Hub 11

Hub is the official newsletter of BBMRI-NL

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Second phase to set up unique NL-Biobank

BBMRI-NL joins forces with EPI2 and CTMM-TraIT

In July 2014, BBMRI-NL embarks upon its second phase: BBMRI-NL2.0. The new endeavour comprises BBMRI-NL and all the biobanks connected with it, and joins forces with two other Dutch projects that aim to facilitate innovative biomedical research: the European Population Imaging Infrastructure (EPI2) and the Translational Research IT project of the Center for Translational Molecular Medicine (CTMM-TraIT). The goal: a truly nationally integrated 'NL Biobank Research Facility', offering fully integrated access for research on how genetic and environmental factors contribute to disease. The Netherlands Organisation for Scientific Research, NWO, has awarded BBMRI-NL2.0 a grant of just over €9.8M as part of the National Roadmap of Large Research Infrastructures.

The research results from BBMRI-NL2.0 will drive new and improved ways to diagnose and predict disease, and highlight factors critical to disease prevention, healthy ageing or optimal development, and thus to the quality of life. Also, it will cement the Netherlands' leading position in biobank-based biomedical research. The envisioned NL-Biobank, with its content ranging from genes, molecules and images to their clinical cognate, will provide a unique repository of integrated data that makes BBMRI-NL2.0 a highly visible and attractive partner for international collaborations.

It has always been BBMRI-NL's aim to promote collaboration and bring together the various biobanking initiatives in The Netherlands. So, after enlisting some 200 Dutch biobanks (f.i. Generation R, the Netherlands Twin Register and Leiden Longevity Study) and joining forces with the Parelsnoer Institute (PSI) and LifeLines in 2012, the next step appeared clear, as director Cisca Wijmenga explains: "Biobanks are a goldmine of biomedical samples and data associated to it. They are expected to transform our understanding of disease mechanisms and contribute to new diagnostic tools and preventive measures. This however requires the integration of novel approaches and data from genomics, phenomics, imaging and computational sciences. We need to harmonize and standardize data and methods and enrich biobanks with additional levels of information, including the connection to national registries. And once data is gathered, it

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Professors Aad van der Lugt (photo Ton Everaers), Cisca Wijmenga (photo UMCG), and Gerrit Meijer (photo Jaap van Velthuisen, VUmc pathology photo service): building a truly integrated NL Biobank Research Facility.

Rainbow project 12: Phenotype 2.0 - proof of principle for large scale phenotyping: major depression

"We want to lay the foundation for harmonized phenotypic assessments in ongoing studies"

In October 2012, a stir was created at the World Congress of Psychiatric Genetics in Hamburg, when the findings of a GWA-study for schizophrenia were presented: more than one hundred loci had been found. The study confirmed what many researchers already believed, but had no evidence for: that major psychiatric disorders are subject to, and caused by genes. It triggered BBMRI-NL's Rainbow project 12, which will use existing biobank collections to set up a GWA-study into Major Depressive Disorder (MDD). Principal investigators are Professor Dorret Boomsma (VU University Amsterdam, Biological Psychology) and Professor Brenda Penninx (VUmc Psychiatry).

The idea is ingenious. Professor Boomsma explains: "The problem with research on psychiatric disorders is sample size. When you want to set up a relevant study for a disorder as common as MDD (13% of men and 24% of women in the Netherlands suffer from MDD at least once in their lifetime), you need thousands upon thousands of participants, who have been carefully phenotyped and for whom DNA and GWAS data are available. Moreover, at the moment, cohorts of subjects suffering from MDD are often compared on their genetic profiles to unscreened controls. This is a problem, as depression is so prevalent, and many controls thus may be cases. So we said: why don't we use the cohorts that are already there and contain DNA and GWAS data, and ask the participants of those studies to take part in a phenotypical assessment, to ascertain whether or not they have ever suffered from MDD, or are still suffering from it?"

An email was sent out to all biobanks

participating in BBMRI-NL, asking if they would be interested in participating in an MDD study. "As participating meant that they would have to approach their own participants, gather the information themselves—in a way that makes it possible to link the phenotypical assessment to the correct DNA and GWAS data, without revealing to any third party the identity of the participant—perform the meta-analyses and then provide us with the aggregated data, we knew we were asking for quite an effort on their part", says Professor Penninx.

