NORMENT
Norwegian Centre for
Mental Disorders Research

CoE NORMENT - structure of the centre and scientific goals

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UiO : University of Oslo
Oslo University Hospital
UNIVERSITY OF BERGEN
Haukeland University Hospital
Norwegian Centre of Excellence
The Research Council of Norway

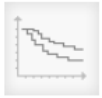
Research topics

Genetics

Disclose the complete genetic architecture of psychotic disorders and determine their functional impact

Brain Imaging

Identify novel brain imaging phenotypes linking genes and clinical phenotypes in a longitudinal setting



Outcome Prediction

Use genetic, environmental and clinical factors to predict disease progress and outcome

Clinical Intervention

Translate pathophysiological discoveries into clinical and pharmacological interventions

News

NORMENT

NORMENT is a Centre of Excellence (CoE) funded by the Research Council of Norway.

Our main goal is to find answers to why some people develop severe mental illness.

→ Read more about NORMENT

NORMENT in social media

Scientific vision for NORMENT

- **Disease mechanisms**
- **Tools for outcome prediction**

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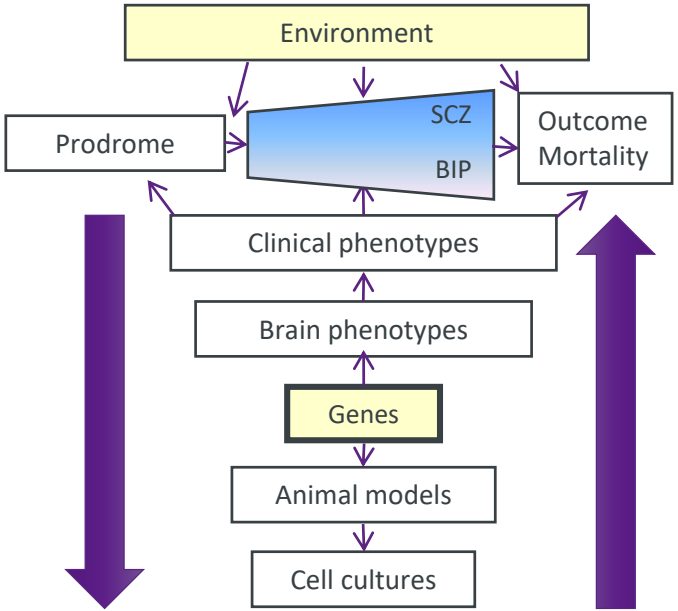
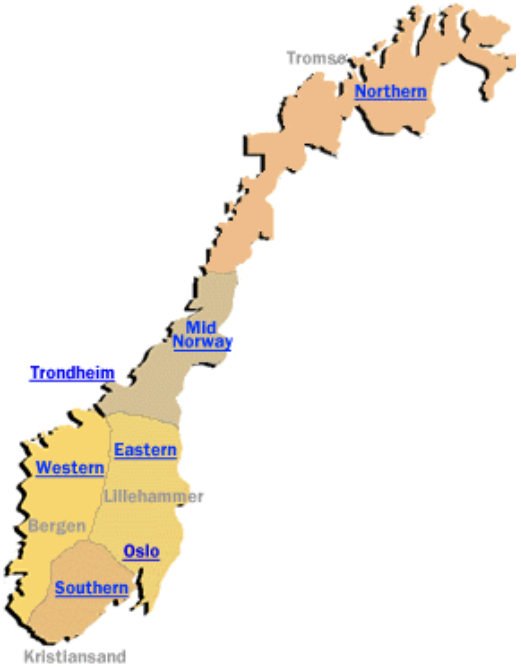
- Severe mental illness
  - Schizophrenia
  - Bipolar disorder
- New approach
  - Norwegian advantage
  - Vertical synergy

Added value of NORMENT

Vertical synergy



Norwegian advantage



Population-based: longitudinal and comorbidity

genotyped
N=400k

Registries
Birth registry
Diagnoses (NPR)
Pathology
Drug use
Cause of death
Family,
Education
Helath surveys

