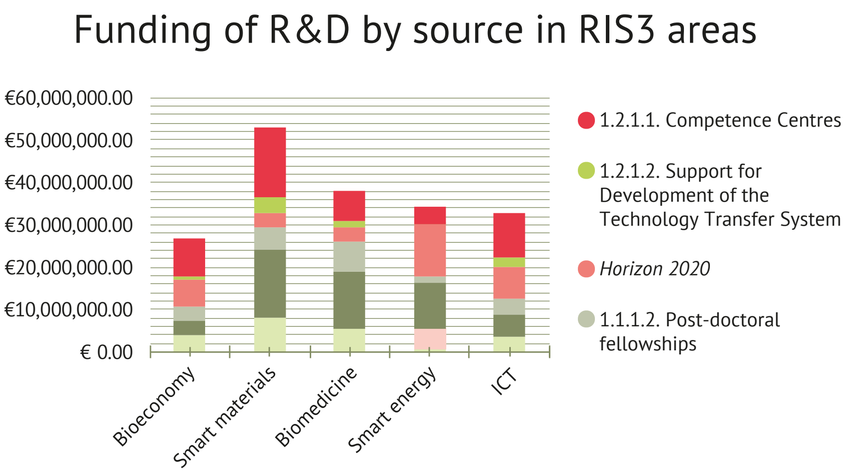


Figure 3. Distribution of investments by RIS3 specialisation area

1. http://www.unesco.org/new/en/media-services/single-view/news/what_is_the_optimal_balance_between_basic_and_applied_resear

4 *Horizon 2020*

4.1. Competition for funding

Latvia's achievements in the *Horizon 2020*, programme significantly surpass performance of Lithuania while falling behind Estonia's result (situation in March 2019).

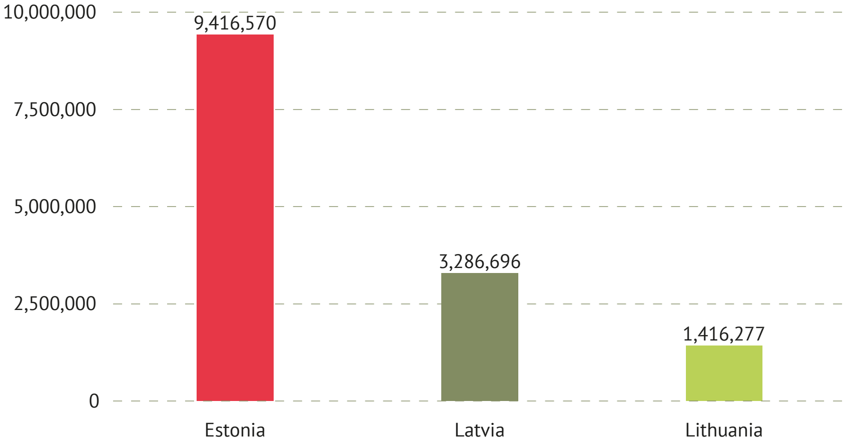


Figure 4. Funding received from the EU Framework programme *Horizon 2020* in 2014–2018.

4.2. Thematic breakdown of research projects within *Horizon 2020*

The largest amount of funding, analogous to national instruments, was obtained in the field of translational medicine. Thus, national priorities are also reflected in the framework programme. The section on environmental health is important, which in the national funding only appears within the framework of SAM 1.1.1.2 activity of human resources development in post-doctoral studies and therefore would be insufficient on national level.

Funding in the area of infectious diseases/AMR was only obtained with the launch of the Innovative Medicines Initiative project ERA4TB, and in the field of digital health with the launch of the PERSIST project. Both projects were conducted in 2020 and, therefore, they are not yet shown in this chart.

H2020 2014–2018.

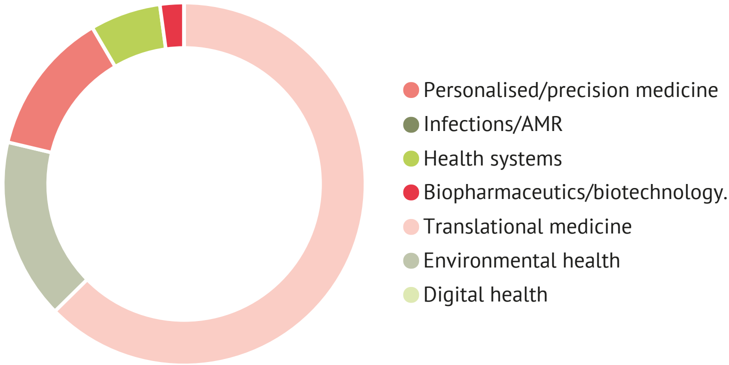


Figure 5. Breakdown of *Horizon 2020* funding by thematic division

It should also be noted that the health sector benefits from funding under other *Horizon 2020* priorities – information technologies, widening participation and spreading excellence, Marie Curie Initial Training Networks.

4.3 Geography of *Horizon 2020* projects

Obtained *H2020* funding in biomedicine

The geographical distribution of the attracted funding shows the absolute trend of centralisation in BM. All funding is concentrated in Riga and its immediate surroundings. This fact is determined by several factors: BM investments in recent years, especially investments in infrastructure have been concentrated in the capital; both national research centres that are active in the sector are located in Riga. Objectively, research resources would also be found outside the Riga region, especially in the area of biology. However, highly integrated BM knowledge ecosystem cannot be easily emulated outside the capital, which is determined to an even higher degree by the trend of concentrating high level medical services in Riga. Unfortunately, research on the interface with bioeconomy, such as pharmacognosy and functional food, as well as environmental science, such as recreation, spa, environmental and climate services, which would have good preconditions in Latvia, has failed to receive support or has been developed on the basis of short-term projects, which prevents the development of capacities for a successful start in the framework programmes.

It should be noted that in Lithuania and Estonia, the funding of framework programmes is multicentric, as there are objectively two main BM activity centres: Vilnius and Kaunas in Lithuania and Tartu and Tallinn in Estonia.

5 Analysis of thematic niches

Research projects corresponding to several niches, will be shown in each of the niches. The niches have been selected according to the thematic division of *Horizon 2020*, which in some cases has been further subdivided, if significant market segments in Latvian RIS3 exist.

A review in the format of a heatmap:

***H2020* area**	**Area**	**"Horizon 2020"**	***ERA-NET***	**FARP**	**ERDF 1111**	**CF**	**Competence Centres**	**ERDF 1112**
PHC, personalised medicine, precision medicine and data lakes	Precision medicine	1	1	6	6	10	1	1
	Pharmacogenetics			1	2			
BHC, translations medicine, innovation in health care	Cancer research	2	3	7	10	8 (4 + 4)	1	7
	Genetics and molecular biology			1	8			4
	Pharmacology, Toxicology and biological pharmaceutical science			1	4	1	6	5
	Neuroscience		5	3	3	2		2
	Diagnostic technologies				4	2	1	5
	Immunology (general)	2	–	4	1			1
	Dermatology			1	3	1		3
	Rare diseases	2			3			
	Endocrinology			1	2			2
	CVD	1		2		2		1
	Therapeutic technologies			2			1	2
	Autoimmunity			2				1
	Mental health		1	2				
	Reproductive technologies					1		1
	Dentistry							1
	Sensory organs							1
Environmental and climate impact on health	**Environmental health and exosome**	1						4
	Nutrition science							4

