



Fotograf: Wisse, A. B. / Oslo byarkiv



UiO • Det medisinske fakultet

Gluten Free Museum Removes All Gluten From Famous Works Of Art



Knut E. A. Lundin, overlege, dr.
med., professor Utdanningsleder
Klinmed

Hvete gluten
– basis for et
sunt liv eller
en trussel mot
menneskehet
en?

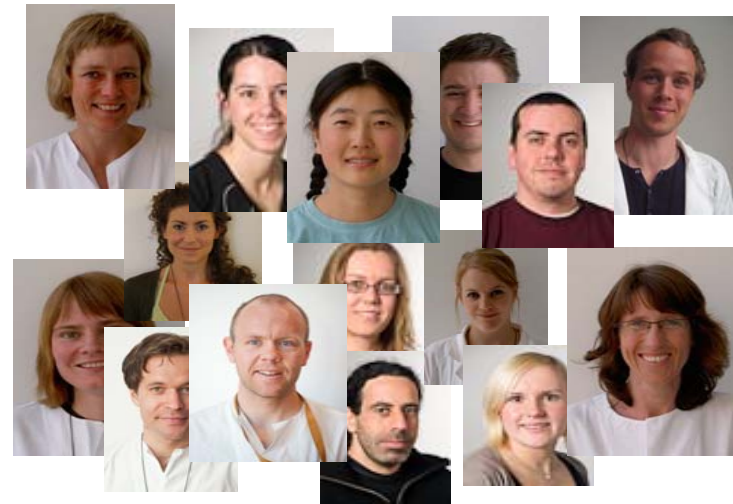


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Vi har tenkt på fremtiden i 200 år



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Federation of Clinical Immunology Societies
www.focis.org



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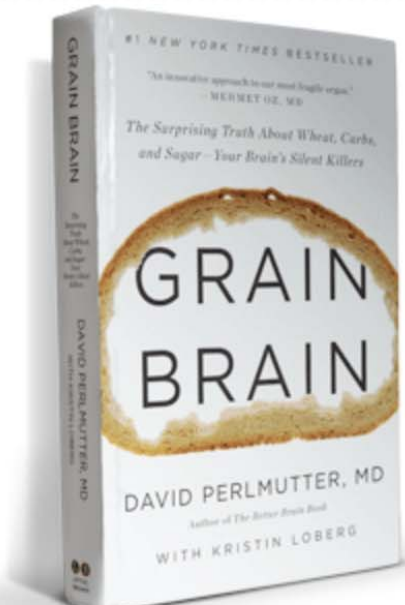


**IT'S BEEN DISCOVERED THAT 1% OF THE
POPULATION IS ALLERGIC TO GLUTEN**

**AND 99% OF THE POPULATION IS SICK OF
HEARING ABOUT IT**



Menneskeheten utryddes ila 1 generasjon?



**INTERNATIONAL
BEST SELLER**

#1 **The New York Times**

#1 **amazon.com**

#1 **THE GLOBE AND MAIL**

**USA
TODAY**

WALL STREET JOURNAL

Grain Brain by David Perlmutter, MD

Renowned neurologist David Perlmutter, MD, blows the lid off a topic that's been buried in medical literature for far too long: carbs are destroying your brain. And not just unhealthy carbs, but even healthy ones like whole grains can cause dementia, ADHD, anxiety, chronic headaches, depression, and much more. Dr. Perlmutter



Randomised clinical trial: gluten may cause depression in subjects with non-coeliac gluten sensitivity – an exploratory randomised clinical study

S. L. Peters*, J. R. Biesiekierski†, G. W. Yelland*‡, J. G. Muir* & P. R. Gibson*†

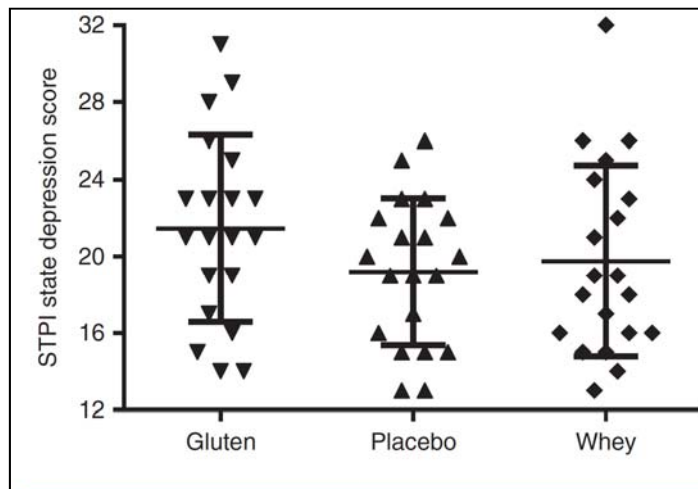


Figure 1 | STPI state depression scores during the gluten, whey and placebo dietary challenges. A linear mixed model of fixed effects revealed that condition had a significant effect on STPI state depression score. Pairwise sub-analyses revealed that state depression was significantly higher in the gluten condition than placebo. No differences were found between gluten and placebo or placebo and whey.