Analyses
Lab results
MR/CT results
Traditionel X-ray
Microbiology

PIN number

eHealth
Readmissions
Hospital acquiered inf.
Days in hospital
Health care costs
Income
Disability insurance

Biobanks
DNA
Plasma, serum
Sample tissue
Spinal fluids
Urine
Amniotic fluids
Saliva
Fecal samples
Genetic analyses

By courtesy of M Melbye

AIMS for NORMENT

- *Explore the underlying **pathophysiology** of psychotic disorders, based on our recent discoveries of genetic risk factors*
- *Develop **tools** for **stratification** and outcome **prediction**, and translate findings to clinical interventions*.

AIMS for NORMENT

Subgoals:

1) *Disclose the genetic architecture of psychotic disorders and determine their functional impact.*

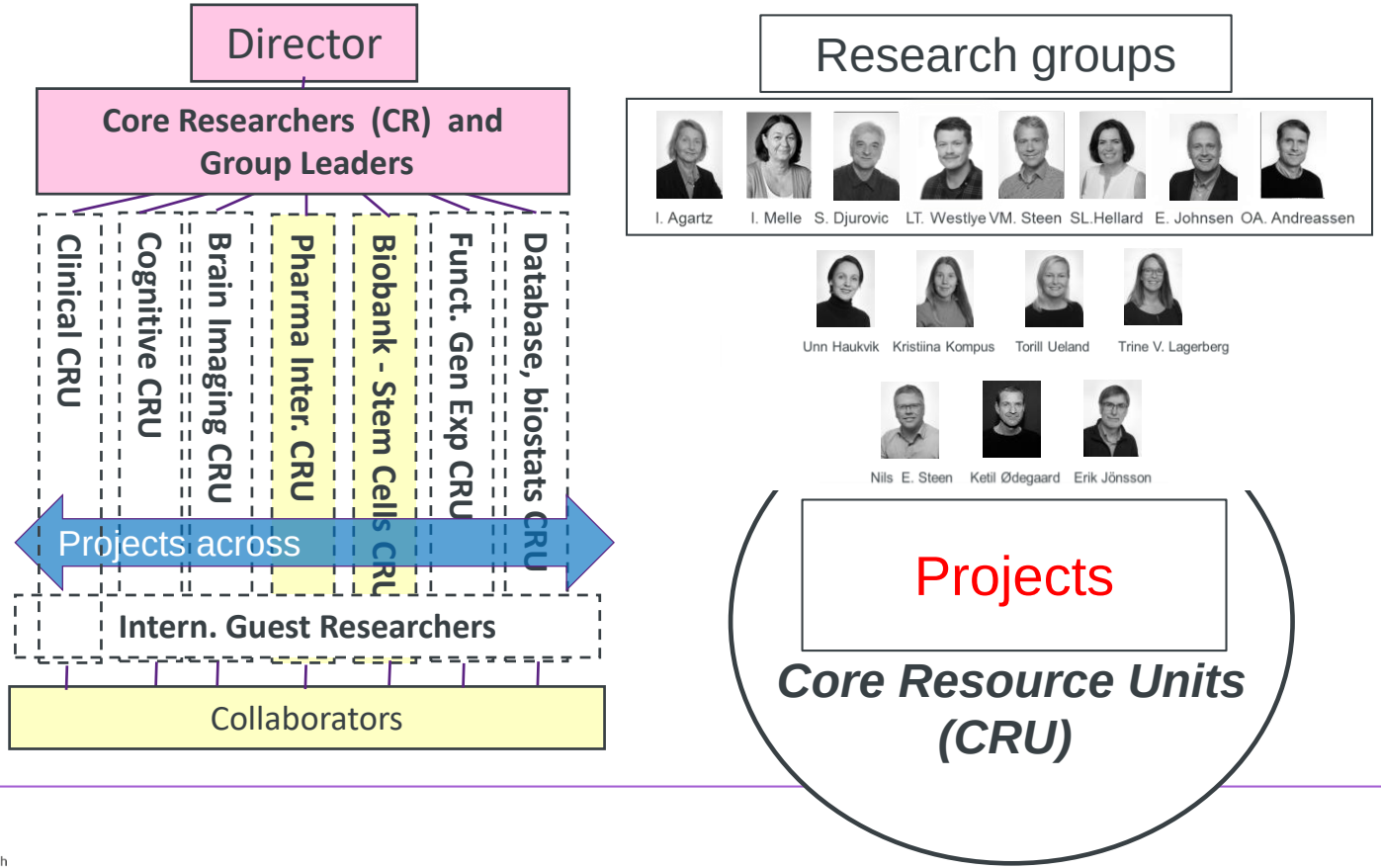
2) *Identify novel brain imaging phenotypes linking genes and clinical phenotypes in a longitudinal setting.*

