Session 1

DUSRA meeting 19-05-2017

John Mathers (Newcastle)
'Personalizing lifestyle intervention in improve healthy aging'

In his talk Prof. Mathers introduced that in an aging societies with increased life expectancy, there is increased disease and disability burden, mostly due to poor exercise and diet. However, the effects of changing behavior with interventions are mostly quite modest, due to several personal factors. He pointed out the need for personalized lifestyle interventions for the elderly (from both biological and behavioral psychological rationales). To have the highest impact these interventions need to be personalized, scalable to large populations and sustainable. Prof. Mathers argued that internet-based tools would be most suitable to meet these requirements. He discussed two interventions he recently set up: LiveWell and Food4Me.

LiveWell was set up as a pragmatic intervention in later life (around retirement age) in a couple of districts around Newcastle, with as a secondary goal to establish monitoring measurements in this group. Individuals were recruited around retirement age, via their employers. Individuals were randomized to a personal program (via web-based questionnaires) or as a control a website with standard lifestyle information. All in all, this program was very well used and accepted by the target group.

Food4Me was founded from a European consortium, and aimed to investigate whether personalized nutrition is more effective than generalized guidelines and whether genetic or phenotypic data would provide additional benefit in the personalized nutritional advices. Participants from several European countries were randomized into one of four arms: a website with generic nutritional advices (as a control arm) or personalized advices based on eating patterns, the former with additional phenotypic data or the former with the additional information of risk variants of five genes. Food4Me resulted in a better outcome measures for the individuals with personalized advices, but without additional benefit in the arms with phenotypic or genetic data.

In the discussion the need of long-term follow-up of individuals after lifestyle interventions, in order to evaluate sustainability was discussed. This is mostly unachievable in trials due to financial concerns. Furthermore, whether the best motivation to adherence would be a positive reward instead of pointing out negative points (as is done in most trials) would be best. Prof. Mathers noted that providing information of risk alleles to individuals can lead to lifestyle changes as an example that warnings seem to give the best changes.

Edo Richard (Radboud, Nijmegen and AMC, Amsterdam)
'Healthy aging through internet counseling in the elderly'

Dr. Richard introduced that dementia prevalence is increasing, due to an aging society, but also due to an increase in modifiable risk factors (that constitute ~30% of the dementia risk). Dr. Richard introduced in his talk two trials that aimed to delay dementia onset through beneficially changing these modifiable risk factors. The Prediva trial randomized general practitioners in the Netherlands to either standard care or to enhanced vascular care in order to decrease dementia incidence in six years of follow-up. However, no significant differences were found between the two study arms, most likely due to also enhanced vascular treatment in the standard care arm. Moreover, current prevention strategies are known to be only moderately effective mostly due to incomplete adherence. Self-management strategies could lead to better and longer adherence of the participants. To evaluate this, dr. Richard is currently Involved in a European consortium (HATICE trial, currently ongoing) to evaluate whether an internet-based interactive platform for lifestyle changes in the elderly would lead to better outcomes than a static platform. After 18 months of follow-up, risk factors for dementia (including blood pressure, LDL-cholesterol levels and body mass index) will be evaluated. Finally, he stressed out that the timing of a lifestyle intervention trial is crucial: too early in life will require very long follow-up to evaluate effectiveness, and too late in life and no effects will be observed.

In the discussion, the requirement for randomized controlled trials (RCTs) for lifestyle interventions was discussed. The problem with RCTs in these interventions is that the control group also seems to be 'treated' with similar beneficial effects as the investigated treatment group (too small to show significant differences). Dr. Richards argued that RCTs are necessary, otherwise there would be a risk of treatment allocation with bias due to effects of the distinct group of individuals that volunteer to participate in trials.

Valter Longo (USC Davis School of Gerontology)
'Caloric restriction mimicking diets in clinic & aging research'

Prof. Longo introduced the importance of the growth-hormone (GH) pathway in aging research, as a conserved pathway across organisms that regulates several 'pro-aging' genes. In several model organisms GH-deficiency leads to increased lifespan. Moreover, humans with a GH-deficiency, seem to be spared from insulin resistance, even in the presence of obesity. Protein intake is a key activator of the GH-pathway, and lowering protein intake seems to decrease mortality risk. Furthermore, a period of fasting (72h) leads to an improvement of the metabolic state. For this end, Prof. Longo developed an intermittent fasting mimicking diet (FMD) which consists of several cycles in which proteins, sugars and overall caloric intake is reduced with increased intake of complex carbohydrates. This intervention led in mice to a reduction of the detrimental visceral fat and even when administering the intervention in mice after midlife, this leads to an increased lifespan and a reversal of hyperglycemia in type 2 diabetes model mice. Finally, he observed that FMD in mice in midlife lead to an increased expression of fetal development genes with enhanced regeneration of pancreatic beta-cells and development of stem cells.

The first trial of FMD in humans (N=100) included 3 FMD cycles (each cycle for five days, once a month) was generally well-tolerated (with a dropout rate of ~30%) and led to improved metabolic parameters. The trials seemed most effective to decrease the metabolic risk in those individuals that were most at risk at baseline. Finally, Prof. Longo noted that a FMD trial for type 2 diabetes patients will commence shortly in Leiden.

In the discussion, it was discussed whether the outcome measures of FMD could differ between tissues. Prof. Longo noted that that would indeed be very interesting, although the focus of the measurements was towards measures relevant for diabetes. Furthermore, the risk of lowering protein intake in the elderly was discussed. Prof. Longo remarked that indeed lowering protein intake would be most beneficial in younger individuals, while elderly individuals require higher levels of protein intake. Finally, the underlying mechanism of the enhanced stem cell regeneration that was observed in FMD was discussed. Prof. Longo speculated that the underlying mechanism could be in two steps: first a shrinkage of the stem cell pool due to the fasting, followed by a regeneration step.

Eline Slagboom (LUMC)
'DuSRA now and in the future'

Prof. Slagboom summarized the meeting, and noted that many scientists work on investigating the aging theories (e.g. nutrient sensing and senescence), while other work on interventions in the elderly. To bridge to gap between these two, would require investigation of means to effectively monitor and classify individuals (for instance with biomarkers). The aim of DuSRA is to connect between these three steps. She introduced as an example the biobanking BBMRI-omics initiative in which 25.000 samples are available to discover disease-specific markers and generic markers of biological age. Prof. Slagboom noted that funding agencies are very much interested in the DuSRA community and in opportunities for public-private-initiatives. She mentioned that we need to map the diversity of aging research in The Netherlands, what kind of initiatives with industrial partners are currently running and what the opportunities are for translating research. Finally she brought up that in the aging field we need to establish realistic goals In order to obtain the much needed funding for the field.