



“Science Advice and Non-Communicable Diseases” Perspectives from the Netherlands



A comprehensive top 100 university

Established by the People of the City and the Province of Groningen in 1614



1. Improving student success: from <50% 4-yr B.Sc. to > 75%
2. Strengthening research quality: rise in rankings: 113=>66
3. Strengthen internationalisation: from 7% intl to 21%
4. Contribute to solutions for societal challenges by quadruple helix: knowledge institutions, government, industry and the population



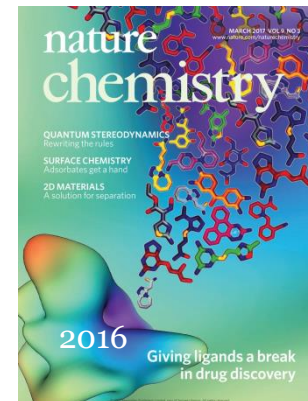
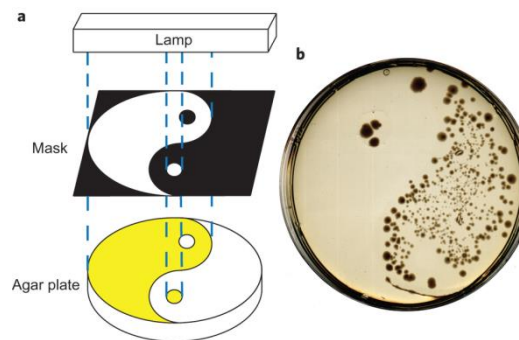
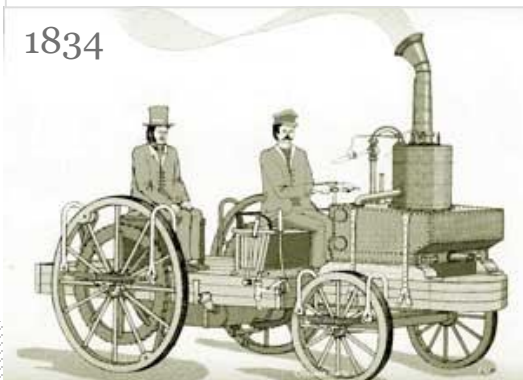
First electrical car in the world
Prof. Sibrandus Stratingh

1835







First steam engine car in
Groningen

1834



First molecular nanocar and first light switchable antibiotics
Prof. Ben Feringa



Institution	Post War Nobel Prizes	ARWU	Times
Utrecht University		51	74
University of Groningen	 	66	79
Leiden University		74	68
Erasmus University		79	70
University of Amsterdam		101-150	62
Free University Amsterdam		101-150	166
Radboud University		101-150	123
Wageningen University		101-150	59
Delft University of Technology		151-200	58
Maastricht University		201-300	128
Eindhoven University of Technology		301-400	167
Twente University of Technology		-	184
Tilburg University		-	201-250



university of
 groningen

Clinical Medicine: 2015-2019

Data from Clarivate Analytics

RANK	INSTITUTION	COUNTRY	ARTICLES 2010-2019	C/P 2015-2019
1	University of Oxford	UK	17,462	15.96
2	Yale University	USA	16,798	14.40
3	Imperial College London	UK	19,820	14.10
4	University of Cambridge	UK	11,326	13.88
5	McMaster University	Canada	12,791	13.87
6	Emory University	USA	17,299	13.68
7	Cornell University	USA	14,724	13.26
8	University of Barcelona	Spain	13,718	13.15
9	Erasmus University	Netherlands	18,372	13.08
10	UC San Diego	USA	14,728	13.07
11	Columbia University	USA	19,655	13.06
12	Harvard University	USA	83,159	13.03
13	University of Washington Seattle	USA	24,446	13.03
14	University of Alabama Birmingham	USA	14,261	12.91
15	Washington University St Louis	USA	16,796	12.90
16	UC San Francisco	USA	26,720	12.86
17	KU Leuven	Belgium	13,758	12.83
18	Vanderbilt University	USA	15,401	12.81
19	John Hopkins University	USA	35,889	12.74
20	University of Montreal	Canada	11,812	12.70
21	Stanford University	USA	22,755	12.60
22	University of Sydney	Australia	22,556	12.59
23	UC Los Angeles	USA	22,996	12.53
24	University of Oslo	Norway	12,312	12.47
25	Mount Sinai	USA	14,320	12.38
26	Northwestern University	USA	17,115	12.34
27	University of Groningen	Netherlands	13,203	12.28
28	Duke University	USA	23,286	12.26
29	University of Heidelberg	Germany	18,697	12.21
30	University College London	UK	28,225	12.11
31	Kings College London	UK	14,650	11.79
32	University of Pittsburgh	USA	24,823	11.76
33	University of Pennsylvania	USA	29,782	11.58
34	McGill University	Canada	14,079	11.55
35	University of Toronto	Canada	42,908	11.51
36	Mayo Clinic	USA	34,269	11.36
37	University of Zurich	Switzerland	12,211	11.35
38	University North Carolina Chapel Hill	USA	17,393	11.35
39	University of Colorado HSC	USA	13,855	11.30
40	University of Amsterdam	Netherlands	19,507	11.27