3) *Use genetic, environmental and clinical factors to predict disease progress and outcome, applying novel statistical tools.*

4) *Translate pathophysiological discoveries into stratification strategies, prevention efforts and clinical interventions.*

Have fun!

Organisation - synergy



Database – Biobank Oct 2019

- Baseline case/control n=**3600** (cont=**1300**), total=**6600**
- Follow up case/control n=**1300** (cont=**270**)
- Neuropsych case/control : n=**2900** (cont=**1280**)
- Brain imaging case/control: n=**1850,** total n=**65 000** incl UKBiobank

- Genotyped: n=**700 000** incl MoBa, UKBiobank (2020: **900 000**)
- Immune: n=**5500** (**800** longitudinal)
- mRNA: n=**1800**
- Methylation: n=**2500**

Scientific production Oct 2019

- Publications (PubMed)
  - ✓total 649, last year 166 (Oct 2018)

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Nat Genet 8,
Nat Neurosci 1,
Nat Commun 4,

JAMA Psychiatry 2,
Am J Psychiatry 1,
Mol Psychiatry 8,
Biol Psychiatry 5,

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Background Big Data

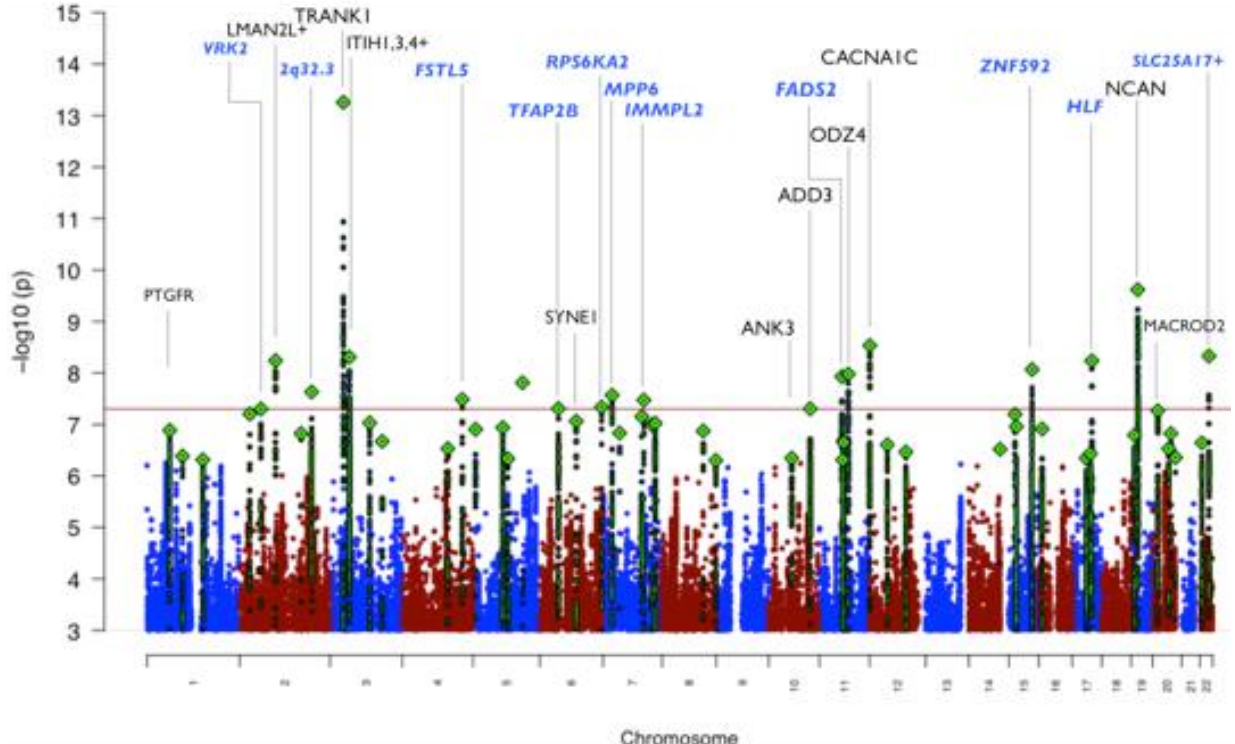
- Most common diseases are complex
  - Multiple genes and environmental factors
- Reduced genotyping costs
  - «Chipping (genotyping) your DNA is soon cheaper than parking at your hospital»
- Complex genetics: polygenic architecture
  - Many variants, each with small effect (OR 1.05-1.1)
- Brain imaging – new technology – data collection hospitals
  - multiple small effects
- *Small effects - The New Normal*