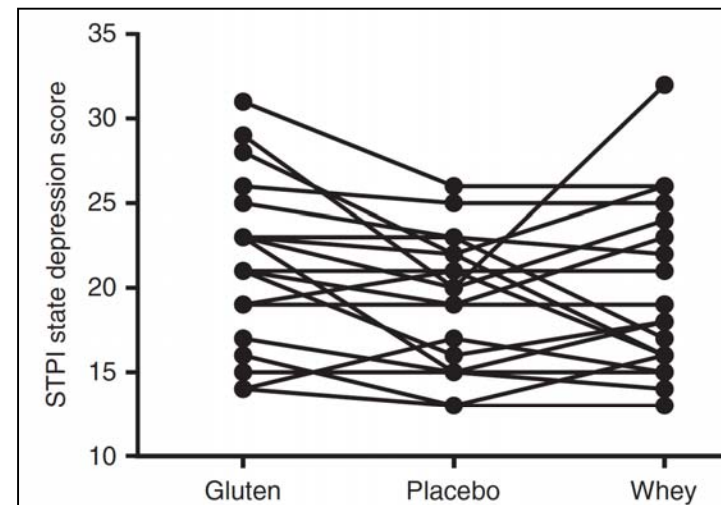


Figure 2 | Paired STPI state depression scores across the gluten, whey and placebo dietary challenges. State depression scores were significantly higher in the gluten condition compared to placebo. No significant differences were found between gluten and whey or placebo and whey.



Gluten – ADHD – “brain fog”

- Lenge kjent at gluten peptider kan finnes i urin hos autister og cøliakere
- Kan påvises i urinprøve
- Hyppig grunn til gluten fri kost
- Svakt vitenskapelig grunnlag



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ORIGINAL ARTICLE

The Oslo definitions for coeliac disease and related terms

Jonas F Ludvigsson,^{1,2} Daniel A Leffler,³ Julio C Bai,⁴ Federico Biagi,⁵ Alessio Fasano,⁶ Peter H R Green,⁷ Marios Hadjivassiliou,⁸ Katri Kaukinen,⁹ Ciaran P Kelly,³ Jonathan N Leonard,¹⁰ Knut Erik Aslaksen Lundin,¹¹ Joseph A Murray,¹² David S Sanders,^{13,14} Marjorie M Walker,¹⁴ Fabiana Zingone,¹⁵ Carolina Ciacci¹⁶

- **Gluten intoleranse**

- Bred betegnelse på alle reaksjoner på gluten
- Cøliaki (1-2% av befolkningen)
- En slimhinnebetennelse i tynntarmen, virker på hele kroppen, alle har genet HLA-DQ2 eller 8, vanligvis også typisk blodprøve (IgA-TG2)
- Hvete allergi en rask, allergisk reaksjon (sjeldent)
- Non-coeliac gluten sensitivity (2-6% ????)
- Klinisk ganske likt cøliaki disease, men uten typisk betennelse og blodprøve

