THE POTENTIAL BENEFITS OF DAIRY PROTEINS ON CARDIOVASCULAR HEALTH

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EVIDENCE FROM PROSPECTIVE COHORT STUDIES
Recent meta-analyses of prospective studies on dairy and cardiometabolic diseases

<table>
<thead>
<tr>
<th>Dairy</th>
<th>Outcome</th>
<th>RR (95% CI)</th>
<th>Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milk</td>
<td>AC mortality</td>
<td>1.00 (0.93-1.07)</td>
<td>Guo et al., 2017</td>
</tr>
<tr>
<td>Milk</td>
<td>CVD</td>
<td>1.01 (0.93-1.10)</td>
<td>Guo et al., 2017</td>
</tr>
<tr>
<td>Cheese</td>
<td>CVD</td>
<td>0.98 (0.95-1.00)</td>
<td>Guo et al., 2017</td>
</tr>
<tr>
<td>Milk</td>
<td>Stroke</td>
<td>0.93 (0.88-0.98)</td>
<td>De Goede et al., 2016</td>
</tr>
<tr>
<td>Cheese /40 g/d</td>
<td>Stroke</td>
<td>0.97 (0.94-1.01)</td>
<td>De Goede et al., 2016</td>
</tr>
<tr>
<td>Yoghurt/80g/d</td>
<td>Diabetes</td>
<td>0.86 (0.83-0.90)</td>
<td>Gijsbers et al., 2016</td>
</tr>
</tbody>
</table>
Association of dairy intake with cardiovascular disease and mortality in 21 countries from five continents (PURE): a prospective cohort study

Mahshid Dehghan, Andrew Mente, Sumathy Rangarajan, Patrick Sheridan, Viswanathan Mohan, Romaina Iqbal, Rajeev Gupta, Scott Lear, Edelweiss Wentzel-Viljoen, Alvaro Avezum, Patricio Lopez-Jaramillo, Prem Mony, Ravi Prasad Varma, Rajesh Kumar, Jephat Chifamba, Khalid F Alhabib, Noushin Mohammadifard, Aytekin Oguz, Fernando Lanas, Dorota Rozanska, Kristina Bengtsson Bostrom, Khalid Yusoff, Lungiswa P Tsolkile, Antonio Dans, AfzalHussein Yusufali, Andres Orlandini, Paul Poirier, Rasha Khatib, Bo Hu, Li Wei, Lu Yin, Ai Deeraili, Karen Yeates, Rita Yusuf, Noorhassim Ismail, Dariush Mozaffarian, Koon Teo, Sonia S Anand, Salim Yusuf, on behalf of the Prospective Urban Rural Epidemiology (PURE) study investigators*

Methods The Prospective Urban Rural Epidemiology (PURE) study is a large multinational cohort study of individuals aged 35–70 years enrolled from 21 countries in five continents. Dietary intakes of dairy products for 136 384 individuals were recorded using country-specific validated food frequency questionnaires. Dairy products comprised milk, yoghurt, and cheese. We further grouped these foods into whole-fat and low-fat dairy.

Interpretation Dairy consumption was associated with lower risk of mortality and major cardiovascular disease events in a diverse multinational cohort.
HRs (95% CIs) of CVD for SFA from dairy and meat

de Oliveira Otto et al. 2012
EVIDENCE FROM RANDOMISED CONTROLLED TRIALS
Milk proteins and blood lipids

Fekete et al., AJCN (2016)

Δ baseline (mmol/L)

TC  LDL-C  TAG

Whey protein  Ca-caseinate  Control

a  a,b  b

a,b different = P<0.05
Milk proteins and blood pressure

Fekete et al., AJCN (2016)

Peripheral SBP & DBP

\[ p = 0.023 \]

\[ p = 0.002 \]

Central SBP & DBP

- Overall treatment effect for C\_SBP \( p = 0.010 \)
- Overall treatment effect for C\_DP \( p = 0.094 \)
- Overall treatment effect for C\_MeanP \( p = 0.024 \)

\( n = 38, \text{ Means } \pm \text{ SEM} \)

Overall treatment effect for P\_SBP \( p = 0.007 \)
Overall treatment effect for P\_DP \( p = 0.095 \)
Overall treatment effect for P\_MeanP \( p = 0.009 \)

\( n = 38, \text{ Means } \pm \text{ SEM} \)
Potent ACE inhibiting peptides from milk proteins