Assessment tool

"But at the same time, we knew many biobanks would be interested. Firstly, because the data forthcoming from the phenotypical assessment remains in their possession. And secondly, because the tool we are going to build for the phenotypical assessment is not exclusively for psychiatric testing, it can be used for any phenotypical assessment. So participating in our study also means preparing your biobank for future phenotypical assessments, for instance yearly. The advantage of having such a tool readymade, and using the same tool as other biobanks, is evident."

Professor Boomsma adds: "Developing this assessment tool will help to strengthen the framework of data and knowledge already there. It will enable closer collaboration between biobanks and studies, and all new data can be gathered in a uniform way. And the phenotypical data need not be exclusively linked to DNA and GWAS data, it can also be tied to biological data, metabolomics for instance, such as is now being gathered and analysed in Rainbow projects 3 and 4. So you see, the 'web' becomes ever more closely knit."

Up until now, twenty-two biobanks have expressed their interest in participation in the MDD assessment, among which LifeLines (*n*=165,000), the Netherlands Twin Register (*n*=22,000), the Rotterdam Study (*n*=14,926), EPIC-NL (*n*=40,011), Leiden Longevity (*n*=3,359), and HEBON (*n*=27,000). In total, 397,905 samples are stored in the participating biobanks. "Allowing for the fact that not in all cases GWAS data has been gathered, we still are very hopeful that this amount of samples will lend us the scope to perform the meta-analyses we want", says Professor Boomsma. "We are very lucky to be able to perform imputation of the data through reference sets of the Genome of the Netherlands project, BBMRI-NL's first Rainbow project."

Beautiful data

Professor Penninx continues: "At any rate, the phenotypical assessment will give the biobanks—and us—beautiful, clean data, not only on the occurrence (and recurrence) of MDD in their participants, but also on which type of MDD; there are several subtypes, and until now, differentiation between those has never been properly performed. Our assessment will provide us with that information. And, of course the assessment will not only provide us with MDD cases, but also with screened controls."

Although some preliminary work has been ongoing for over half a year now, the official start data for the Rainbow project is 1 July, with a time scale of 36 months and a budget of ca € 795K. There are of course several challenges to be faced during the project. The development of the online tool is the first one, explains Professor Penninx: "The tool itself will be based on the Composite International Diagnostic Interview short form, or CIDI-sf. There have already been experiments with such an online tool in Australia and the USA, so that looks promising. The challenge lies in the encryption. How do you provide a key that at the same time guarantees anonymity to the participant, but can be traced back to the individual DNA and GWAS data? It is a puzzle, but one we will be able to solve."

"The biggest challenge is to persuade as many people as possible to participate", concludes Professor Boomsma. "For participants, the possibility of a better treatment for one of the most prevalent diseases will be a factor, but also the degree of anonymity with which they can participate. For the biobanks, we feel that the extra work incurred is well worth the trouble: the biobanks gain an online phenotypical assessment tool, plus they co-operate in gathering data for a project that will prepare the Netherlands for valuable future research and international collaboration."

RP12's principal investigators, Professors Dorret Boomsma (l) and Brenda Penninx (r). Photo: Thijs Rooimans

UMC Biobanks: ErasmusMC

"Building uniformity without comprimising diversity"

At ErasmusMC in Rotterdam, there are 52 clinical departments. Thirty-three of these have biobanks or are planning to set one up. How these biobanks are governed, how they store and process their samples and data, and what type of lab work is done on them, has always been pretty much up to the department concerned. Until now: a steering committee has been appointed to categorize and standardize the ErasmusMC clinical biobanks. Dr. Mieke Hazes is in charge of the committee.

You have your work cut out for you.
I do. And I asked for it myself (laughs). I had been in charge of the Arthritis Pearl (of the Parelsnoer Institute) at ErasmusMC for some years, when I was asked to set up a steering committee for biobanks. I stipulated that this committee would be in charge of all clinical biobanks at ErasmusMC. My experience with setting up a biobank for arthritis, 14 years ago, and the setting up of standards for the PSI biobanks within ErasmusMC made me feel that this was the right time to see if we could centralize all clinical biobanks, that is, set up the same systematology, using the same standards, set up freezer management, and so on.