Ludvigsson et al, Gut 2012

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The Neolithic period

Fertile crescent

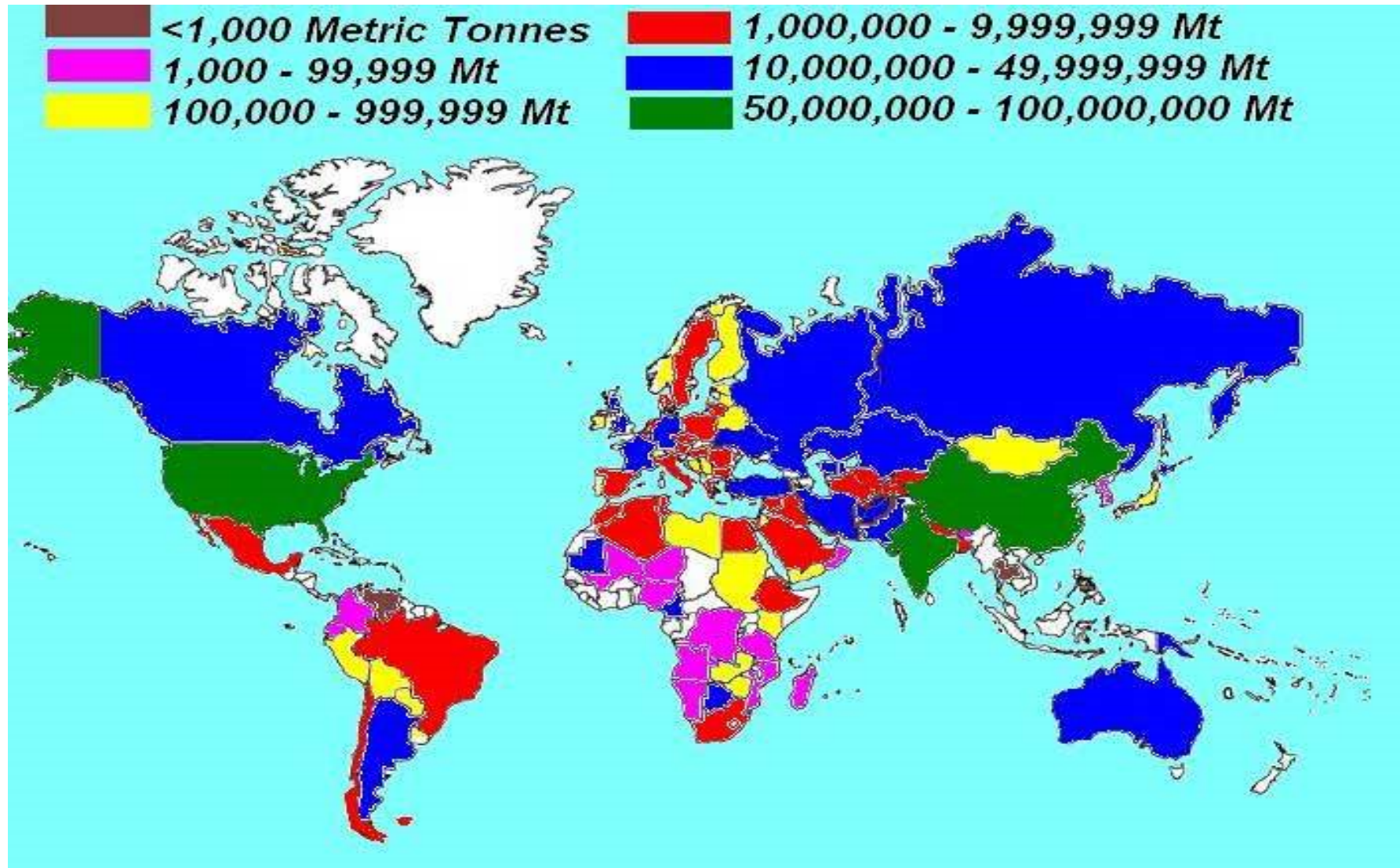


- Started about 9500 BC
- First signs of cultivation of grains



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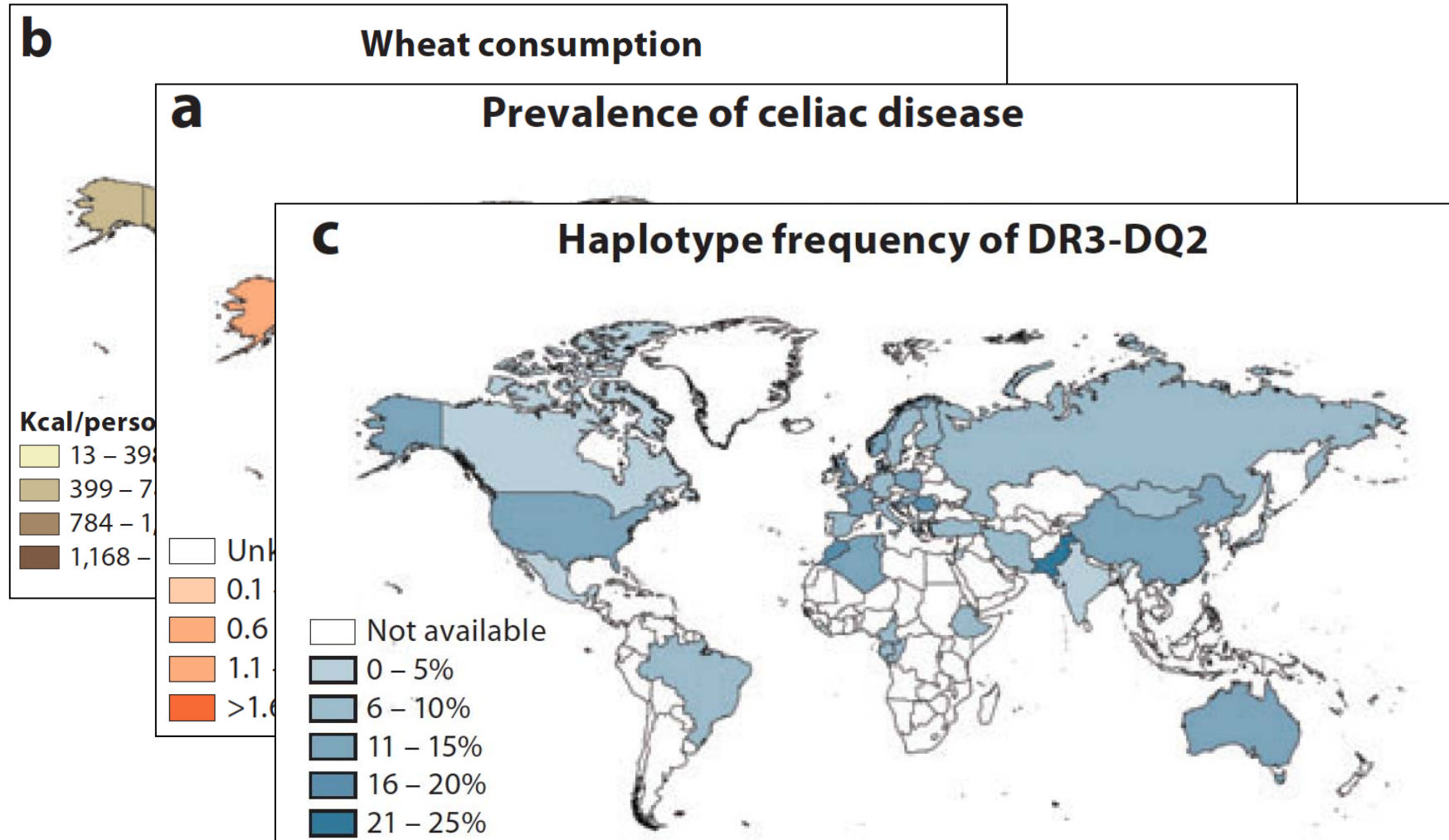
Vi har tenkt på fremtiden i 200 år