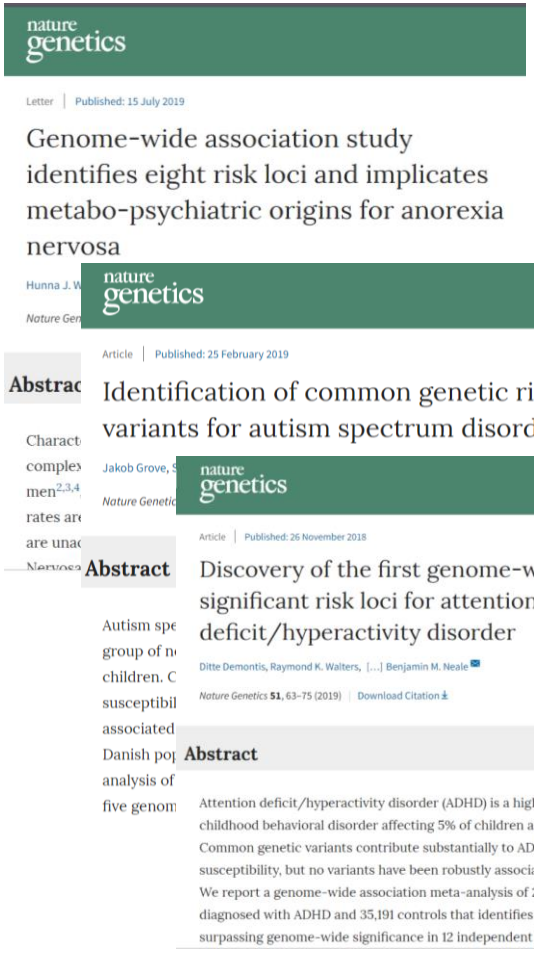
Paulus MP, Thompson WK. JAMA Psychiatry

nature genetics

Article | Published: 01 May 2019

Genome-wide association study identifies 30 loci associated with bipolar disorder





nature genetics

Letter | Published: 15 July 2019

Genome-wide association study identifies eight risk loci and implicates metabo-psychiatric origins for anorexia nervosa

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Nature Gen...

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nature genetics

Article | Published: 25 February 2019

Identification of common genetic risk variants for autism spectrum disorder

Jakob Grove, S...