Clin Medicine: C/P last 10 years

Countries with more than 50,000 papers

8/14/2019 | 6

	Countries/Regions	Web of Science Documents	Cites	Cites/Paper
1	NETHERLANDS	101,559	2,378,936	23.42
2	SWITZERLAND	60,637	1,397,123	23.04
3	CANADA	134,617	2,941,606	21.85
4	ENGLAND	204,168	4,414,358	21.62
5	SWEDEN	58,944	1,257,444	21.33
6	FRANCE	125,411	2,545,988	20.30
7	ITALY	148,068	2,867,805	19.37
8	AUSTRALIA	116,173	2,175,238	18.72
9	USA	869,400	15,923,217	18.32
10	SPAIN	86,973	1,592,735	18.31
11	GERMANY (FED REP GER)	199,960	3,573,429	17.87
12	JAPAN	174,434	2,061,884	11.82

Multidisciplinary & Public participation

- 1. Healthy ageing (2005)**
(How to get more healthy years)
- 2. Energy transition (2010)**
(How to get from fossil to sustainable)
- 3. Sustainable Society (2015)**
(How to achieve a more...)



GLOBAL
CENTER ON
ADAPTATION



Modern Healthcare and Hygiene have prolonged the lifespan, resulting in an aging population.

However, now the major causes of illness are chronic diseases: obesity, diabetes, hypertension, cancer, heart/lung diseases, depression, dementia

Resulting in Living Longer with Disease

Hypothesis:

Chronic diseases result from combination of genetic, lifestyle and environmental factors.



Centenarians



Bien Bos-van der Laan
Born 1919
2189 >100 in Netherlands
85% are women





- › Malaysia 7% >65
- › China 10% >65
- › Netherlands 19% >65
- › Japan 27% >65

- Malaysia now: ~10% > 60 (3.5M)
- Malaysia in 2030: ~15% > 60
- Malaysia in 2040: ~20% > 60 (6.3M)



Consequences of Aging Population

Shortage in labour market

High Healthcare costs

High Pension costs

Results of Healthier Aging

Ability to continue working past 65

Lower Healthcare costs

Lower Pension costs



Pathologists know everything....

But too late...

Isn't this true for all of medicine?



*Medical science provides many answers...
But not to the big questions!*

*Why are some people healthy till old age
and others already have several diseases
during midlife?*

*Why are we ageing, when we have stem
cells to replenish damaged and old cells?*



university of
 groningen

European Research Institute on the Biology of Ageing



Question: What are the Biological
 Mechanisms of the Ageing of Stem Cells



rijksuniversiteit
 groningen



umcg



Ministerie van Economische Zaken





Question: What are the Biological Mechanisms of the Ageing of Stem Cells

Aim: Fundamental insights and breakthroughs, therapies

[Clearance of p16Ink4a-positive senescent cells delays ageing associated disorders.](#)

Baker DJ, **Wijshake T**, Tchkonina T, LeBrasseur NK, Childs BG, **van de Sluis B**, **Kirkland JL**, **van Deursen JM**.

Nature. 2011, 479:232-6.

[Local clearance of senescent cells attenuates the development of post-traumatic osteoarthritis and creates a pro-regenerative environment.](#)

Jeon OH, Kim C, Laberge RM, **Demaria M**, Rathod S, Vasserot AP, Chung JW, Kim DH, Poon Y, David N, Baker DJ, **van Deursen JM**, Campisi J, Elisseff JH.