Vi har tenkt på fremtiden i 200 år

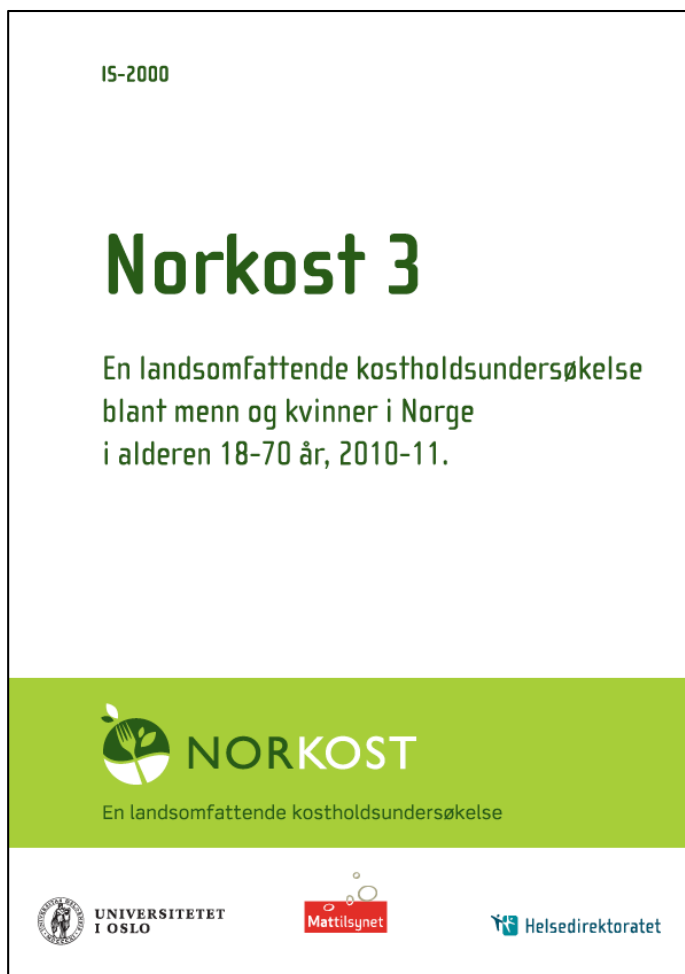


Wheat consumption - CD - HLA





Helseeffekt av hvete



- Brød og kornvarer viktigste kilde til:
 - Karbohydrater
 - Kostfiber
 - Jern
 - Magnesium
 - Tiamin
 - Folat
 - Selen