Nature Genetic...

Abstract

Autism spe... group of n... children. C... susceptibil... associated... Danish pop... analysis of... five genom...

nature genetics

Article | Published: 26 November 2018

Discovery of the first genome-wide significant risk loci for attention deficit/hyperactivity disorder

Ditte Demontis, Raymond K. Walters, [...] Benjamin M. Neale

Nature Genetics **51**, 63–75 (2019) | Download Citation

Abstract

Attention deficit/hyperactivity disorder (ADHD) is a highly heritable childhood behavioral disorder affecting 5% of children and 2.5% of adults. Common genetic variants contribute substantially to ADHD susceptibility, but no variants have been robustly associated with ADHD. We report a genome-wide association meta-analysis of 20,183 individuals diagnosed with ADHD and 35,191 controls that identifies variants surpassing genome-wide significance in 12 independent loci, finding

nature genetics

Article | Published: 25 March 2019

Gene expression imputation across multiple brain regions provides insights into schizophrenia risk

Laura M. Huckins, Amanda Dobbyn, [...] Eli A. Stahl

Nature Genetics **51**, 659–674 (2019) | Download Citation

nature genetics

Article | Published: 19 August 2019

A global overview of pleiotropy and genetic architecture in complex traits

Kyoko Watanabe, Sven Stringer, Oleksandr Frei, Maša Umićević Mirkov, Christiaan de Leeuw, Tinca J. C. Polderman, Sophie van der Sluis, Ole A. Andreassen, Benjamin M. Neale & Danielle Posthuma

Nature Genetics **51**, 1339–1348 (2019) | Download Citation

Abstract

After a decade of genome-wide association studies (GWASs), fundamental questions in human genetics, such as the extent of pleiotropy across the genome and variation in genetic architecture across traits, are still unanswered. The current availability of hundreds of GWASs provides a unique opportunity to address these questions. We

nature genetics

Comment | Published: 15 April 2019

Roadmap for a precision-medicine initiative in the Nordic region

Pål Rasmus Njølstad, Ole Andreas Andreassen, [...] Kári Stefánsson

Nature Genetics **51**, 924–930 (2019) | Download Citation

The Nordic region, comprising primarily Denmark, Estonia, Finland, Icela... for b... inclu... and ...

nature genetics

Article | Published: 07 January 2019

Genome-wide meta-analysis identifies new loci and functional pathways influencing Alzheimer's disease risk

Iris E. Jansen, Jeanne E. Savage, Kyoko Watanabe, Julien Bryois, Dylan M. Williams, Stacy Steinberg, Julia Sealock, Ida K. Karlsson, Sara Hägg, Lavinia Athanasiu, Nicola Voyle, Petroula Proitsi, Aree Witoelar, Sven Stringer, Dag Aarsland, Ina S. Almdahl, Fred Andersen, Sverre Bergh, Francesco Bettella, Sigurbjorn Bjornsson, Anne Brækhus, Geir Bråthen, Christiaan de Leeuw, Rahul S. Desikan, Srdjan Djurovic, Logan Dumitrescu, Tormod Fladby, Timothy J. Hohman, Palmi V. Jonsson, Steven J. Kiddle, Arvid Rongve, Ingvild Saltvedt, Sigrid B. Sando, Geir Selbæk, Maryam Shoai, Nathan G. Skene, Jon Snaedal, Eystein Stordal, Ingun D. Ulstein, Yunpeng Wang, Linda R. White, John Hardy, Jens Hjerling-Leffler, Patrick F. Sullivan, Wiesje M. van der Flier, Richard Dobson, Lea K. Davis, Hreinn Stefansson, Kari Stefansson, Nancy L. Pedersen, Stephan Ripke, Ole A. Andreassen & Danielle Posthuma - Show fewer authors