Nature Med. 2017 23:775-781.



university of
 groningen



umcg



LifeLines



In 2004, a dream to build a large scale biobank to answer these questions and add healthy years for the inhabitants of the 3 northern provinces.

This dream became Lifelines, a prospective cohort study including 167,000 citizens (10% of the population).

Healthy Ageing became a strategic agenda, at UMCG, in the region, nationally and in Europe.

...How to get more healthy years...



university of
 groningen



LifeLines

since 2006

A **prospective** study following **167,000** participants in a **3-generation** design for at least **30 years**.

The focus is on **multifactorial** genetic, lifestyle & age-related disorders.

More than **8 million** samples in Lifestore.

Challenge: How to get more healthy years?

Question: What are the contributions of Genetics and Lifestyle to Health and Disease?

Aim: Personal Prevention and Precision Medicine



Ministerie van Economische Zaken



rijksuniversiteit
 groningen



umcg





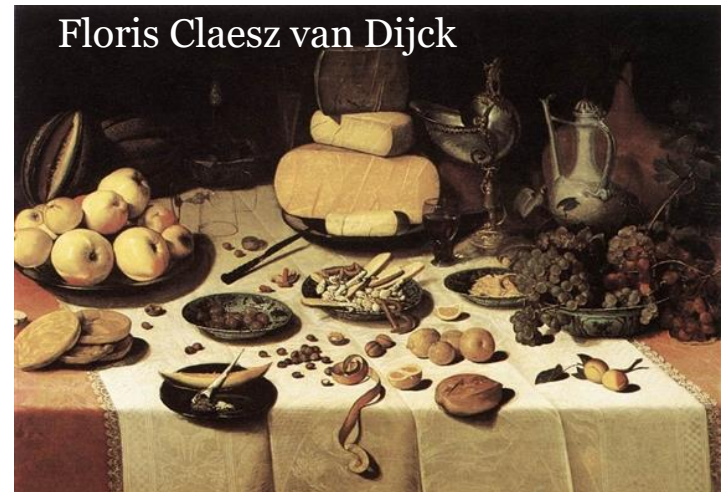
Res nonnaturales: Hippocrates, Galenus



1. De Lugt.
2. Spys en Drank.
3. Beweeging en Rust.
4. Slaapen en Waaken.
5. Ontlasting en Terughouding.
6. Gemordsbeweegingen.

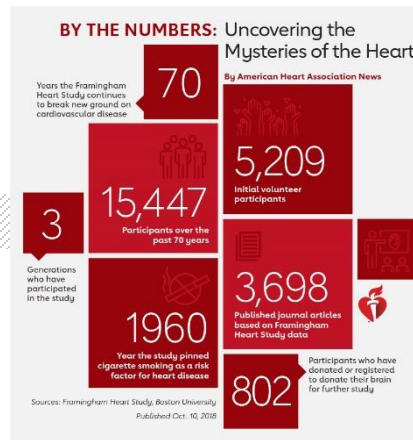
1. Quality of Air, Water, Climate.
2. Eating and Drinking.
3. Exercise and Rest.
4. Sleep and Wakefulness.
5. Excretion and Retention
6. Emotional Balance

- ❑ Jan van Wijck, 1775
- ❑ Lifestyle and environmental factors influencing our health.
- ❑ All are about the right balance.





university of
 groningen



Twenty First Century version of the Framingham study

- Around the same time in 2006, first (very expensive) technology became available to perform **large scale genetic association** studies enabling the identification of genetic **risk factors and profiles**.
- Lifelines aims to identify **actionable factors** that can help **prevent** disease by **empowering** and encouraging citizens.



- ❑ Pilot in 2006: 2,000; 2011: 50,000; 2013: 167,000.
- ❑ Probands aged 25-50 yr, spouses, parents, children.
- ❑ Thus 3-generations, mostly between 19 and 64, but also 12,000 over 65 and 15,000 under 18.