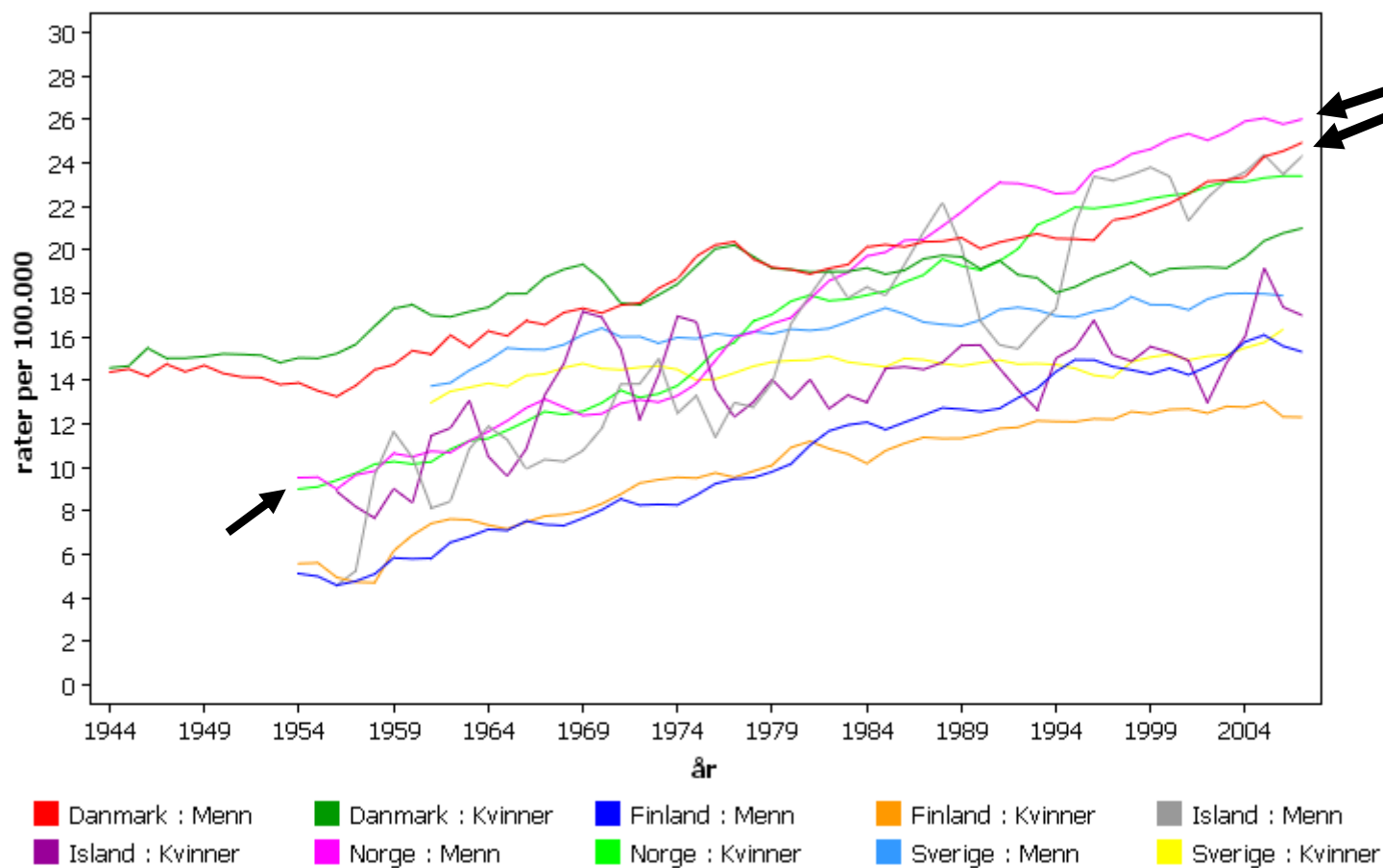




Norden: kolon cancer insidens

Tykkertarm

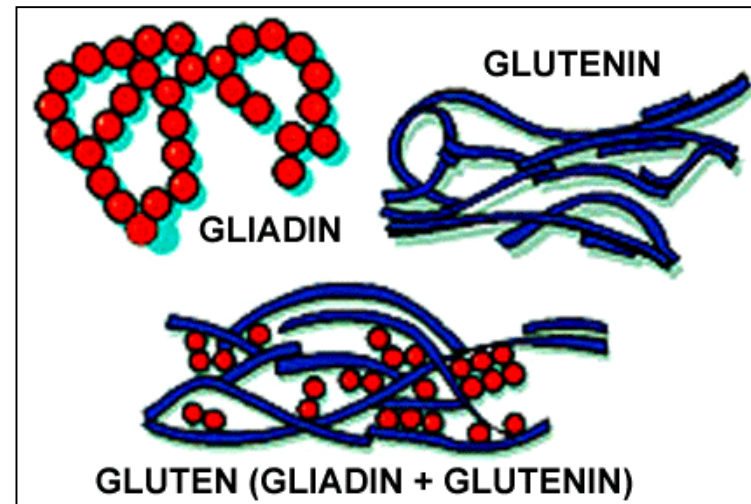
Insidens: ASR (W) alder (0-85+)