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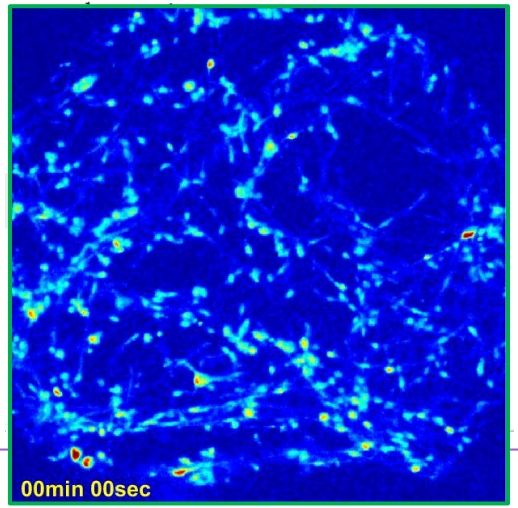

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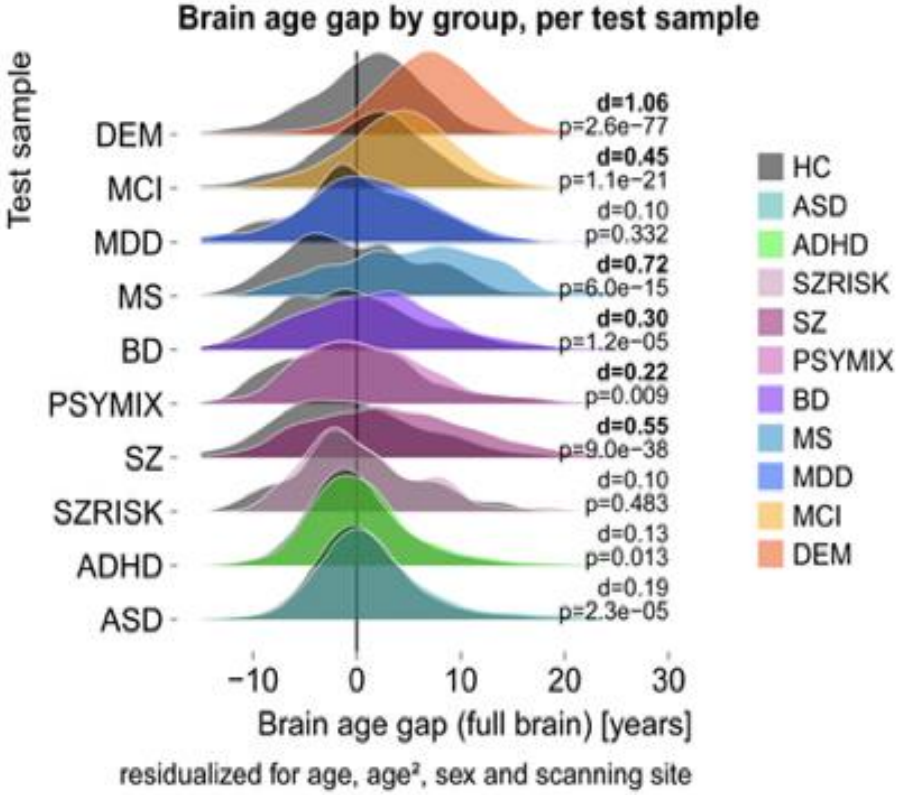
Have fun!

Common brain disorders are associated with heritable patterns of apparent aging of the brain



Kaufmann et al., *Nat Neurosci* 2019

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Journal of Affective Disorders
Volume 256, 1 September 2019, Pages 348-357

Research paper

Tobacco smoking and other substance use disorders associated with recurrent suicide attempts in bipolar disorder

R. Icick [a, b, c, d], I. Melle [e, f], B. Etain [a, b, c, d], P.A. Ringen [e], S.R. Aminoff [e, f], M. Leboyer [d, g, h, i], M. Aas [e, f], C. Henry [d, h], T.D. Bjella [e, f], O.A. Andreassen [e, f], F. Bellivier [a, b, c, d], T.V. Lagerberg [e, f]