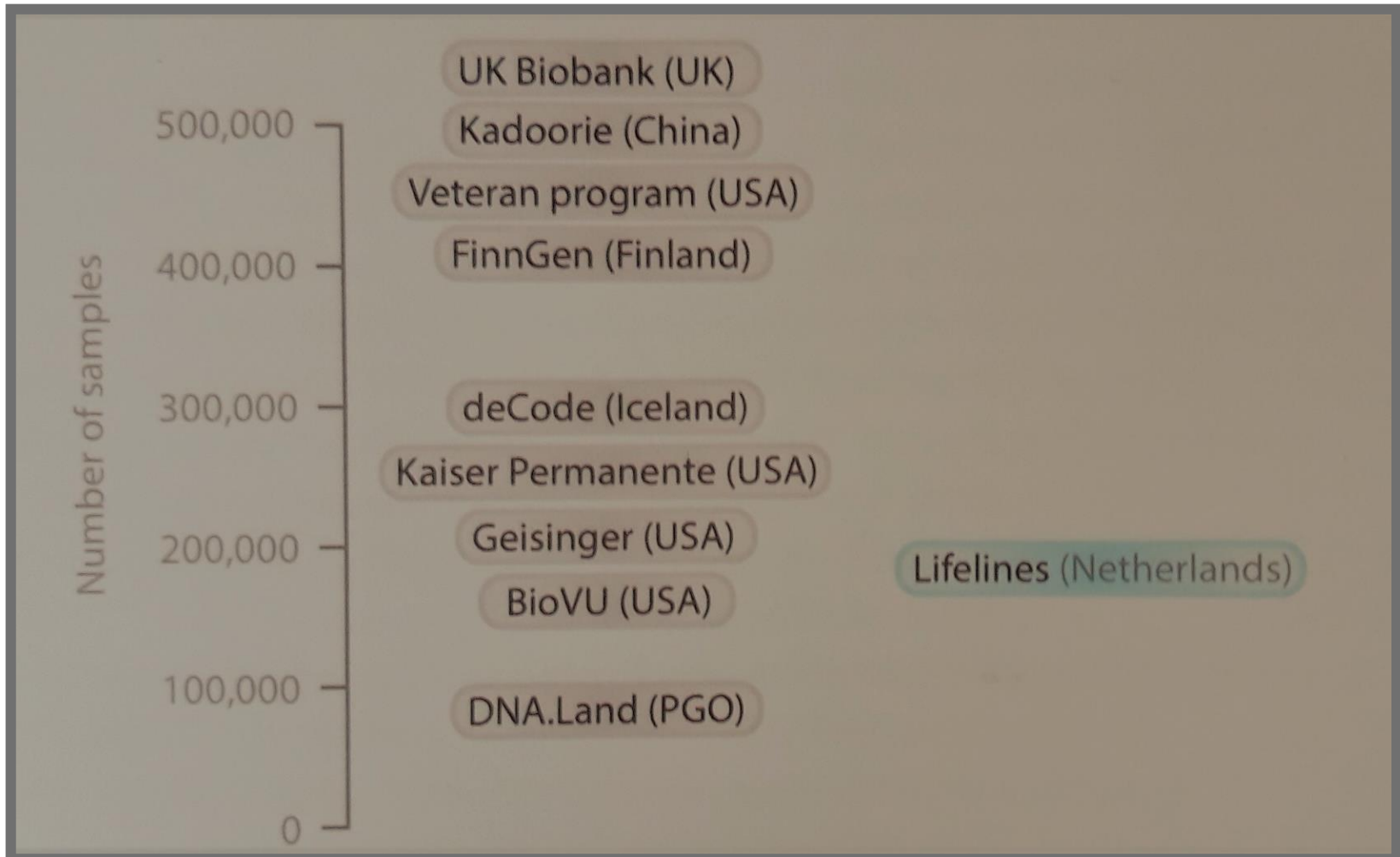
- ❑ Funding from EU, Dutch government and region
- ❑ Over 120 Million Euro (~ 10 M per year)
- ❑ Next years 8 M per year



- ❑ In Lifelines individuals are followed long enough (*>30 years*) to identify risk factors before disease development.
- ❑ The collection of data on non-genetic factors can be greatly enhanced by body monitors and/or smart homes (collaboration Philips Healthcare).



Smaller than some cohorts, but powerful in impact





Family-based design in 3 (4) generations

Now 4,500 families with at least 6 participants; based on municipal archives larger clusters of families can be identified.
UK biobank only collects single individuals.

Genetic homogeneity

The Northern Dutch population is a founder population.
UK biobank multiethnic

Prospective design

Five-year follow-up planned for all 167,000 over 30 years.
UK biobank will only follow 25,000.



