CANDIDATE GENE STUDIES AND GENOME WIDE ASSOCIATION STUDIES (GWAS) ON HEALTH-RELATED QUALITY OF LIFE (QL) OF MOTHERS AND YOUNG CHILDREN; THE GENERATION R STUDY

Hein Raat, MD, PhD
Erasmus MC – University Medical Center Rotterdam
Vincent Jaddoe, MD, PhD
Cornelia van Duijn, PhD
Albert Hofman, MD, PhD
Andre Uitterlinden, PhD
Erasmus MC - University Medical Center Rotterdam
Jeanne M. Landgraf, MA
HealthActCHQ, Boston, MA

Genetic Disposition & Patient-reported Quality of Life Outcomes
AMC Amsterdam meeting, 2-3 December 2009
Background

• Determinants of health-related quality of life and other patient-reported outcomes:
  Biological, psychological and environmental

• Study the role of genetic factors:
  Direct effects
  Interaction with other factors
Background

- Mother and Child Care & HR-QoL:
  
  Women (Mothers): Self-report measures
  Children: Proxy-reports (~mothers)

The proxy’s traits may affect response
Background

- Public Health:
  Explaining socio-economic and ethnic differences in health, and perceived health
  
  Do genetic factors play a role?

  ![Diagram]
  
  SES/Ethnicity → Mediators → (Perceived) Health
  Genetic factors

  ???
Aims / This presentation

• Study of genetic factors associated with HR-QoL Mother and Child:
  1. Gene-finding (GWAS) → Children
  2. Candidate gene studies → Mothers & Children

• This presentation:
  1. Generation R study
  2. Genetic information and HR-QoL
  3. Collaboration
Generation R Study: Rotterdam birth cohort study

- Inclusion in early pregnancy
  - 2002 – 2006 (Now: 4-7 yrs old)
  - n=9,778 mothers
  - mean age 29.7 (SD 5.3)
  - 58% Dutch ethnicity
  - 55% first pregnancy

- Postnatal informed consent n=7,893 life born children

- 2008-2011 Renewed consent: GenerationR@5
Generation R: Research areas

(1) growth and physical development
(2) behavioral and cognitive development
(3) diseases in childhood
(4) health and healthcare for mothers & children

Many PRO's, including HR-QoL
Generation R HR-QoL measurements: Women (mothers)

• Pregnancy:
  18 weeks: SF-12, EQ-5D, VAS
  25 weeks: SF-12
  32 weeks: SF-12

• After birth:
  2 months: SF-12, EQ-5D, VAS
  6 months: SF-12
Generation R HR-QoL measurements: Children (proxy reports)

- **1 year old:**
  - Infant-Toddler Quality of Life (ITQOL) Q.
  - Generic health profile measure; 103 items; 12 scales

- **2 years:**
  - ITQOL (subset 55 items)

- **3 years:**
  - Health Status Classification System-Preschool (HSCS-PS)
  - Preference-based measure; 12 dimensions; 3-5 levels

- **4 years:**
  - Child Health Questionnaire Parent Form (CHQ-PF28)
  - Generic health profile measure; 28 items; 13 scales

- **5/6 years:**
  - CHQ-PF28
DNA

• Blood mother (mid&late pregnancy):
  8,055 samples
  DNA extraction
  25 (candidate) genes

• Cord blood newborns (& child blood 5/6yrs)
  5,908 samples
  DNA extraction complete
  Genome wide association scan
  (Illumina 610K platform)
Genetics of HR-QoL

• Monogenic traits
  ‘Easy’

• Polygenic traits
  e.g. 50 genes interacting with environment
  Law of independent assortment
  Only (e.g.) 0.2% or 2% variance explained

Samples of 50,000 required (ideally)
Replication studies needed
Gene finding
Replication earlier results
Candidate genes studies

• Genome wide association studies (GWAS)
  Children in Generation R (n=6,000)

• Replication or Candidate gene studies
  Children (n=6,000)
  Women (Mothers) (n=8,000)
Conclusions

• Large and multiple samples are needed to study genetic disposition of PRO’s

• Collaboration is therefore essential

• Generation R study offers collaboration

  Women/mothers: Candidate gene studies
  Replication of results

  Children: GWAS
  Candidate gene studies
  Replication of results