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https://doi.org/10.1016/j.jad.2019.05.075

INTPART

PREDICTOR SUICIDAL BEHAVIOR?
Tobacco smoking and other substance use disorder can be risk factors of suicide attempts recurrence in bipolar disorder - clinical implication

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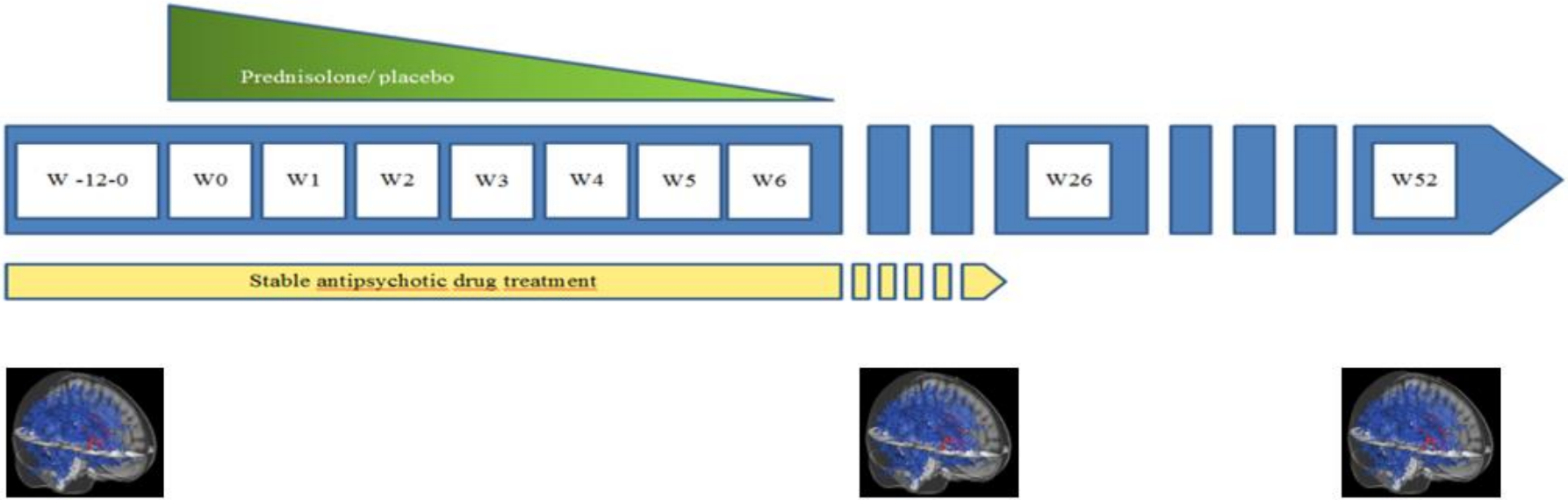
Schizophrenia RCT – Immune modulation



Johnsen et al.