Recruitment

Through their family physicians

Centers throughout the 3 Northern Provinces

All ages (0-93 years).

UK biobank only recruited 40-69 year olds.

Detailed medical history

Medication history as well as self medication use available.

Not in UK biobank.

Special phenotypes:

Thyroid, liver, immune, lung and kidney function measurements.

Not in UK biobank



Genetic studies

performed on subset of 14,000 (Nolte, Eur J Hum Gen)

Entire genome analysis

60 trio families in Genome of the Netherlands project
(Francioli et al, Nature Genetics 2014)

Currently genetic analysis

of additional 50,000 participants

lifelines timeline adults

pilot

2006 2007 2008 2009 2010 2011 2012 2013 2014 2015 2016 2017 2018 2019

baseline assessment

questionnaire 1A

visit 1A1: measurements
AGE reader, anthropometry, blood pressure, ECG, lung function test, RFFT, MINI, MMSE

visit 1A2: biological samples
fasting blood, DNA, 24-hour urine, fasting urine (EMS)

follow-up: questionnaire 1B

follow-up: questionnaire 1C

second assessment

questionnaire 2A

visit 2A1: measurements
anthropometry, blood pressure, ECG, lung function test, Cogstate, jump test, MINI

visit 2A2: biological samples
fasting blood, 24-hour urine, feces, scalp hair

follow-up: questionnaire 2B



- ❑ Data on heart, lung, kidney and liver function
- ❑ Blood for serum, plasma and DNA
- ❑ 24hr urine and morning samples
- ❑ Stool samples
- ❑ Total: 53 test tubes of biological material per participant

- ❑ Large warehouse, the Lifestore, built to store 8 million samples at -80°C

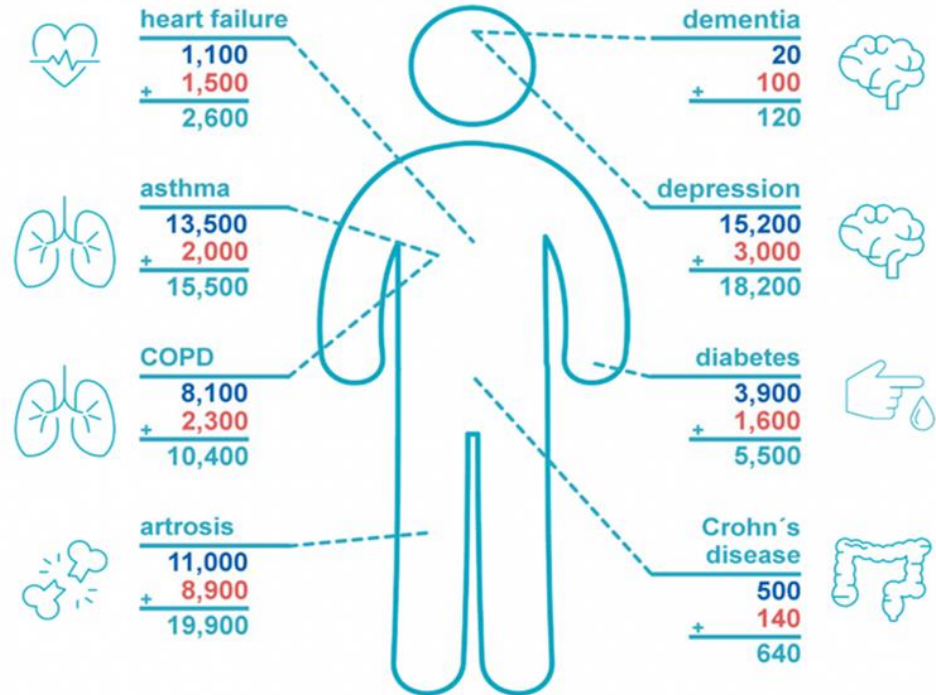




Detection of life-threatening diseases, like leukemia, heart failure, kidney insufficiency

Participants = Ambassadors

lifelines prevalence&incidence



participants baseline # participants follow-up # participants total

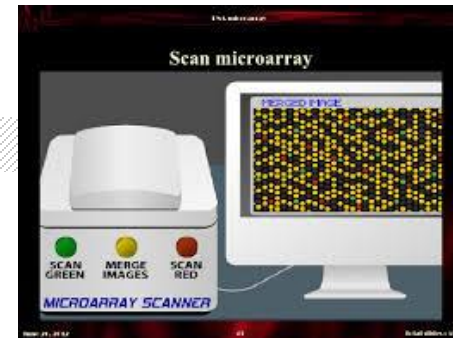
Self-reported data collected between 2006 and 2017