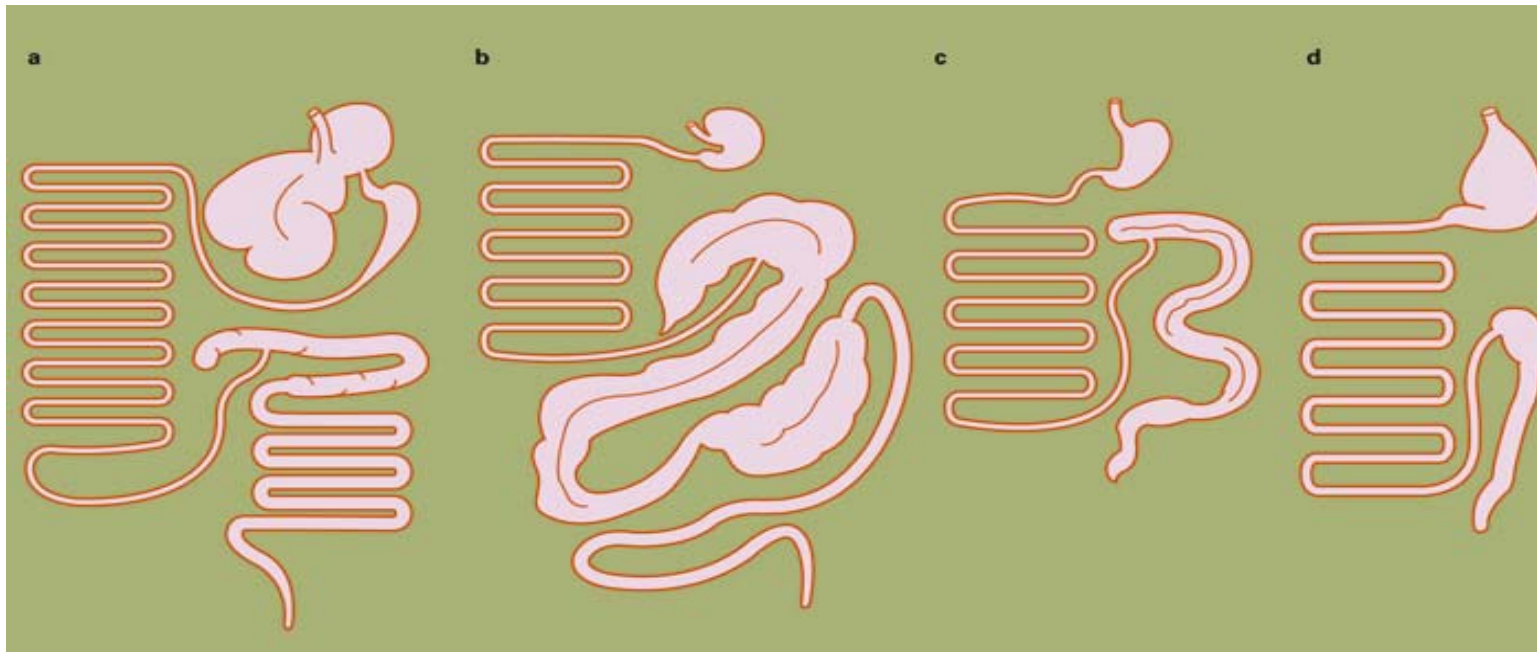
Gluten – definitions

- Gluten as in
 - Gluten free food
 - The glue-ish mass after washing of flour
 - The gliadin and glutenin proteins in wheat, hordeins of barley and secalin of rye





Mammalian digestive system



Ruminating
herbivores
(sheep)

Non-ruminating
herbivores
(horse)

Omnivores
(humans)

Carnivores
(dog)

Valeur and Berstad 2008



Areteus the Cappodoccian



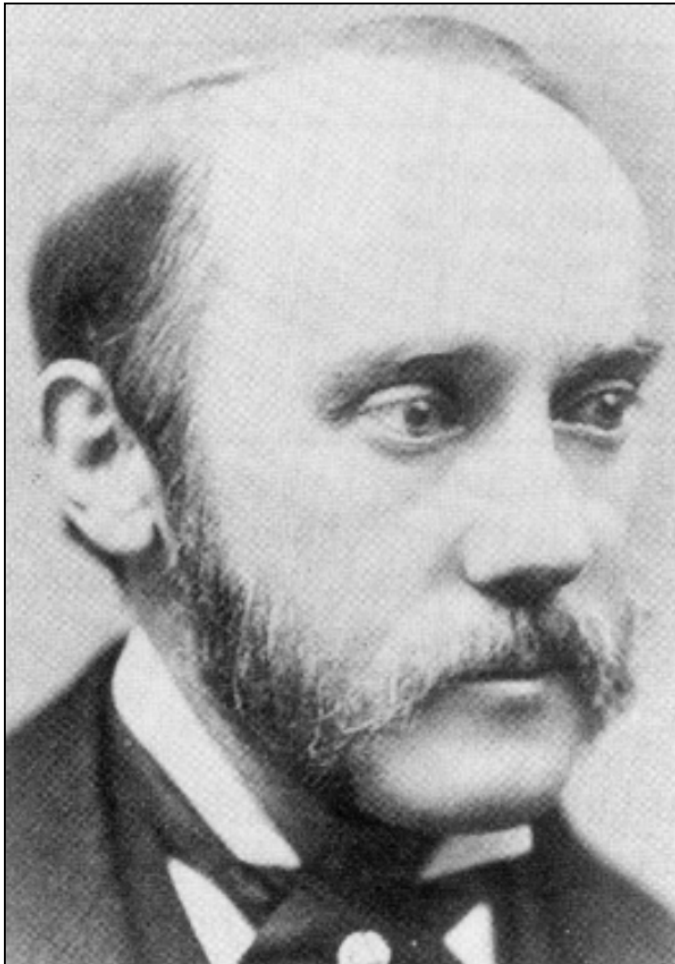
- Greek physician
- Recorded a malabsorptive syndrome with chronic diarrhoea
- "Coeliac affection" (coeliac from Greek: κοιλιακός koiliakos "abdominal")
- Stomach pain, atrophied, pale, feeble....
- Diarrhoea white, malodorous and flatulent....

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Samuel Gee 1888



- "...a kind of chronic misdigestion...."
- "Occurs mainly in children but may be seen at all ages...."
- "If the disease can be cured, it must be by means of the diet..."

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Willem K. Dicke oppdaget cøliaki som livslang og hveteutløst tilstand



- Nederlandsk barnelege.
- På sporet av gluten som årsak fra ca 1934.
- Motstand fra kirkelig hold.
- Hvete, rug, bygg (og havre) utløsende faktor.
- Fett i avføring terapimål.