Why hadn't such a project been set up before?
Well, the philosophy at ErasmusMC is, and always has been, 'let a thousand flowers blossom'. By that, we mean that we don't want to hamper the departments in their approaches by inflicting too many standards and rules. But it is also evident that, without standards and rules, collaboration and communication becomes much more difficult. So we are basically trying to find a middle way.

You are speaking only of the clinical biobanks, why is that?
There are, as you know, some major population biobanks at ErasmusMC: the

Rotterdam Study (ERGO), the Erasmus-Rucphen Family Study (ERF), and Generation R. These are long-established endeavours, with their methods and standards well in place. Telling the researchers who set up those biobanks that they should come 'into the fold', so to speak, would not be a good idea. Still, it is useful to take their methodology into account when we are setting up ours, of course. So we will be talking to the principal investigators, like Professor Cornelia van Duijn.

When you say 'a middle way', what do you mean?
Well, for instance, we don't have a physical central facility for the biobanks, and we don't know if there is enough space in ErasmusMC to set one up. So, the actual freezers might have to stay in the departments where they are now. That's not necessarily a bad thing, and also, I don't believe in trying to ban freezers and small biobanks in the departments, I don't think you can ever convince the researchers that they should put everything into central storage.
Also, I need to make clear that what we want to set up is a way of working that will prove profitable to the researchers, so that they will want to participate. They will gain by making use of standardized storage methods, uniform clinical data software, etc. There is no point in trying to force a system and a set of rules on the departments here; that would simply never work.

So, a system like in Maastricht Biobank, where a researcher enters into an agreement with the biobank, and certain lab analyses and preparatory tests can be performed at an attractive fee is more in line with what you are planning?
Yes, I think that is the way to go. But every biobank that does participate will have to store their clinical data in the same way, so as to be ready for the Electronic Patient File (EPF). That really is the trigger behind much of what we are doing, because the EPF forces us to find a way to store information that can be used outside our own departments. Uniformity is the mission; the challenge, building that uniformity without compromising the existing diversity.

Dr. Mieke Hazes: "The philosophy at ErasmusMC is, and always has been, 'let a thousand flowers blossom'. Photo: Thijs Rooimans

European BBMRI News

BBMRI-ERIC Vacancies: Quality Manager & IT/Data Protection manager

BBMRI-ERIC is looking for a Quality Manager and an IT/Data Protection Manager for its office in Graz, Austria. The Quality Manager will be responsible for quality management issues related to BBMRI-ERIC in close interaction with the Director General. The IT/Data Protection Manager will be responsible for IT strategy and core IT competencies in the BBMRI-ERIC Central Executive Management Office. Deadline for both applications is 15 July, 2014; anticipated start of work during Q4 2014. You can find the full vacancy text on http://bbmri-eric.eu/news

BBMRI-ERIC and EATRIS-ERIC sign MoU

EATRIS-ERIC (the European Infrastructure for Translational Medicine) and BBMRI-ERIC (the Biobanking and BioMolecular Resources Research Infrastructure) have signed a Memorandum of Understanding (MoU) in March. The MoU is the first step in a close collaboration between the two research infrastructures. The main objectives of this collaboration will be to advance the development of biobanking and translational research infrastructures, and to improve quality and access to biobanking and biomarker development resources and expertise throughout Europe. By combining the significant resources and expertise residing in these two permanent international infrastructures, Europe is better positioned to tackle the significant challenges of innovation in the age of personalized medicine.

BBMRI-LPC call for research proposals

BBMRI-LPC, the BBMRI organization for large population cohorts, has opened a call for research proposals. Researchers whose proposals are selected will gain access to the more than 1 million samples stored in the BBMRI-LPC member cohorts. The call is open until 15 July and mainly targets common disease research proposals (f.i. diabetes type 2, cancer, and cardiovascular disease). Research proposals involving metabolomics and/or genomics can also be submitted. Read the full call text on http://www.bbmri-lpc.org/node/48.