❑ 84,000 overweight, including 24,000 obese



- 3 million plasma and serum samples
- 2 million urine samples
- 54,000 hair samples
- 11,000 stool samples (analysis of gut flora),
constitutes largest collection in the world
- 10,000 nose and throat samples

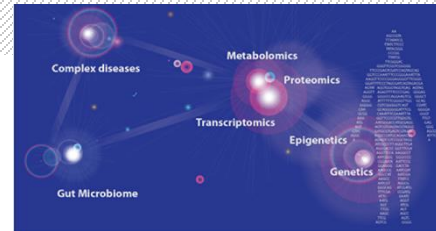




DNA array technology allows the analysis of genetic variation by genome-wide association studies (GWAS).

In 10 years, risk factors have been identified for most diseases and traits, explaining 10-50% of the total risk for a given disease.

This allows for prediction of individual risk of developing a disease, the so called polygenic risk profile.



Lifelines-DEEP (n=1,500)

Profiled DNA, RNA, proteins and metabolites as well as the microbiome. (Tigchelaar et al, BMJ Open 2015)

Lifelines-DAG3 (n=10,000)

Collected nose, throat and gut material to profile microbiome and culturing of life bacteria

Lifelines-NEXT (n=1,500)

Ongoing cohort with *4th generation* by including newborns from Lifelines participants (Wijmenga & Zhernakova) Nature Genetics 2018)



1. Genetics of Dupuytren's disease, (Dolmans et al, NEJM, 2011)
2. Genome of the Netherlands (Francioli et al, Nature Genetics 2014)
3. Largest microbiome study showing that life style factors determine gut flora (Zhernakova, Science 2014, Falcone, Science 2014) and gut flora is associated with diseases



1. Integrated health portal IkDus <http://ikdus.nl>

Platform implemented in Lifelines, that already has genetic risk profiles, gut flora profiles and pharmacogenetic passport. Innovative test environment for self monitoring devices

2. Newborn project (EU funded project) will test the use of smart toothbrushes, scales and health watches, baby monitors, sensors in diapers, environmental meters. **Participants will gather info and make this available for research: Citizen's Science**



- ❑ Funding more than 100 Million Euros for 10 yrs.
- ❑ For the next 5 years 8 Million per year available.
- ❑ At 100 Million, and 167,000 participants, this is less than 600 Euro (60 Euro/yr) per participant for 2 full physical exams, lab tests, storage of biomaterials.
- ❑ Lifelines already has saved many lives through early detection of cancer, heart, kidney disease.



1. Groningen on the map as top destination for genetic epidemiology and genomics
2. Has helped securing grants and personal grants
3. So far, more than 300 articles, including 42 in Nature* or Science
4. 10% of the population are proud participants and ambassadors
5. Value will increase with time passing!
6. Will enable **meaningful advise** and **interventions** in lifestyle and in healthcare provision.