Adult coeliac disease

W. T. COOKE, D. J. FONE, E. V. COX, M. J. MEYNELL,
AND R. GADDIE

From the General Hospital, Birmingham

EDITORIAL SYNOPSIS A clinical, biochemical, and pathological study is recorded of 50 patients in whom a diagnosis of idiopathic steatorrhea had been made and who had 'flat' jejunal biopsies. It is suggested that there is an underlying constitutional defect, not yet clearly defined, and that possibly secondary intestinal infection allows the intestinal mucosa to become sensitized to substances in the diet. Of these gluten is the commonest; milk adversely affects others; and there may be other factors.

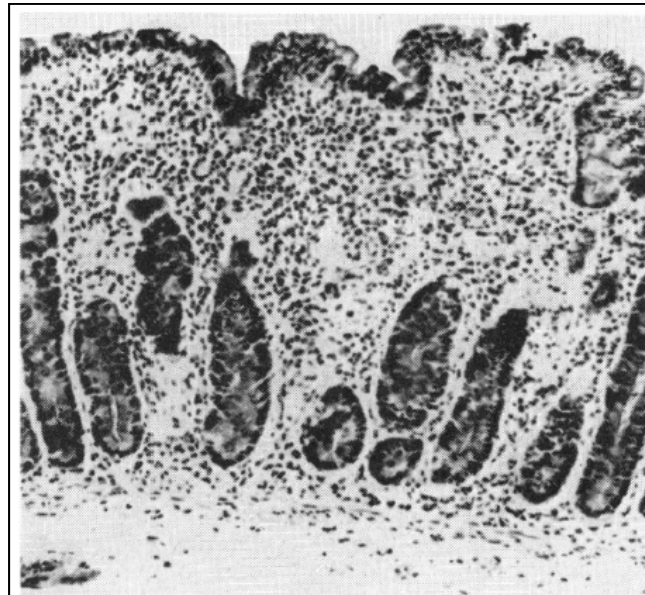
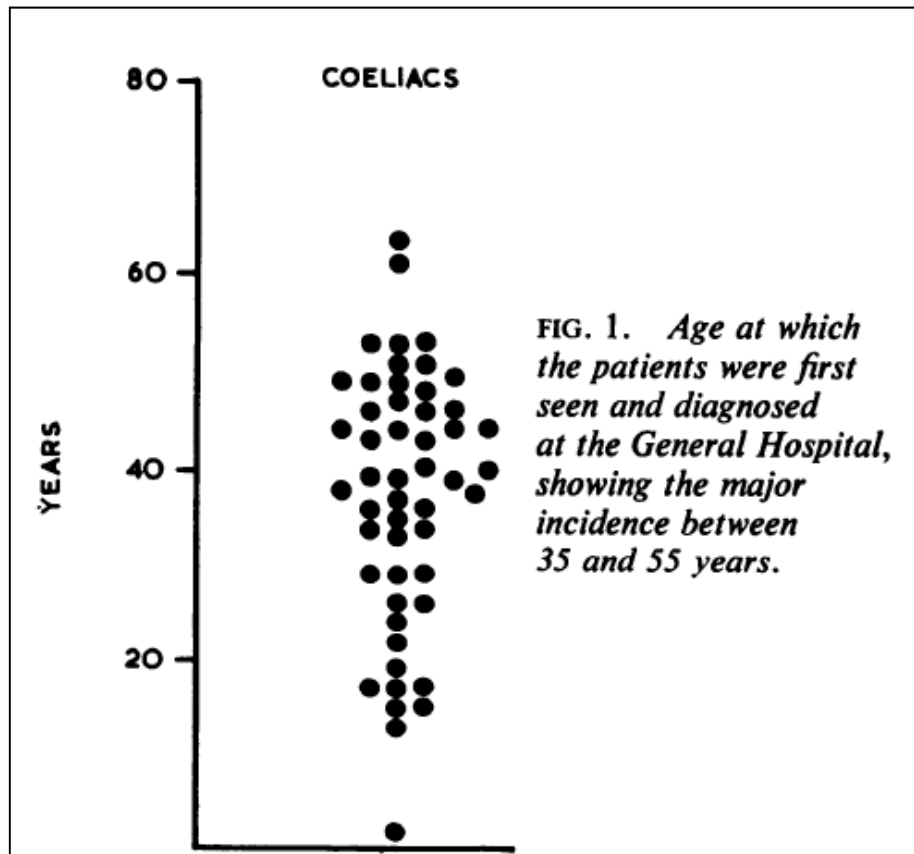
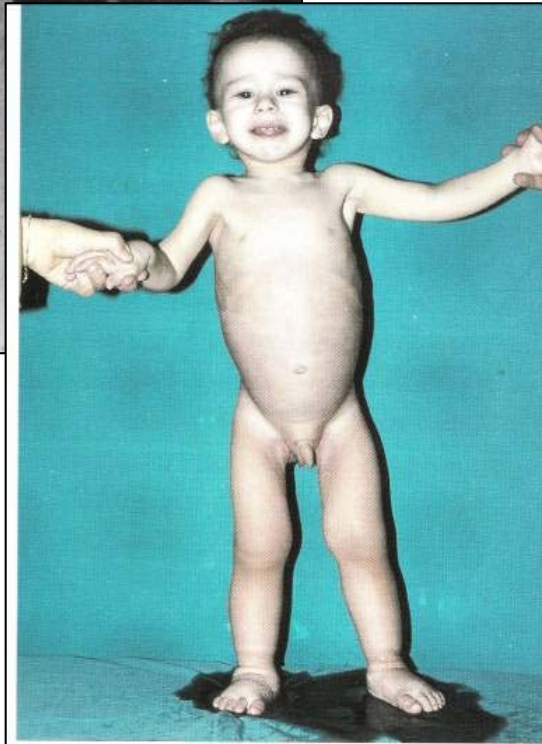
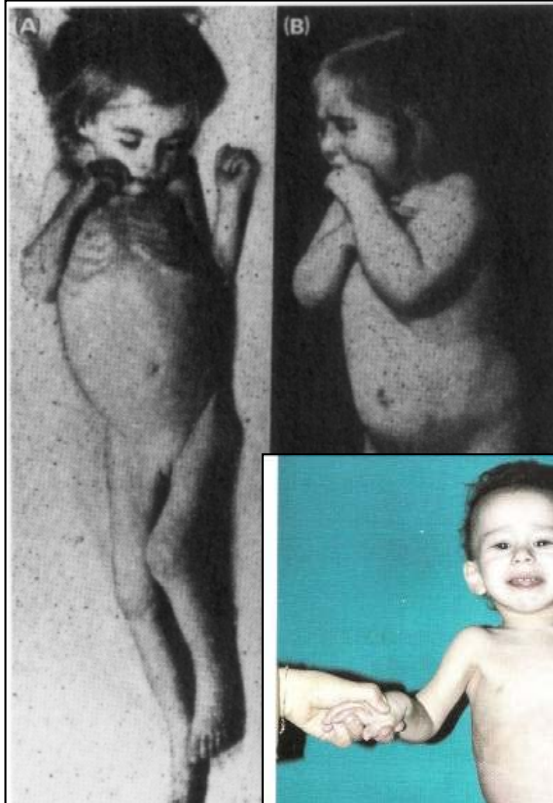