H2020 area	Area	"Horizon 2020"	*ERA-NET*	FARP	ERDF 1111	CF	Competence Centres	ERDF 1112
Infectious diseases and global health	AMR		3	1	2			2
	Vaccines			1	1	2		1
	Microbiology and virology	1			1			4
	HIV/AIDS		2					
	Malaria				1			1
	Tuberculosis				1			
Innovative in health care systems, integrated care	**Health systems**	1						2
	Nursing science							2
Digital transformation in health care	M-health	1			1	1		2
	Simulators, augmented reality in health	1						
The big data solutions and cybersecurity						2		
LEIT, biotechnology and materials, raw materials	Pharmaceutical chemistry and drug technology	1		1	6		14	7
	Biotechnology	1	1		4	1		7
	Biomaterials	1	1	2				3
	Pharmacognosy				2	3	12	3

In the area of personalised and precision medicine (analogous section of *H2020 – PHC*) all institutions active in BM area are operating. Special activities are carried out by BMC, which is also the Latvian hub organisation for the European Biobank and Molecular Resources Infrastructure (BBMRI *ERIC*). BMC maintains a national biobank, performs bioinformatics data processing. Within the framework of RIS3, BMC, in cooperation with other institutions, is specialising in **precision medical** research conducted on the basis of the so-called data lake. RSU, on the other hand, is the Latvian representative on the Flagera platform in the *IT Future of Cancer* project, which is preparing a EU Flagshipproject.

LU and IOS work intensively in the area of biomarker research. BMC and LU are implementing projects in the area of pharmacogenetics.

In the section of **precision medicine**, the assessment of data lake related marketable activities demonstrates that they focus on providing high value-added services (*know-how*-based services), especially for the pharmaceutical industry, by developing therapy algorithms for personalisation and – which is especially innovative – predictive modelling of safety and efficacy. There is a demand for precision-based (taking into account patient and disease profiling at the molecular and imaging level), *ADME* modelling and prediction of therapeutic effect. As genome-based precision approach is the most advanced, the widest research area is tumour research, as it provides an opportunity for the analysis of the genetic profiles of both the patient and the specific tumour, and intensive accumulation of case-specific knowledge occurs worldwide. High-level research services as a way of knowledge transfer should by no means be viewed negatively, as development processes in modern biomedicine are so complicated that the transfer of knowledge in traditional ways by means of a patenting or other registration of intellectual property is quite limited; furthermore, the implementation of these methods requires personnel with many years of intensive training and experience. It is much more efficient, if the scientific service is provided by the inventor or validator of the method, who is aware of the finest details. An additional argument is open innovation, where the increasing amount of the risk of early stage research is absorbed by the public sector, and this is a key factor in attracting industry to a particular country.

There are some limitations – Latvian hospital and laboratory environment does not allow for the performance of xenobiotic tests, for example, in order to perform the interpretation of variants. Meanwhile, the concept of the digital twin requires high-performance computers with high availability, which should also be concentrated at specialised IT centres.

The link with the IT industry and the relatively fast implementation of applications is particularly promising in the *PHC* area. Therefore, 62.5% of the Commercialisation Fund projects in biomedicine relate to this topic.

Investments in the planning period (number of projects, funding in EUR)

***H2020* area**	**Area**	**“Horizon 2020”**	***ERA-NET***	**FARP**	**ERDF 1111**	**CF**	**Competence Centres**	**ERDF 1112**
PHC, personalised medicine, precision medicine and data lakes	**Personalised medicine total**	1 299,375	1 200,000	7 1,698,000	8 5,140,069	10 1,406,207	1 171,355	1 133,806
	including precision medicine	1 299,375	1 200,000	6 1,398,000	6 3,843,186	10 1,406,207	1 171,355	1 133,806
	including pharmacogenetics	–	–	1 200,000	2 1,296,883	–	–	–

An analysis of project funding in the *PHC* section shows that this sub-sector is competitive in the initial and middle stages of the value chain. It is expected that the implementation of Commercialisation Fund projects will lead to developments for further commercialisation in the competence centres and the commercial sector. The sub-sector is well equipped with human resources, therefore the attraction of postdoctoral students was not necessary. Pharmacogenetics is promising, since it directly links to industrial research.

Thus, precision medicine as a more compact section of personalised medicine is well suited for the development of the ecosystem. It includes activities that are relevant to *EDP* and has the potential for commercialisation.

Research in **translational medicine** (associated with *H2020 BHC – Better Healthcare*) deals with the study of specific diseases and research into specific solutions and products to address health problems. The previous section on *PHC* is partially considered to be included into the translational medicine. It is only included in this section, if the projects are disease-specific, i.e. the research is conducted to improve health care measures and approaches for the therapy of a specific group of patients.

Cancer research accounts for the highest intensity of research in major diseases. It is already a tradition in Latvia and many EU countries, since this is the area, where significant scientific progress has been made over the recent years. Starting with two cancer research projects within the *Horizon 2020* programme, the total sequence consists of 28 projects in this section. The main drawback of the biomedical ecosystem of Latvia in the area of cancer research is the insufficient provision of high-quality innovative registers to include a wide range of personalised – *omics* – information along with modern visualisation data (for instance PET). Such registries are required for involvement in the planned *Horizon Europe's* cancer mission and the development thereof is a part of the *PHC*.

The contribution of *Horizon 2020* to **cancer research** comes not only from the traditional health priority, but also from the Widening priority, where a technology-intensive project in the area of cancer research has been implemented.

Cardiovascular diseases are clearly the most important mortality factor in Latvia; furthermore, the mortality rate is more than twice the EU average. In Latvia, higher mortality is observed in younger age groups. CVD is the second most important factor in the loss of healthy life years, for women – the most important. Research in CVD is centred at the Latvian Centre of Cardiology and cooperating RIs, as well as at other hospitals. In the case of CVD, several specialised registers have been set up.

Neuroscience has seen an intensification of early research in recent years. Thus, this area is promising for further focused tenders in applied and commercialised research to move further along the translation chain.

H2020 area	Area	"Horizon 2020"	*ERA-NET*	FARP	ERDF 1111	CF	Competence Centres	ERDF 1112
BHC, translational medicine, innovations in health care	**Translational medicine total**	5 1,459,108	9 1,831,763	16 3,996,622	16 9,721,673	13 1,601,028,	6 882,895	15 2,007,082
	including cancer research	2 867,575	4 830,000	7 1,799,895	10 5,971,736	8 1181203	1 171,355	7 936,635
	including cardiovascular diseases	1 82,500	–	2 499,081	–	–	2 268,861	1 133,805
	including neuroscience	1 376,125	5 1,001,763	3 798,740	3 1,804,406	2 299,820	–	2 267,612
	including metabolic diseases	1 109,408	–	1 199,000	2 1,296,883	–	1 204,495	2 267,612
	including other	1 399,625	–	3 699,906	1 648,648	5 428,004	2 238,184	3 401,418

In the area of **infectious disease** research, the specific resource of Latvia is connected with the operation of the specialised research institute – RSU Institute of Microbiology and Virology (formerly LAS A. Kirhenstein Institute of Microbiology and Virology), the research is localised also in BMC and IOS, as well as BIOR and universities. Studies on antimicrobial resistance is an important major societal challenge. UL and BIOR are actively involved in AMR studies. This area is characterised by excessive emphasis on early-stage research and the lack of commercialisation activities, although diagnostics and therapies related products could be feasible on the market. One of the reasons is highly limited opportunities for clinical trials, which would require cooperation, for instance, with the EDCTP.