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is crucial to find uniform ways to make it available to the wider research community for translational research, while sticking to the ethical and legal issues related to data sharing. Allying BBMRI with EPI2 and CTMM-TraIT was a logical step, since it combines the gathering of various types of data—biobank data and population imaging data—with the processing of that data to make it optimally accessible for translational health care research."

Professor Aad van der Lugt, co-founder of EPI2, sees great synergetic advantages in the collaboration. "The quality of imaging is now at a standard where it offers relevant and valuable information for research. The combination of biobanking resources with imaging data can reveal links hitherto unthought of; images can be viewed as a source of biomarkers in their own right. With standardized data acquisition and automated post-processing in image analysis pipelines a broad range of quantitative imaging biomarkers can be extracted. These biomarkers have the unique benefit that they can provide temporal and localized information about the normal and diseased tissue. Therefore, image data will enrich biobanks".

Professor Gerrit Meijer (CTMM-TraIT) adds: "Even in public opinion, the big data debate is now starting to develop; of course, the questions being asked are mostly privacy questions. In research, the need for tools to render data accessible and shareable is prevalent. Our focus lies there: in unravelling the immense and growing amount of data, making it usable. BBMRI-NL and EPI2 are two major 'players' in the area of gathering data; joining forces with them means creating the opportunity for gathering data in a uniform way. So instead of unravelling a tangle, you build an infrastructure into which the several strands of data can be stored intelligently."

About EPI2

The European Population Imaging Infrastructure (EPI2) was initiated in 2011 by the NFU, the Netherlands NeuroImaging Network (3N) of the National Initiative Brain & Cognition (NIBC), and the Netherlands eScience Center (NLeSc). The infrastructure was put on the Dutch Roadmap for Large-Scale Research Facilities in 2012. The objective of EPI2 is "to establish a Dutch infrastructure for large-scale harmonized acquisition and analysis of medical images in controlled population cohorts, with open access to all users". Although started with a focus on healthy cohorts the infrastructure can also be used for patient cohorts. EPI2 aims to utilize advanced imaging for the prediction of optimal normal development, understanding the etiology and pathophysiology of disease, performing preclinical diagnosis, identifying persons at risk for disease, and developing preventive strategies. EPI2 is involved in large-scale projects such as the Rotterdam Study, ImaGene and the Biomarker Boosting project. It is also involved in the development of an ethical approach of incidental findings through imaging in research.

The first results for the population imaging infrastructure initiative EPI2 (€2.8M in 2013) include the inclusion of large-scale imaging in existing population health studies, a setup for harmonized data acquisition, development of the first image analysis pipelines, and the setting up of a neuroimaging data sharing working group.

About CTMM-TraIT

The CTMM Translational Research IT (TraIT) initiative was launched in October 2011 and aims to develop a long-lasting IT (information technology) infrastructure for the Netherlands that will facilitate the collection, storage, analysis, archiving and securing of the data generated in research projects. CTMM-TraIT will use proven IT to create an IT infrastructure to accelerate translational research. Since its inception, CTMM-TraIT has grown from 10 partners to 30, including the Dutch UMCs, PSI, DTL (Dutch Techcentre for Life Sciences), NLeSc, charities like the Dutch Cancer Society and the Netherlands Heart Foundation, and a broad range of private partners.

Key achievements of the CTMM-TraIT initiative include the TraIT OpenClinica service, the fully searchable, central research image archive 'Biomedical image archival and retrieval' (BMIA), a shared service centre, implementation of the tranSMART integrated data warehouse and research portal, and the implementation of the first BBMRI-NL biobank catalogue.

The National Biobank

The initiators of BBMRI-NL2.0 share the feeling that the onset of genomics and the modern imaging era has led to an urgent need for a national, standardized, biobank infrastructure to ensure the efficient use of research resources and avoid redundancy, to create more efficient research workflows, and to ensure effective data integration and data access. The national biobank infrastructure that BBMRI-NL2.0 aims to set up will enable ground-breaking biomedical research, resulting in the faster development and delivery of new life style interventions or ways to prevent disease, and the development of better diagnostics and therapeutics.