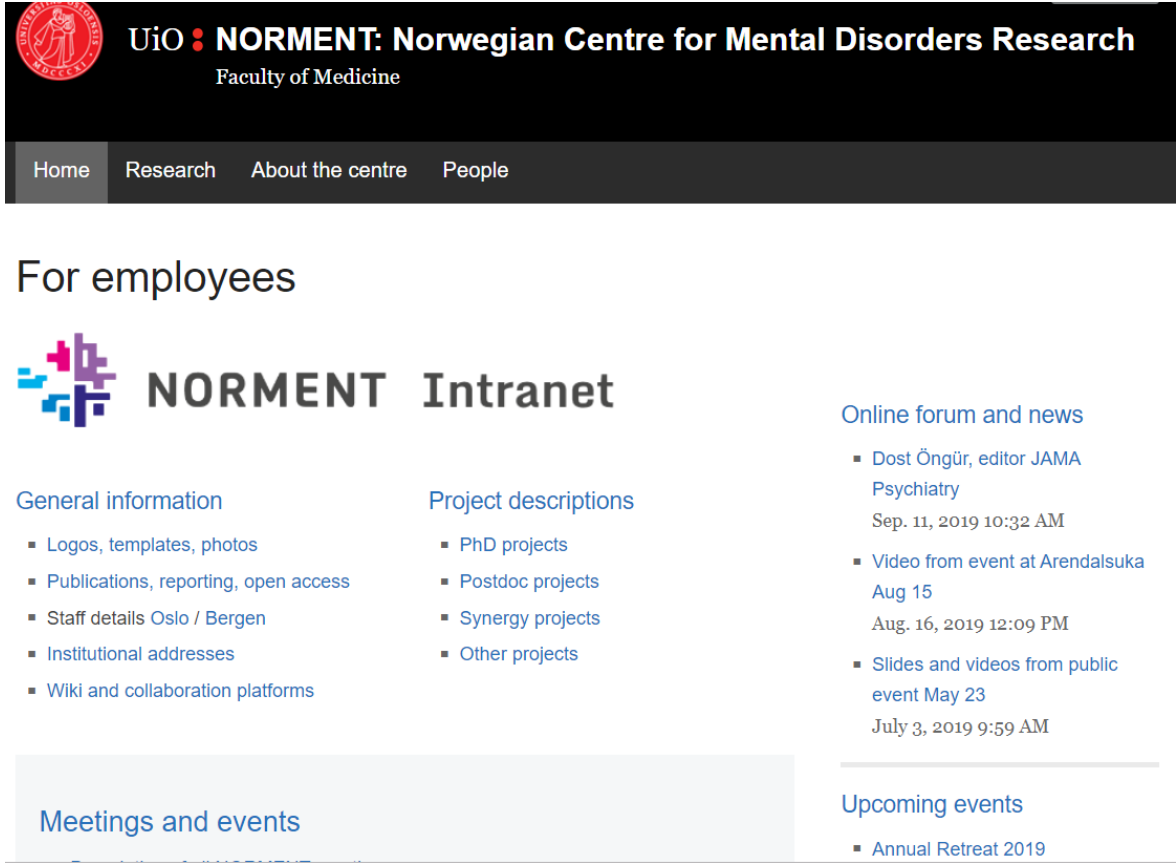
eNORMENT

Digital - data collection

Real life (apps)

Web based recruitment

Wiki, intranet

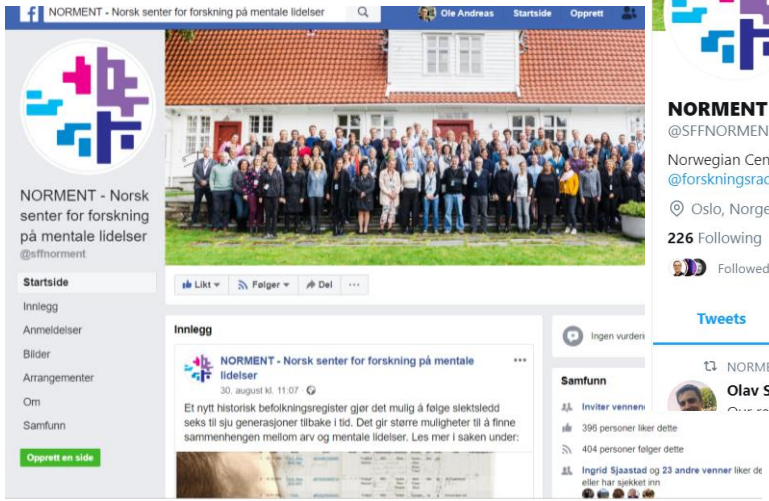


User group and dissemination

Twitter

Facebook

Open meetings



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- Study participants
- PGC, ENIGMA, deCODE, UCSD, ImageMend
- NORMENT team:

Opportunities Moscow-Oslo Collaborations

Viking age