FitzGerald et al., 2004

<table>
<thead>
<tr>
<th>Protein</th>
<th>Peptide fragment</th>
<th>Primary Sequence</th>
<th>ACE IC₅₀ (µmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Casokinins</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>αₛ₁-casein</td>
<td>f(25–27)</td>
<td>VAP</td>
<td>2.0</td>
</tr>
<tr>
<td>αₛ₂-casein</td>
<td>f(174–179)</td>
<td>FALPQY</td>
<td>4.3</td>
</tr>
<tr>
<td>β-casein</td>
<td>f(74–76)</td>
<td>IPP</td>
<td>5.0</td>
</tr>
<tr>
<td>κ-casein</td>
<td>f(185–190)</td>
<td>VTSTAV</td>
<td>52.0</td>
</tr>
<tr>
<td>Lactokinin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>α-lactalbumin</td>
<td>f(104–108)</td>
<td>WLAHK</td>
<td>77.0</td>
</tr>
<tr>
<td>β-lactoglobulin</td>
<td>f(142–148)</td>
<td>ALPMHIR</td>
<td>42.6</td>
</tr>
<tr>
<td>BSA</td>
<td>f(208–216)</td>
<td>ALKAWSVAR</td>
<td>3.0</td>
</tr>
</tbody>
</table>
In vitro ACEi activity of dairy and plant proteins

Giromini et al., 2017

Dairy proteins

Plant proteins
Measuring vascular endothelial function by flow mediated dilation (FMD)

1. Baseline measurement (up to 1 min)
2. Inflate cuff. Distal occlusion (5 min)
3. Ischemia below cuff. Distal vasculature dilates, decreasing vascular resistance
4. Cuff release
5. Dramatic increase in blood flow
6. Shear stress
7. Endothelium releases vasodilators and NO
8. Healthy artery dilates
Milk proteins and endothelial function

Fekete et al., AJCN (2016)
Milk proteins and vascular stiffness in young hypertensive women

Figueroa et al. AJHypertens (2014)
Diabetes and heart disease

When you have diabetes, you're more at risk of heart disease. This is also called cardiovascular disease (CVD) or coronary disease, and can lead to heart attacks and strokes.
Carbohydrate-rich meal +/- whey protein on blood glucose in T2DM patients

Frid et al., 2005

$+ 28g$ whey

$P, \text{Treat x time } = 0.022$
Fat rich meal +/- whey protein, casein or CHOcontrol on blood insulin in subjects at risk of T2DM

Fekete et al. 2018
Effect of whey protein on insulin release

Whey protein has a rapid gastric emptying rate

GLP-1 slows GE

DPP-IV is inhibited → increases in GLP-1, GIP

GLP-1 suppresses glucagon secretion

GIP and BCAAs stimulate insulin secretion

GLP-1: Glucagon-like peptide 1
GIP: Glucose-dependent insulino-tropic peptide
DPP-IV: Dipeptidyl peptidase-4
BCAA: Branched chain amino acids
A few conclusions……

• There is functionality beyond nutrient supply BCAA important…

• Many nutrition and health benefits from dairy-derived foods/proteins, both at population and individual levels and for young and old including BP and haemodynamics…..

• Negative association of milk proteins and milk/fermented dairy and T2DM may become the most important findings. Needs development…..

• If food sustainability is driven by replacing animal with plant derived foods be careful what you wish for so……

• Not sensible to consider protein in isolation, need to consider foods
Thank you!
Spare slides
Changes in total and LDL-chol after consumption of ~80 g/d fat (~36g/d SFA) as cheese or butter

Hjerpsted et al. AJCN 2011;94:1479–84.
Protein quality of dairy alternatives?
Contributors to dietary protein in the EU

EFSA, 2012
Bonetrophic nutrient interactions
Effects of milk on bone mineral density

82 girls mean age 12.2 years randomised to 568ml/d whole or fat-reduced milk or habitual diet for 18 months
Micronutrient status of UK children and adult females

NDNS 08/09 + 09/10

Dairy food intake in UK females
Bone mass changes with age

Weaver et al. (2016)
Effect of protein and GI on body weight regain after loss

Diogenes
Larsen et al.
Benefits for sarcopenia

Resistance training induced changes in lean mass

Phillips et al., 2009 JACN 28:343
Response to dairy fat differs when in cheese matrix (~40g fat/d; 6w parallel)

Feeney et al., 2018