H2020 area	Area	"Horizon 2020"	*ERA-NET*	FARP	ERDF 1111	CF	Compe-tence Centres	ERDF 1112
Infec-tious diseases and global health	**Infec-tious diseases, total**	1 299,375	3 497,844	1 200,000	7 4,475,857	1 24,503	1 238,130	7 936,642
	including antimic robial re-sistence (AMR)	–	3 497,844	1 200,000	2 1,232,337	–	–	2 267,612

A specialised agency is operating in the sub-area of **environmental health and exosome** research – RSU Institute of Occupational Safety and Environmental Health (IOSEH). Research within the European Biomonitoring Initiative is carried out by the IOSEH and UL. The development of the sub-sector in Latvia is insufficient, although investment in this area is seen as an investment in mitigating climate change and promoting safe production processes. Increased interest in the control of microbiological contamination is expected.

H2020 area	"Horizon 2020"	*ERA-NET*	FARP	ERDF 1111	CF	Compe-tence Centres	ERDF 1112
Environment and climate impact on health	1 255,325	–	–	–	–	–	4 535,224

Innovative health care systems, integrated care. Although this sub-area has been identified as important for the development of the health sector in Latvia, and a priority research direction *Public Health* has been selected, investments to date have been low. A larger contribution to the sector has been made from the National Research Programme concluded in 2017. To ensure the development of the sector, a purposeful new programme is required; optimally it should be longer than the traditional three-year period. In the area of integrated care, implementation projects within the framework of the INTERREG programme are being implemented, for instance, BaltCityPrevention.

H2020 area	"Horizon 2020"	*ERA-NET*	FARP	ERDF 1111	CF	Compe-tence Centres	ERDF 1112
Innovative health care systems, integrated care	1 39,875	–	–	–	–	–	4 512,921

Digital transformation in health care is important for the process of business discovery, as Latvia has an active ecosystem of start-ups in the area of digital health, as well as it has potential in the reduction of health care costs and addressing social problems, especially in the care for the elderly. Latvia's accession to the knowledge and innovation community of the European Institute of Innovation & Technology is a considerable milestone, as a result of which Latvia became a member of its Regional Innovation Scheme. It should be noted that Latvian applicants have also been active in the *H2020* digital health theme, however activities in this section have not resulted in specific projects yet. The Institute of Electronics and Computer Science, RTU, VUAS are active in the area.

H2020 area	"Horizon 2020"	*ERA-NET*	FARP	ERDF 1111	CF	Compe-tence Centres	ERDF 1112
Digital transforma-tion healthcare	1 (EIT) 50,000	–	–	1 648,586	1 24,969	–	2 267,612

Big data solutions and cybersecurity are a challenge and an opportunity in the health sector. In the area of big data, one project has been implemented within the framework of CF, in both rounds. However, there have been a number of highly-rated projects, which have failed to reach the necessary number of points required to obtain funding, which shows that Latvia has an adequate capacity. Cyber security should become a part of a focused call.

H2020 area	"Horizon 2020"	*ERA-NET*	FARP	ERDF 1111	CF	Compe-tence Centres	ERDF 1112
The big data solutions and cybersecurity	–	–	–	–	2 299,968	–	–

Active research in the **biopharmaceutics and biotechnology** sub-areas corresponding to the RIS3 specialisation is being implemented – mainly in applied research and commercialisation. It should be noted at the outset that, in the area of biotechnology, it is not easy to draw a distinct line from the areas of bioeconomy; there is often an overlap with materials used in the pharmaceutical and organic chemistry. For practical purposes, pharmacy is identified as a separate sub-sector, although, for instance, in the *H2020* classification, it is integrated into innovative production processes. In the area of pharmacy, a specialised centre of competence is operating in this planning period, which explains the high investment intensity at this stage (in the previous planning period, there was also a specialised biotechnology centre of competence, which was discontinued).

H2020 area	"Horizon 2020"	*ERA-NET*	FARP	ERDF 1111	CF	Compe-tence Centres	ERDF 1112
Biotechnology, material conversion, raw materials	1 50,000	1 210,000	1 200,000	2 1,288,640	1 24,503	4 521,583	7 936,642
Pharmacy and pharmacognosy	2 100,000	–	2 599,970	10 5,460,907	3 297,431	22 7,499,776	14 1,873,282

Institutional specialisation

Institutional specialisation in BM shows a relatively high degree of parallel activities in research, and limited complementarity.

In essence, all four major research organisations are carrying out similar research. Specialisation is observed in certain directions, for instance, IOS – in pharmacy, UL – in medical physics, RSU – in public health, BMC – in the development of a data lake. In general, however, the BM sector is characterised by very tough internal competition, and although it provides really high-quality research, greater specialisation would be welcome.

BM research focuses on the discovery and explanation of naturally occurring processes in naturally occuring systems or in relation to external effects. A completely experimental approach has only emerged in recent years with the development of synthetic biology. Consequently, the epistemological principles of BM are different from other areas of RIS3. The core of BM research is a group or team of researchers (not an institution or a laboratory), who are working on a specific problem, attracting the best experts in a specific area to the group. When the problem is resolved (or it is proven that it cannot be resolved), the group, as a rule, ceases to exist and researchers regroup to work in other teams that are working on current issues. The establishment of virtual long-term institutes in BM should be seen as a hindrance rather than a facilitator, since it reduces the dynamism of the industry. This also explains why it is not easy to get involved in international projects in the area of BM – because the institutional forms of cooperation are not strong here; personal experience of cooperation on an individual profile based on publications dominates the area. Starting of first-time collaboration with another research group is not simple; it has not only science-based, but also important psychological, financial and organisational aspects. However, if this form of interaction has been developed, then, as a rule, long-term collaboration with group members, no matter what configuration they work in during their future research career, is already much easier to establish if based on previous experience. BM not only needs research money; it also needs resources to visit laboratories abroad and for short-term visits. In the case of BM, the ecosystem must have a strong diffusion of knowledge in relation to the external world, the personnel must be mobile and the processes must be agile.

6 Personnel

The number of research personnel that, according to the indicators of 2019, refer to the BM RIS3 area, amounts to 1,337 people. The breakdown by institution is as follows:

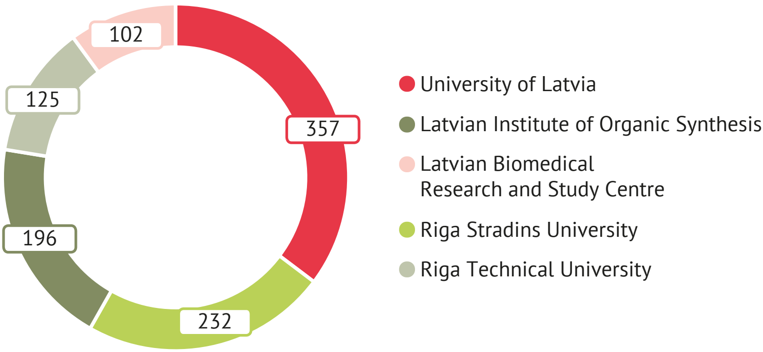


Figure 6. Number of research personnel in the largest institutions of the area

Another 19 research institutions and universities have at least one researcher related to the area of RIS3. Researchers in the area of chemical engineering, without subdividing them into potential sub-sectors, have also been taken into account.

