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BMD meta-analysis - Replication phase - 1st teleconference

Date: 19-02-2010 16:00-17:00 h (CET)

Attendees

Present	**Abscent**
Rotterdam: Fernando Rivadeneira & Karol Estrada	UFO: Ulrika Pettersson (Apologies)
DeCode: Unnur Styrkarsdottir	AOS: Kim Brixen (Apologies)
APOS: Lynne Hocking	FLOS: Maria Luisa Brandi
Ioannina: Vangelis Evangelou	AUSTRIOS: Barbara Obermayer-Pietsch
CABRIO: Jose A. Riancho	AROS: Bente Langdahl
GEOS: Francois Rousseau	EPIC: Stephen Kaptoge (Apologies)
INDIANA: Dan Coller	LARISSA: Panagoula Kollia
MrOS: Liesbeth Vandenput	AOGC: Emma Duncan (Apologies)
BARCOS: Daniel Grinberg	SHEFFIELD:Eugene McCloskey
SLO-PREVAL: Simona Mencej	SOF: Steve Cummings
CAMOS, MANMC: Brent Richards	CARLANTINO: Paolo Gasparini
GEVUR: Elza Khusnutdinova	EPOLOS: Marcin Kruk
LASA: Paul Lips	NEMO: JM Kaufman
	OPERA: Kristina Åkesson
	VIGGOS: Marie-Christine DeVernejoul
	HUNT: Siri Forsmo

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Participants were welcomed to the first teleconference of GENOMOS genotyping. This strategy is lunched by the GEFOS DXA BMD meta-analysis of genome-wide data.

1. An update on the GEFOS current activities:

GEFOS BMD: Currently finalizing quality control of genome-wide association datasets from 14 studies on lumbar spine and femoral neck BMD as outcome. We expect to find 35 to 45 genome-wide significant loci ($P < 5 \times 10^{-8}$) and some (less than 10) suggestive loci ($5 \times 10^{-8} < P < 5 \times 10^{-7}$) may also be considered as candidates for genotyping. Our GEFOS budget can afford up to 50 SNPs genotyped in 50,000 samples. The objective of this genotyping effort is to perform an association analysis of these BMD loci with BMD and osteoporotic fractures.

GEFOS Bone ultrasound, Hip structural analysis, DXA-based lean mass: Currently gathering data on studies with genome-wide data, may also pursue replication of some SNPs within GENOMOS. More information on GEFOS activities can be seen in the GEFOS website http://www.gefos.org.

2. Replication and genotyping plan

The objective is to recreate the GENOMOS collection used for previous publications on an expanded basis. All studies that have filled the survey on the GEFOS website will be invited to participate in ongoing efforts. This initial effort will focus on studies with DNA and BMD and/or fracture which are now invited to participate. The timeline to have a list of markers to be genotyped is by the end of March. Genotyping will be sponsored through the GEFOS EU project (50 SNP in up to 50,000 samples). The sponsored costs do not include handling or DNA extraction of samples. Studies willing to participate will acquire ownership of the produced genotypes for future analysis in their own cohorts; the only requirement is that no publication will be pursued by individual studies until the larger effort is accepted for publication.

A work group agreement for the BMD meta-analysis was circulated, which specifies the conditions for the replication studies. It was asked to read in detail this agreement and to send it back via email (gefos.inw@erasmusmc.nl and genomos@erasmusmc.nl) or fax no. +31107035430 (attn. Karol Estrada). Cohorts providing GWAS on BMD data have already signed this agreement.

3. Inventory Genotyping centers

Rotterdam offers to be one centralized facility for genotyping, but can currently handle up to 30,000 samples, therefore additional genotyping centers are required. deCODE Genetics can also process a number of samples and will begin with a collection of samples they withhold already. The additional number they can genotype is yet to be established. Each center can select their choice of technology for genotyping, but they have to consider that since we will pursue 50 SNPs, then it has

to be a multiplexed solution. The grant allows a maximum payment of €10 cents per genotype. These funds can be allocated to cohorts outside the European Union. BARCOS Barcelona offers to run their own genotyping. The timeline to do the genotyping is within 4 to 5 months, but on average we expect that studies doing their own genotyping should return genotypes in 2 months. Before doing genotyping on their own samples, these studies have to standardize the results via a common DNA plate of 96 samples that the Rotterdam genotyping centre will provide.

4. Inventory studies/phenotypes/sample sizes

Information attached in the report is based on numbers gathered via the online survey. Individual studies reviewed the numbers and almost all updated information was correct. BARCOS will update their fracture data. It is suggested to all participants to update their data via the GEFOS questionnaire. Rotterdam will circulate an email with the questionnaire login information to all participants. LASA will be extended to ~ 900 - 1300 samples. The GEVUR collection will be enlarged every week, a timeframe has to be set where the dataset will be frozen. SLOVENIA has updated numbers for fracture data. deCODE will ask for owners of other DNA collections for availability to this project. APOS study (not in questionnaire) will update via questionnaire, APOS is over 3000 samples.

5. Draft proposal for the protocol for material transfer and genotyping

DNA can be sent in three different ways (to the Rotterdam genotyping centre):

- o Fifteen 384 PCR-plates (2ng per plate)
- o One 384 DW plate (100ng per plate)
- o One 96 DW plate (150ng per plate)

Dry DNA is preferred for DNA handling, for the CABRIO study it is easier to send DNA in solution, this is always possible as long as the proper protocol for shipping and handling the DNA is used and the original volume and concentration is specified. Vendor plates need to be exactly those established by the genotyping centers. Rotterdam will send an updated protocol with links to the specific plates that are required.

April 30th is the proposed deadline to send DNAs to the centralized genotyping facilities.

6. Other issues

GENOMOS website: Rotterdam will update the website; it will have a similar aspect as the GEFOS website, with news, meetings. This will be a point of reference for general information.

7. Next call

We will circulate a doodle link with time options, next call should be within 1 month.

ACTION POINTS:

- Participants to read the BMD Working group agreement, if agree sign it and send it back either via e-mail to gefos.inw@erasmusmc.nl with cc to genomos@erasmusmc.nl or to the fax no. +31107035430 att. Karol Estrada.
- Rotterdam will send an extended DNA shipping and handling protocol to GENOMOS participants.
- BMD Working group to select final list of SNPs to genotype
- GEFOS Coordination centre to send an email to participants with login information to update the GEFOS questionnaire.
- Rotterdam group will have a new GENOMOS website available for testing on the next call
- Next call within 1 month, doodle link with options will be sent around.