It will also ensure that the leading position of the Netherlands in this area of international science is maintained and enhanced. And, not unimportantly, such a large-scale, multi-faceted infrastructure will assist in generating the 'evidence base' required by registration and reimbursement authorities to assess the impact, quality and cost-benefit ratio of novel screening programmes, drugs and therapies.

News

Dorret Boomsma awarded Academy Professor Prize

The Royal Netherlands Academy of Arts and Sciences (KNAW) has awarded the Academy Professor Prize to Dorret Boomsma, Professor of Biological Psychology at VU University Amsterdam. She owes her reputation to her work setting up The Netherlands Twin Register in 1987.

Each year, two researchers are awarded the Academy Professor Prize, one in the humanities or social sciences and the other in the natural, technical or life sciences. The prize is a lifetime achievement award for researchers between 54 and 59 years of age who are regarded as world-class in their field. The prize consists of € 1 million, to be used for funding scientific research.

See also the article on Professor Boomsma and Professor Penninx' Rainbow project, pp. 2-3.

Human life expectancy regulator discovered

Investigators from the Netherlands Consortium for Healthy Ageing at the Leiden University Medical Center (LUMC), in cooperation with a European research team, have discovered a DNA variant on chromosome 5 that has a positive effect on human life expectancy. This information was recently published in the renowned journal Human Molecular Genetics.

Professor Slagboom (photo Thijs Rooimans)

The DNA variant found was significantly more common in people over the age of 90 than in those younger than 65. "People with this DNA variant have a 10% higher chance of reaching the age of 90 years," explains Professor Eline Slagboom, head of the study.

The genetic aging study is the largest ever performed into longevity anywhere in the world. "We were given the unique opportunity to compare the genetic material of over 20,000 people over the age of 85 from 10 European countries with that of over 75,000 younger people," says Slagboom.

The DNA segment identified does not code for a protein, but for RNA that controls other genes. "It is a regulator, a kind of genetic main switch, that may control dozens of other genes," explains Slagboom. "After APOE, a gene that increases the risk of dementia, among other things, this is the first regulator we have identified with a universal effect on longevity starting in middle age." Which genes are affected, and what tissues this regulator is expressed in, is currently being investigated.

Agenda

To submit your event to the agenda, send an email to m.heesakker@bbmri.nl, stating the name of the conference plus date, venue and a short description of the programme.

Finnish Gulf Biobanking Week - Tallinn, Estonia, and Helsinki, Finland, 22-27 September

No fewer than five biobanking-related events take place in Tallinn, Estonia, and Heslinki, Finland, in the week of 22-27 September:

TALLINN, ESTONIA:

22 + 23/9: the Annual EuroBioForum Conference - 'For research funders and performers in Personalized Medicine'. See www.eurobioforum.eu/2014;

23/9: BBMRI-LPC Forum Meeting - Transferring expertise from existing biobanks to emerging biobanks: 'Starting from Scratch'. See www.bbmri-lpc.org.

HELSINKI, FINLAND:

24/9: International Biobanking Summit III - 'Building the International Code of Conduct for Genomic and Clinical Data Sharing'. See www.p3g.org;

24 + 25 /9: HandsOn: Biobanks Conference -Biobanking with a 'Hands On' approach: Experience the Route, Idea labs and Ethics Café. See www.bbmri.fi;

26 + 27/9: BBMRI-LPC Practical Biobanking Workshop - For emerging biobanks: 'Learn How to Collect, Handle and Store a Large Population Cohort'. See www.bbmri-lpc.org.

NVHG symposium - Papendal, Arnhem, 2 and 3 October

The yearly symposium of the Dutch Society for Human Genetics (NVHG) carries the title 'The Genome: more than just 4 letters' and is organized together with VKGN, VKGL and NACCG. Speakers include Annelien Bredenoord (UMCU), Axel Visel (USA), and Malte Spielmann (Germany). Professor GertJan van Ommen will give the Galjaard lecture on Friday 3 October. See www.nvhg-nav.nl/

LifeLines conference - UMC Groningen, 8 October

The Netherlands' largest population cohort, LifeLines, organizes its third yearly conference. The topic of the conference is 'From Bench to Biobank: biomarker development and challenges of usage in cohort studies'. This year's keynote speakers will specifically address the use of biomarkers in biobank research, a rapidly increasing field. Program details will be announced later. See www.lifelines.nl.