Breakdown by position:

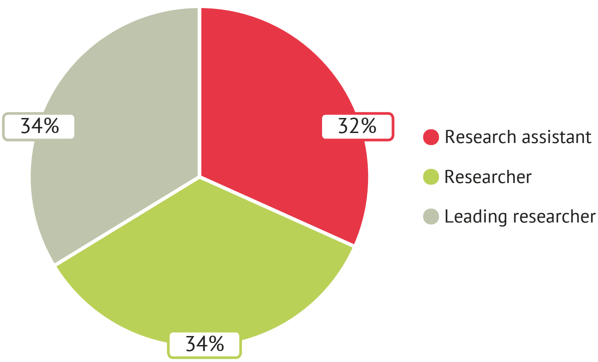


Figure 7. Distribution of research personnel in BM area by positions

This distribution points to an insufficient number of young researchers. This is due to both insufficient generational exchange, as well as the structural problem – since methods and knowledge in this area require a long period of learning, it is quite expectable that experienced researchers are much more valuable in attracting funding; they accumulate in these projects and instruments and dominate in the structure. There are no instruments in the situation of Latvia that would be suitable to assistant researchers and researchers, who do not yet have a doctoral degree, and this is a part of the capacity support problem. The practices of the admission of doctoral students in the status of researchers used among universities also differs greatly.

Age structure

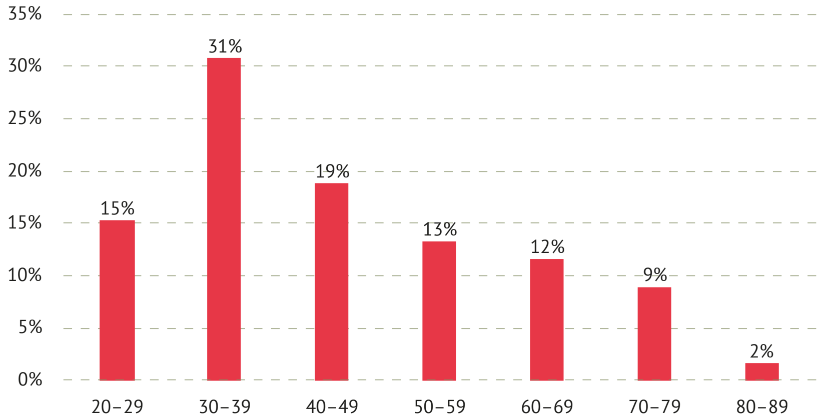


Figure 8. Age structure of research personnel in the BM area

The relatively high number of researchers in the middle age group of 30–39 results from doctoral support programmes implemented in the previous planning period (2007–2013). Clearly, this is also the age, when the most active research activity occurs. Relatively high proportion of research personnel over 60 years of age (23%) is a peculiarity of Latvia, which is also observed in other sectors. This is determined by the consequences of the crisis, during which researchers, who were receiving a state pension, were in a relatively better position, since they could cope with lower remuneration for research activities, as it was not the sole source of income.

Subordinate specialisations in the area of RIS3:

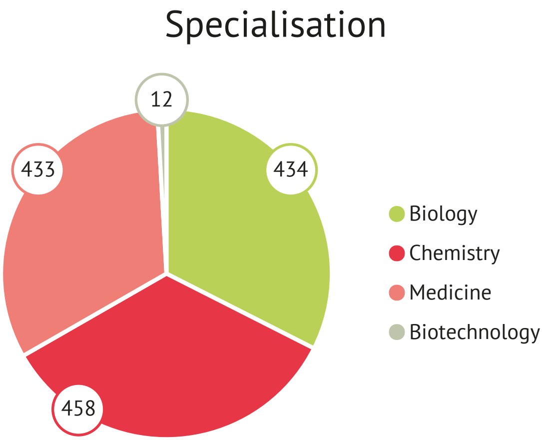


Figure 9. Distribution of BM research personnel by primary specialisation

The structure (which has been developed based on the first indicated specialisation) can be assessed as optimal. The relatively small number of researchers in industrial biotechnology is related to the reduction of the economic influence of this sector, as well as the fact that the expertise in biotechnology is included in programmes of many engineering sciences – food, wood and environmental.

Breakdown by institution

Table 1. Distribution of BM specialisations by scientific institutions

Institution	Biology	Chemistry and chemical technology	Medicine	Biotechnology
Total	**434**	**458**	**433**	**12**
University of Latvia	166	48	132	11
Rīga Stradiņš University	15	2	215	0
University of Institute of Organic Synthesis	7	175	14	0
University of Biomedical Research and Study Centre	99	0	3	0
Other	147	233	69	1

It can be concluded that the number of research personnel in all three main groups – biology, chemistry and chemical technology, medicine – is similar, on the basis of the primary identified activity sector. Thus, in Latvia, the area of specialisation should be considered to be well balanced. Assessment at the institutional level clearly demonstrates the subordinate specialisation: UL and BMC in biology, RTU and IOS in chemistry and chemical technology, RSU in the medical sciences. A significant overlap with the area of bioeconomy is also observed, for instance, in wood chemistry, which could contribute also to the production of important substances for use in medicine. The representation of the commercial sector in the format of small and medium enterprises is also beneficial, although it involves a small number of personnel.

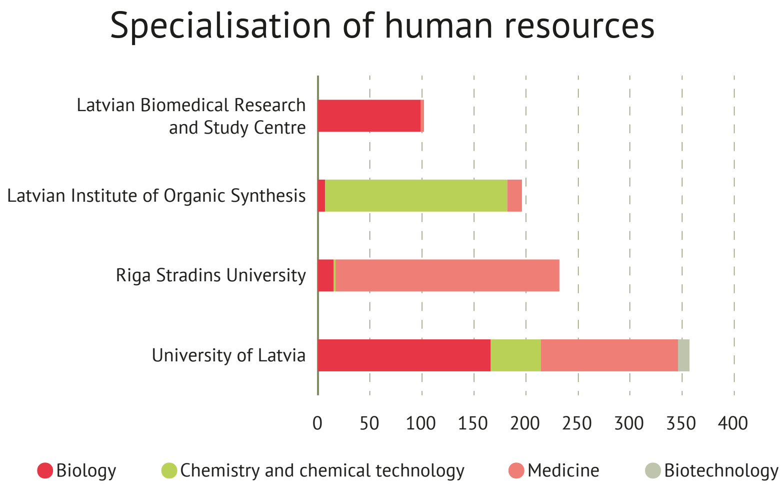


Figure 10. Visualisation of the specialisation of human resources in BM

7 Students

A special phenomenon in the field of BM specialisation is the increasing number of students. This is determined by two factors:

- ability to attract foreign students, higher education in the area of BM is exportable;
- the growing interest of young people in health sciences, which has a relatively large number of jobs; furthermore, this education provides mobility at the European and global level, since the demand for professionals is growing globally.