Aletta Jacobs School of Public Health

Together for more healthy years



To Explore ▾

To Educate ▾

To Resolve ▾

We are Aletta ▾

Events ▾

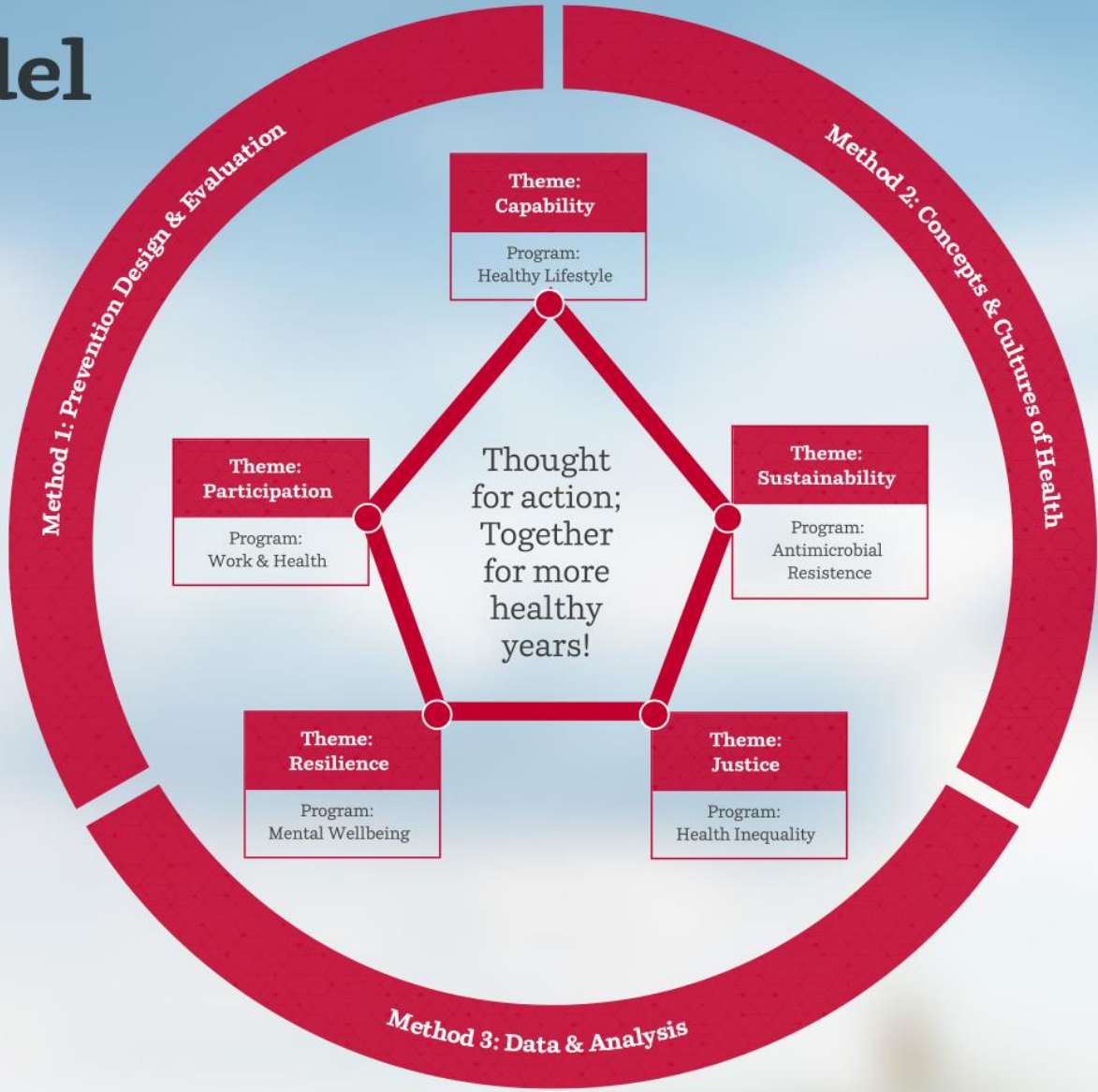
Q Search

Aletta Henriëtte Jacobs (February 9, 1854 – August 10, 1929) was the first woman who successfully graduated as a doctor and obtained a PhD in Medicine (University of Groningen).

She became the first female physician in the Netherlands, accomplished much in the field of medical care for the poor, and was a famous women's liberation activist.

In honour of her memory the school was named after her.

The Aletta model





Aletta Jacobs School of Public Health

Together for more healthy years



To Explore ▾

To Educate ▾

To Resolve ▾

We are Aletta ▾

Events ▾

Q Search

Scaling-up NCD Interventions in South-East Asia (SUNI-SEA)

The European Union has awarded a 4 million grant in order to enhance the prevention and control of chronic diseases in Myanmar, Vietnam and Indonesia. The grant was awarded within the H2020 research programme targeted at scaling up health interventions in Low/Middle Income Countries.

Thank you for your Attention



Groningen was named one of the European Commission's top three finalists for the accolade of European Capital of Innovation 2014.



university of
groningen

SUSTAINABLE
DEVELOPMENT GOALS



- ❖ At the Campus of **University College Fryslan**
Bachelor on Global Responsibility & Leadership (GRL) programme
Inspired by the 2030 UN Agenda for Sustainable Development



Network on Humanitarian Action
International Association of Universities

- ❖ 120 ECTS Erasmus Mundus Joint Degree Master in International Humanitarian Action is an inter-university multidisciplinary master.