Connecting Biobanks - Stadsgehoorzaal Leiden, 28 November

2014 marks BBMRI-NL's 5th anniversary, and this edition of Connecting Biobanks will reflect that. The programme highlights the various projects funded by BBMRI-NL, from Genome of the Netherlands to the ELSI-app, from the first Complementation project to the collaboration with large population cohorts, from the biobank catalogue to the 'Participant disclosure directive'. More details to come on www.bbmri.nl.

Protecting privacy *and* the public interest?

A note for those negotiating the General Data Protection Regulation

Authors: Mark Taylor, Edward S. Dove, David Townend

In January 2012, the European Commission proposed a General Data Protection Regulation to amend Directive 95/46/EC. The Council has not agreed its position on the Regulation or begun negotiations with the European Parliament but, in March 2014, the Parliament adopted its text of the Regulation.

Mark Taylor, (photo Uni of Sheffield) Edward S. Dove (photo Jean-François Ouellette) and David Townend (photo Alice Townend).

Articles 81 and 83 would enable Member States to legislate for an exemption from the need for explicit consent to research use of health data only where research serves 'a high public interest'. The meaning of this is not clarified (the Commission is delegated power to set a definition), but suggests use in only very limited circumstances.

This may be problematic from not only a research perspective. It is also unhelpful from the perspective of privacy protection. It suggests both that privacy is most appropriately protected through explicit consent and that, if the public interest is sufficiently 'high', the claim to this protection may be overridden. Some of the problems with this view of the relationship between privacy and the public interest can be illustrated by the debate now taking place in England.

The 2012 Health and Social Care Act permits the Health and Social Care Information Centre (HSCIC) to require the disclosure of confidential and identifiable patient information by health professionals, notwithstanding a lack of explicit patient consent. An early initiative under these powers, a programme to extract patient information from primary care records and link them with hospital data, has proven extremely controversial. The programme has been paused, for at least six months, while some of the issues are addressed and there have already been some statutory changes. While some concerns have been expressed in relation to the lack of explicit consent, this has not been the only – or even the principal – concern voiced. More prevalent have been concerns relating to transparency (despite a national 'letterbox drop'), control of purposes (especially commercialization), and lack of independent oversight. Many benefits, including those that could have public support, would be lost if explicit consent were required. However, the idea of public interest relied upon, while considered by the architects of the programme sufficiently 'high' to justify the use of patient data without explicit consent, offered insufficient assurance to the public that their privacy expectations would be respected.

If the synergy between privacy and the public interest had been better recognized, and the public interest in the programme had originally been conceived of as dependent upon patients' reasonable expectations, then some of the problems might have been avoided. The EU must develop a clearer determination of 'the public interest', and stop considering it something to be balanced against a claim to individual consent. The alternative may be the collapse of public trust and confidence.

About the authors

Mark Taylor is Senior Lecturer at the School of Law, University of Sheffield.

Edward Dove is an Academic Associate at the Centre of Genomics and Policy (CGP) at McGill University in Montreal.

Dr David Townend is Professor of Law and Legal Philosophy in Health, Medicine and Life Sciences at Maastricht University.

Correspondence to:
Mark Taylor, m.j.taylor@sheffield.ac.uk

Colophon
Hub 11, July 2014

Hub is the official newsletter of BBMRI-NL (Biobanking and Biomolecular Research Infrastructure).
It appears in a circulation of 1,000 copies and as a pdf on the BBMRI-NL website.
To subscribe to Hub, email info@bbmri.nl or register on www.bbmri.nl/en-gb/news/newsletter/subscribe-to-printed-newsletter. Subscriptions are free.

Contributions to this issue:
Mark Taylor, Edward S. Dove, David Townend

Photography:
Ivar Pel
Thijs Rooimans
for incidental credits see relevant photo captions

Lay-out:
Margot Heesakker - Heintz

Print: Printshop Ouwehand

BBMRI-NL is part of BBMRI-ERIC, and is funded by the Netherlands Organisation for Scientific Research (NWO).

BBMRI Biobanking and Biomolecular Resources Research Infrastructure