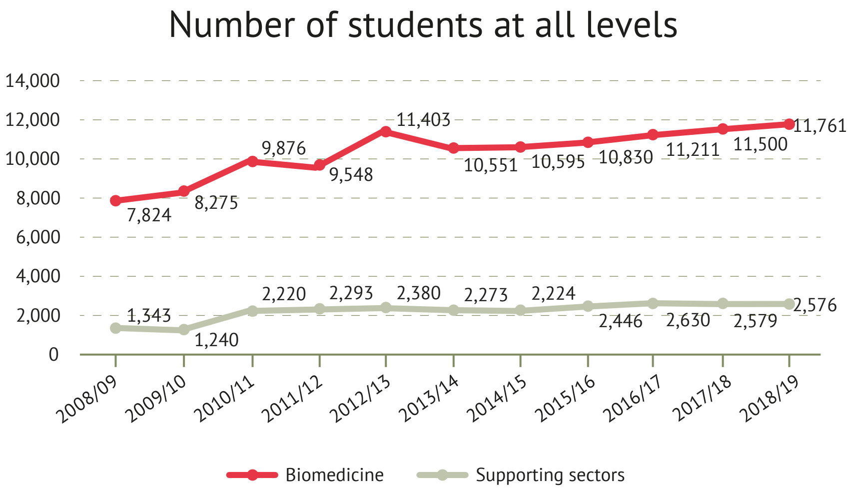


Figure 11. Number of students in BM and supporting sectors over a period of ten years

The number of students in the supporting sector is stable. This ensures both the availability of highly specialised personnel and the availability of specialists in the industry to implement the entrepreneurial discovery principle.

Thus, the proportion of BM and support industries in the total number of students in Latvia is demonstrating an increasing trend and has doubled over the decade.

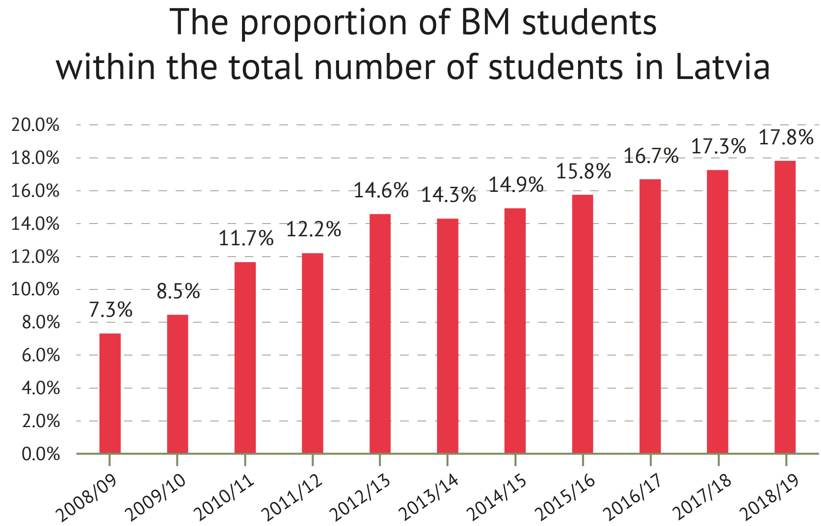
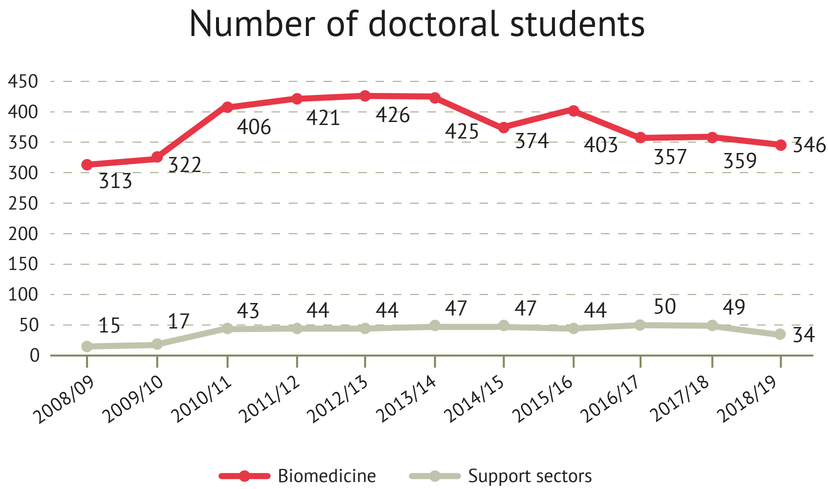


Figure 12. The Proportion of BM students within the total number of students in Latvia

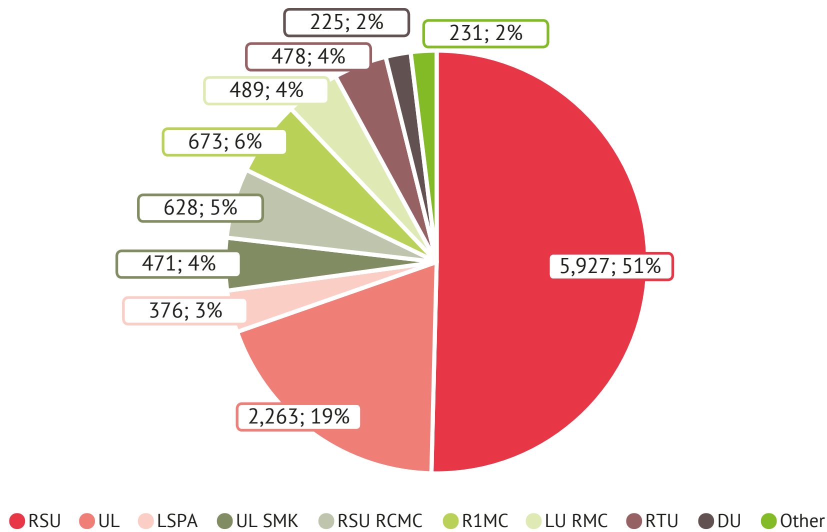
The increase in the proportion is not only a phenomenon of supply, as there are strong pull factors in the human resources area of BM. It is both a strong innovation process that creates new sub-specialities and a rapidly growing public investment, which, although still insufficient, highlights the health sector among others.

The situation is slightly different in the area of doctoral studies. The indicators are more dependent on the specific support programmes that existed in the 2007–2013 programming period (effective until 2015). To ensure research personnel renewal, the development of doctoral studies requires support programmes. This is especially related to the social security of doctoral students, because BM doctoral studies are usually commenced relatively late, after obtaining the professional qualification, and, therefore, doctoral students must take care of the provision for a family, while studies, along with full-time work, interferes with the ability to pay sufficient attention to research work.



Figures 13. Number of doctoral students

7.1. Distribution by higher education institutions in the 2018/2019 academic year



Figures 14. Distribution of BM students by universities

Breakdown of student numbers by university shows that most BM students are studying at RSU, which has traditionally been specialising in BM and offers studies at all study levels. RSU also has the largest number of foreign students in the medical sciences. UL, RTU, LSPA, in turn, are profiling in their respective directions of strategic specialisation.

7.2. Distribution by study levels in the 2018/2019 academic year

Table 2.

	Biomedicine	**Support**
College	2,571	836
Prof. bachelor	1,856	1,011
Acad. bachelor	795	155
Master's	487	79
2nd level higher education with qualification (Industrial Master's)	6	1
Prof. Master	801	460
Degree in medicine, pharmacology, dentistry	4,899	
Doctoral	346	34
Total	**11,761**	**2,576**

23.8% of students in the area of BM are college programme students (BM + Support), which highlights BM among the areas of specialisation. This is primarily due to the traditions of medical personnel training; first level higher education is the standard for work in the professions of nurse, radiology assistant, physician's assistant. In the college system of Latvia, medical professions account for 30% and are thus one of the most important pillars of the college system. This will change significantly with the reform of nursing education. Only 2.7% of students are involved in doctoral studies, which is too low to provide the area with highly qualified human resources.

8 Publications

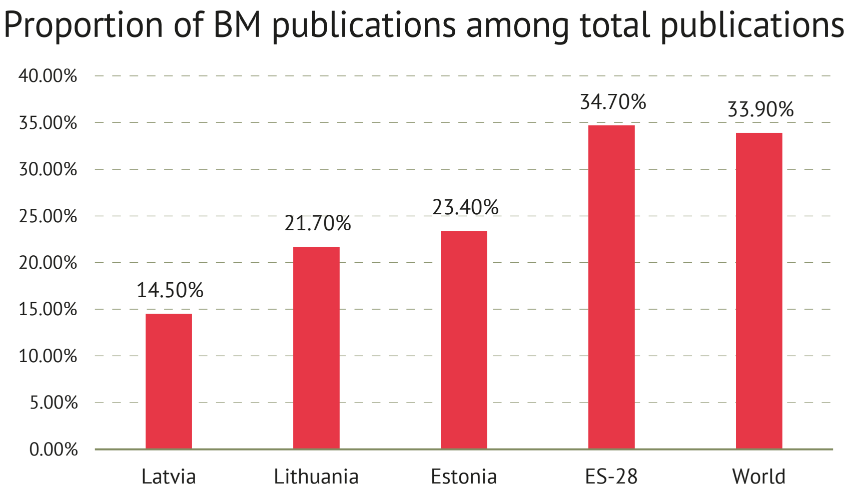


Figure 15. Proportion of BM publications. Source: INCITES

The mass productivity of Latvia's publications in the area of BM lags far behind the global indicators and is also significantly lower than in other Baltic countries. In Latvia, the formula dominating in the area of BM is – high quality publications, but relatively few. This could be explained by the fact that university excellence programmes are relatively underfunded, and therefore, there are relatively few publications in the area, since there is no financial pull, which also leads to comparatively lower university ratings in Latvia. The area of BM is especially promising for the significant increase in university ratings.

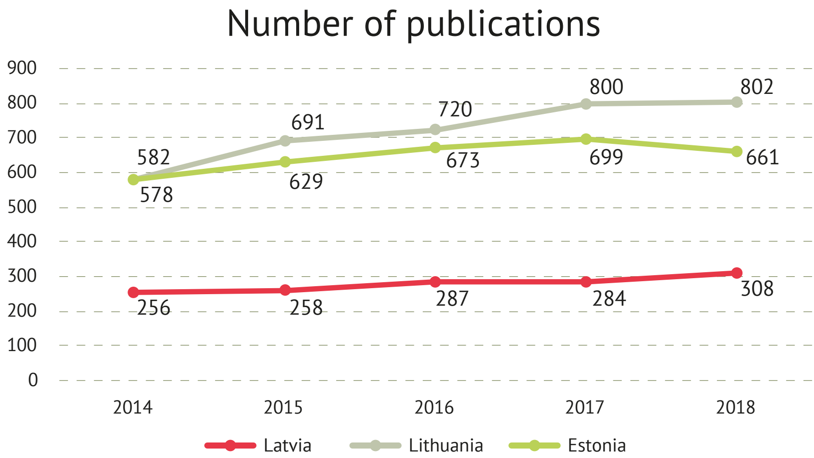


Figure 16. Number of BM publications in the Baltic states. Source: INCITES

By analogy, the number of publications over a 10-year period shows a relatively lower productivity in Latvia compared to Lithuania and Estonia. In terms of scientific quality, Latvia's performance is significantly better than that of Lithuania and is approaching that of Estonia. This is demonstrated both by the *CNCI* index compiled by *Clarivate Analytics*, as well as the high proportion of publications of 10% of the most cited publications. In all reporting years, this figure has been significantly higher for Latvia than for Lithuania, and convergence with the Estonian indicator is being observed.

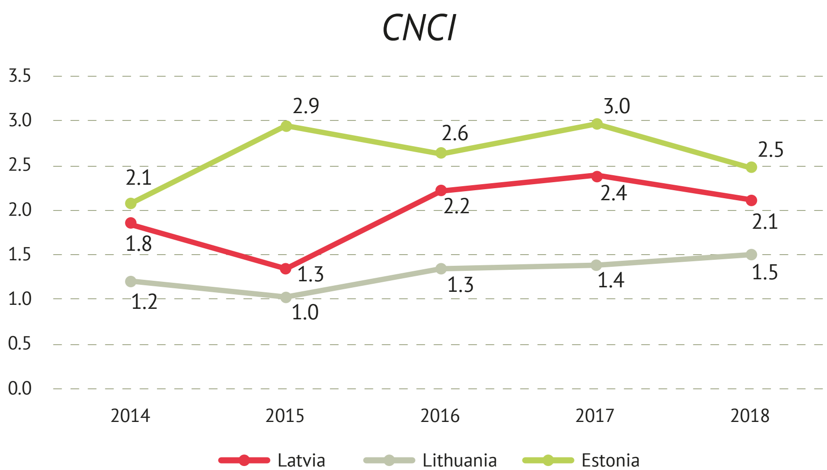


Figure 17. *CNCI* indicators during the BM reporting period. Source: INCITES

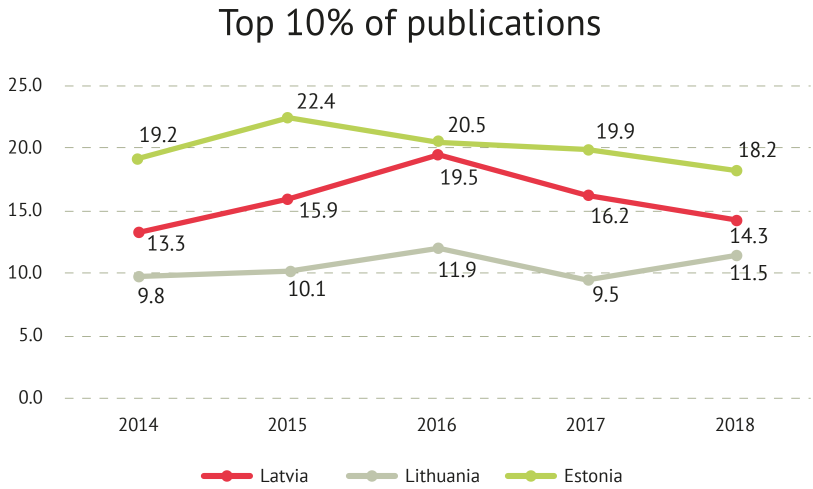


Figure 18. Proportion of publications among 10% of the most cited. Source: INCITES

The sectors with the highest *CNCI* figures are as follows:

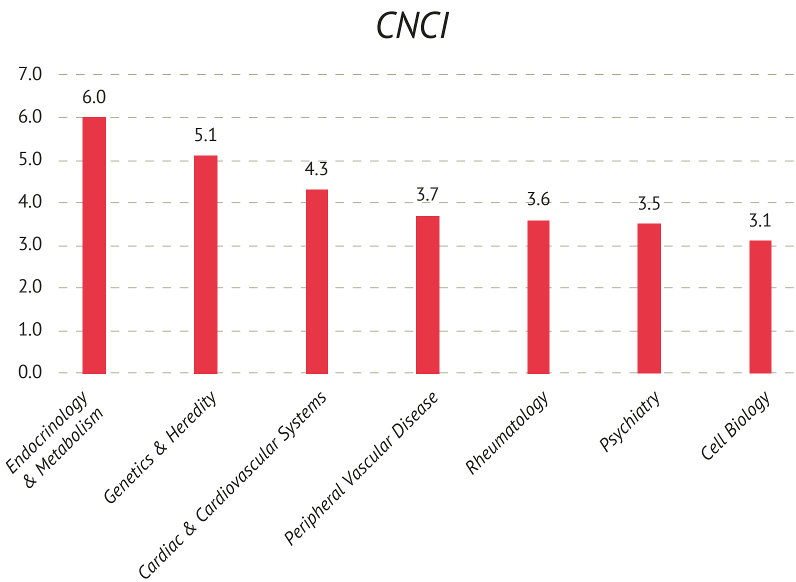
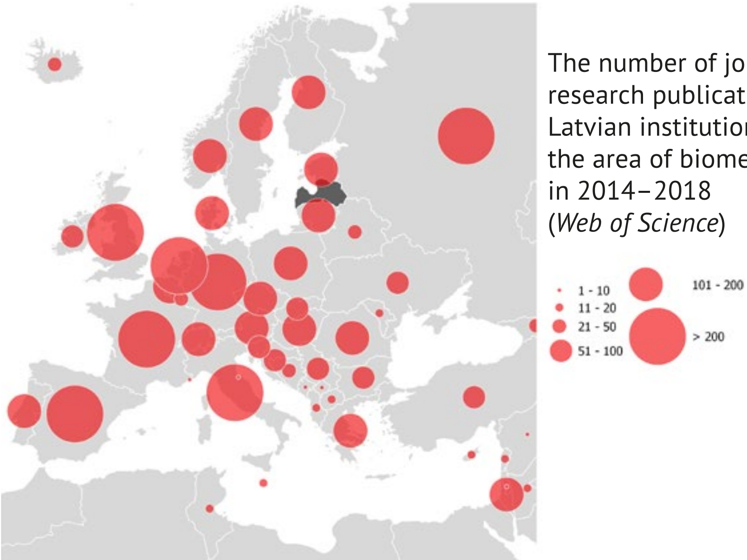


Figure 19. Industries with the highest representative *CNCI*. Source: INCITES

9 International co-operation

The leaders of cooperation with Latvian scientists in the area of BM are European countries; serious cooperation also exists with the United States and Russia.

The contribution of the 12 most important countries in co-operation is demonstrated in the graph.



Figures 20. Latvian co-operation publications in the area of BM. Source – *Web of Science*

Biomedicine is the area of RIS3 specialisation with the highest intensity of international cooperation, where, the analysis of the geographical location of the main cooperation partners demonstrates very wide cooperation with Western European countries at the European level. This is also the area of RIS3, where significant scientific cooperation with non-European countries is observed, which is evidenced by the high level of co-operation intensity with the USA, Japan, South Korea, countries of Southeast Asia and South America. The United States is particularly noteworthy, because although most of the joint publications in biomedicine involve co-operation with European countries, not only Germany, Italy and the United Kingdom, but also the United States are among the 4 countries with the highest cooperation intensity (> 250 joint scientific publications during this period).

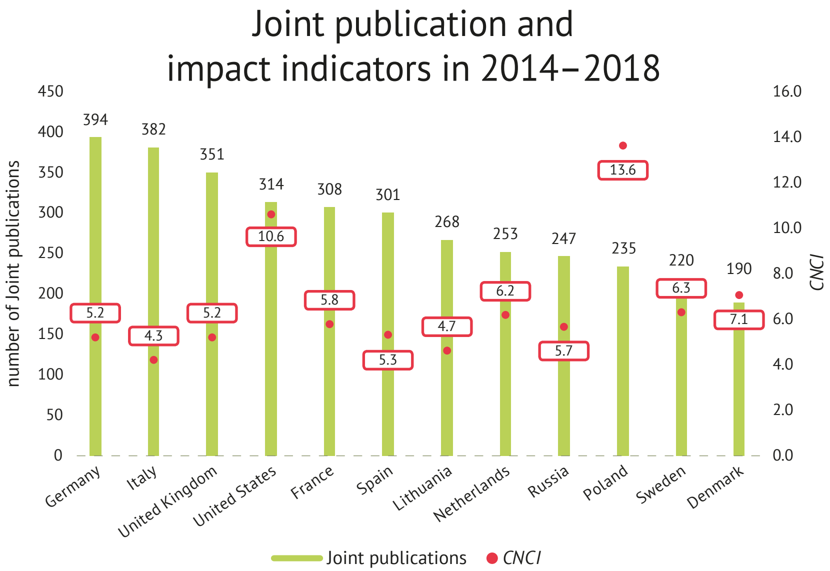


Figure 21. Collaborative publications and the corresponding *CNCI*

It should be noted that Germany, France and Italy are leaders in EU transnational cooperation instruments, of which *ERA-NET* is particularly noteworthy in the area of BM. Since Latvia is relatively active in the *ERA-NET* platforms of the BM sector, it promotes the creation of joint publications with other platform countries.

It is interesting to note that the *CNCI* impact indicator is better for publications in those international co-operation areas, where the number of total publications is lower. Obviously, the principle *less, but better,* works. But in any case, all these collaborative publications have an extremely high impact level, thus sending a clear message to policy planning: Cooperation in the area of BM is an absolutely necessary condition for excellence.

9.1. Co-operation network

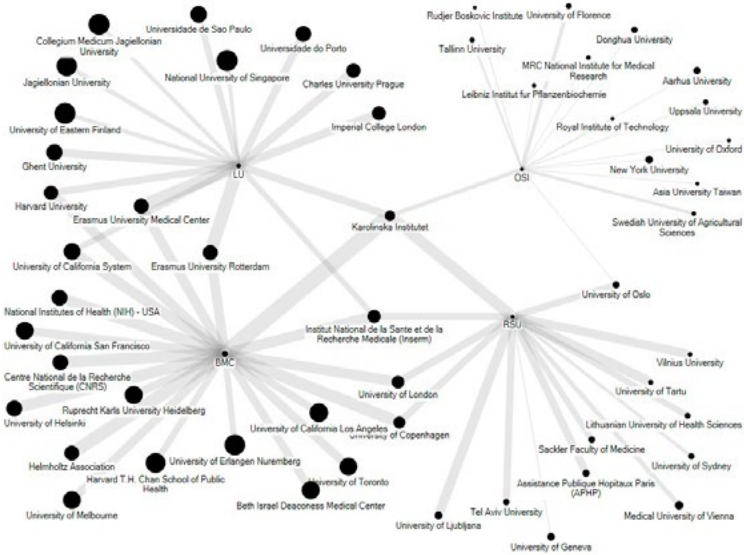


Figure 22. Co-operation network at the institutional level

All research organisations in the BM area cooperate with the most important BM research institution in the region – the Royal (Karolinska) Institute in Sweden. The collaboration network has the highest density in the event of BMC, which is determined by historical and intensive collaboration at European level platforms and organisations, *in particular the ESFRI* platforms BBMRI and *INSTRUCT*.

9.2. Special forms of collaboration

Latvia participates in a number of *ESFRI* platforms in the area of BM, practically all of which have developed an *ERIC* consortium as a legal form. *The ESFRI/ ERIC* map includes BBMRI (Biobank and Molecular Resources) *ERIC, INSTRUCT* (Structural Biology) *ERIC, EATRIS* (European Translation Centre) *ERIC*, *OPENSCREEN* (Substance Screening Repository) *ERIC* infrastructures. The *ESFRI* platform *MIRRIS* (microorganism collections), on the other hand, has not yet established an *ERIC* organisation; Latvia is participating in it at the appropriate preparatory stage, and the start of *ERIC* operation is planned in 2021.

10 Conclusions and recommendations

10.1. Conclusions of the first phase of RIS3 evaluation in BM

The further development of BM as a specialisation area of RIS3 depends on the following processes.

1. How effective are the translation (transfer) processes from the basic research phase to applied and further on to commercialisation?
2. Can we believe that the principle of *EDP* works and what are the forms thereof? How is academy-industry cooperation functioning?

The analysis conducted to date demonstrates the following situation.

1. Translational processes are operating insufficiently exactly due to insufficient transmission from basic research to applied research and application. This is demonstrated by the thematic discrepancy between the profiles of the projects implemented within the framework of Basic and Applied Research Programme, *H2020*, *ERA-NET* as more basic research, further on to the ERDF 1111 applied research support activity (partially also ERDF 1112, but the impact of this activity on practical research is weak; it is primarily a human resource development activity) and followed with the third phase - in the CF and Competence Centre programme. The three main research phases of the translation chain operate autonomously to a certain extent. Research organisations are trying to maintain a high level of research within a certain phase, while the transition to the next phase is risky and the management thereof is limited by existing tools. Projects tend to get encapsulated in one of these phases and develop an ever-increasing scientific excellence, while remaining within a certain phase. In principle there are three wheels that are rotating comparatively autonomously; the system is fragmented. This problem is known, therefore attempts have been made to create mechanisms that could activate the transmission to the next phase, such as the technology scout programme. International peer-review evaluation results in strong positive feedback. Another factor that limits the transmission along the product development chain is the fact that, in Latvia, the possibilities of implementing early *TRL* projects that are based on RIS priorities only exist in a small part of the ERDF 111 activity. Larger basic research programmes, such as the Basic and Applied Research Programme, do not have a direct link to RIS3, and more applied research is often uncompetitive in purely research excellence based funding instruments.
2. An element necessary for the operation of the *EDP* is an effective academia-industry co-operation, which is based on a well-established form of interaction. The following forms of cooperation are topical for BM in Latvia.
   a. Classical valorisation, which works relatively inefficiently. Revenues

from licensing in the area of BM are only possible in the event of IOS; at other RI they are rather low. The causes are primarily on the part of the business sector, which has a low absorption capacity; furthermore, a lack of resources for relatively expensive valorisation persists. Meanwhile, the principle of open innovation is poorly developed in Latvia, but there are positive trends, for instance, accelerated activity of the European Institute of Innovation and Technology in Latvia.

b. Provision of scientific services with high added value. This segment grows and the entry of new large customers is observed. In the event of complex technologies, the demand for scientific-technological services is growing compared to patenting and licensing. This is determined by the high cost of training and the purchase of infrastructure, to implement activities in-house, and outsourcing can be very beneficial for the business sector, since it does not require immediate investment and is economically flexible. Latvia still lacks a functional institutional system for the transfer of knowledge, similar to, for instance, the Steinbeis centres in Germany, which are based directly on the sale of know-how by research services.
c. *EDP* on the basis of human resources (industrial doctoral students) practically does not exist in Latvia, and does not play any role, while globally it is an important form of academia-industry cooperation.

Functioning of BM ecosystem can be quite successful, but it also has certain specifics.

1. On the business side, there is a need for high-level managers of research resources and methods throughout the product value chain, as the business sector needs to address the challenges of transition from the current product development stage to the next. Attracting human resources in the conditions of Latvia is associated with significant challenges in a highly qualified segment - there is a fragmentation of the labour market, there is no stable total manpower demand that would ensure a reasonable stable income for narrow specialisation experts.
2. There is a lack of transparency about the developments in the ecosystem, so the principle of discovery works better on the basis of knowledge that comes directly from research, be it in the start-up sector or in large companies with well-resourced development departments. Small and medium-sized enterprises appear to be the customers of research and development services and to a lesser degree autonomous innovators -.
3. A general problem in Latvia is the uncertainty about “sources” in ecosystems, i.e. financial resources, because the development of traditional credit-based business is impaired, and especially in the BM sector, where product development requires not only large financial but also time resources.

10.2. Recommendations

BM as an area of smart specialisation needs to be further developed by shifting the emphasis within the area. This can be done effectively through specialised thematic calls. BM is the main driving force for the increase of research excellence in Latvian science leading to improvement of university ratings. The entry of entrepreneurs into new sectors beyond the traditional ones requires significant public investment in capacity building and the implementation of pilot projects. The sector of economy specialising in BM is insufficiently active in terms of research and development. Therefore, long-term support mechanisms should be used. Individual funding programmes should taylored to ensure that excellence in basic research affects the value chain of product development. The comparatively good situation in the provision of human resources is a strong argument for the increased support of the sector in order not to miss the favourable period for attracting and renewing research personnel.

11 Research institutions

- **Natural sciences**
- **Material sciences**
- **Modelling**

University of Latvia (UL) was founded in 1919 as the centre of national higher education in the newly established independent Republic of Latvia. It was the leading research institution in the area of BM until the Riga Medical institute was formed as a separate entity. In 1990-ies the Medical faculty was re-established at UL, and this way UL combines the broadest spectrum of scientific areas, from natural sciences to applied medicine.

Staff number in BM – 357

Publications in BM in 2018 (INCITES) – 269

- Thereof Open Access – 33,8%
- Thereof with an international collaboration – 62,8%

- **Translational research**
- **Biomaterials**
- **Infectious diseases**

Rīga Stradiņš University originates in Riga Medical Institute, established 1950 as a very strong higher education and research establishment under the auspices of the Ministry of Health. It is the largest higher educational institution in Baltic region active in all healthcare and medical specialities, at all educational levels, and also a very competitive scientific institution. It has over 20% share of international students, and possesses specialised high-level clinical entities, like Institute of Dentistry.

Staff number in BM – 142

Publications in BM in 2018 (INCITES) – 181

- Thereof Open Access – 51,4%
- Thereof with an international collaboration – 44,2%

- **Chemical biology**
- **Drug design**
- **Structural biology**

Latvian Institute of Organic Synthesis (LOSI) has been established in 1957 under the auspices of Latvian Academy of Sciences, which was that time the major holder of scientific industry. Today an independent scientific institute, LOSI has an excellent track record in drug design and development, and has very strong collaboration with industry, excellent patenting record.

Staff number in BM – 198

Publications in BM in 2018 (INCITES) – 47

- Thereof Open Access – 74,5 %
- Thereof with an international collaboration – 46,8%

- **OMICS**
- **National biobank**
- **Bioinformatics**

Latvian Biomedical Research and Study centre started its activities in the area of molecular biology in 1993, via joining of several entities of Latvian Academy of Sciences and University of Latvia. Since 2006 it is an independent scientific institute with an important contribution to excellent basic biomedical research.

Staff number in BM – 102

Publications in BM in 2018 (INCITES) – 52

- Thereof Open Access – 71,2 %
- Thereof with an international collaboration – 67,3%

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within the framework of "Integrated national-level measures for strengthening interest representation for research and development of Latvia as part of European Research Area"

Ministry of Education and Science

THE NATIONAL DEVELOPMENT PLAN 2014-2020

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