FIG. 3. Typical histological appearance of 'flat' biopsy showing the absence of normal villi; abnormal surface epithelial cells.



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Endret klinisk presentasjon



Moren løste Jacobsens form-mysterium

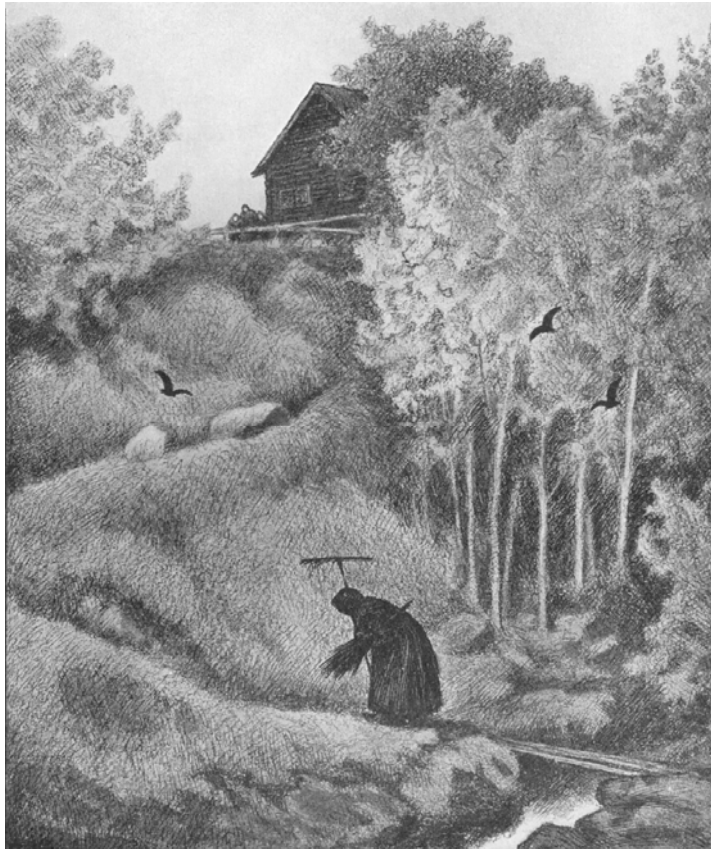
Tok overraskende femteplass i Tour de Ski etter magemareritt



FEMTEPLASS I TOUR-EN: Astrid Uhrenholdt Jacobsen fikk hjelp fra mamma med å få orden på kroppen. Foto: Scanpix



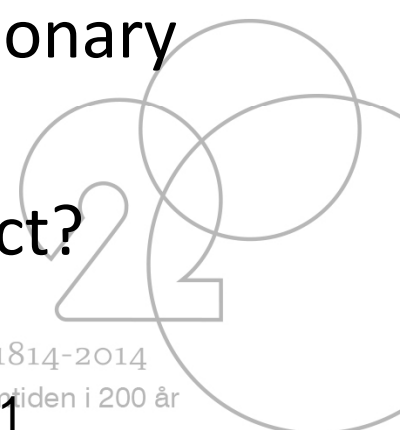
Coeliac disease – the backside of the coin?



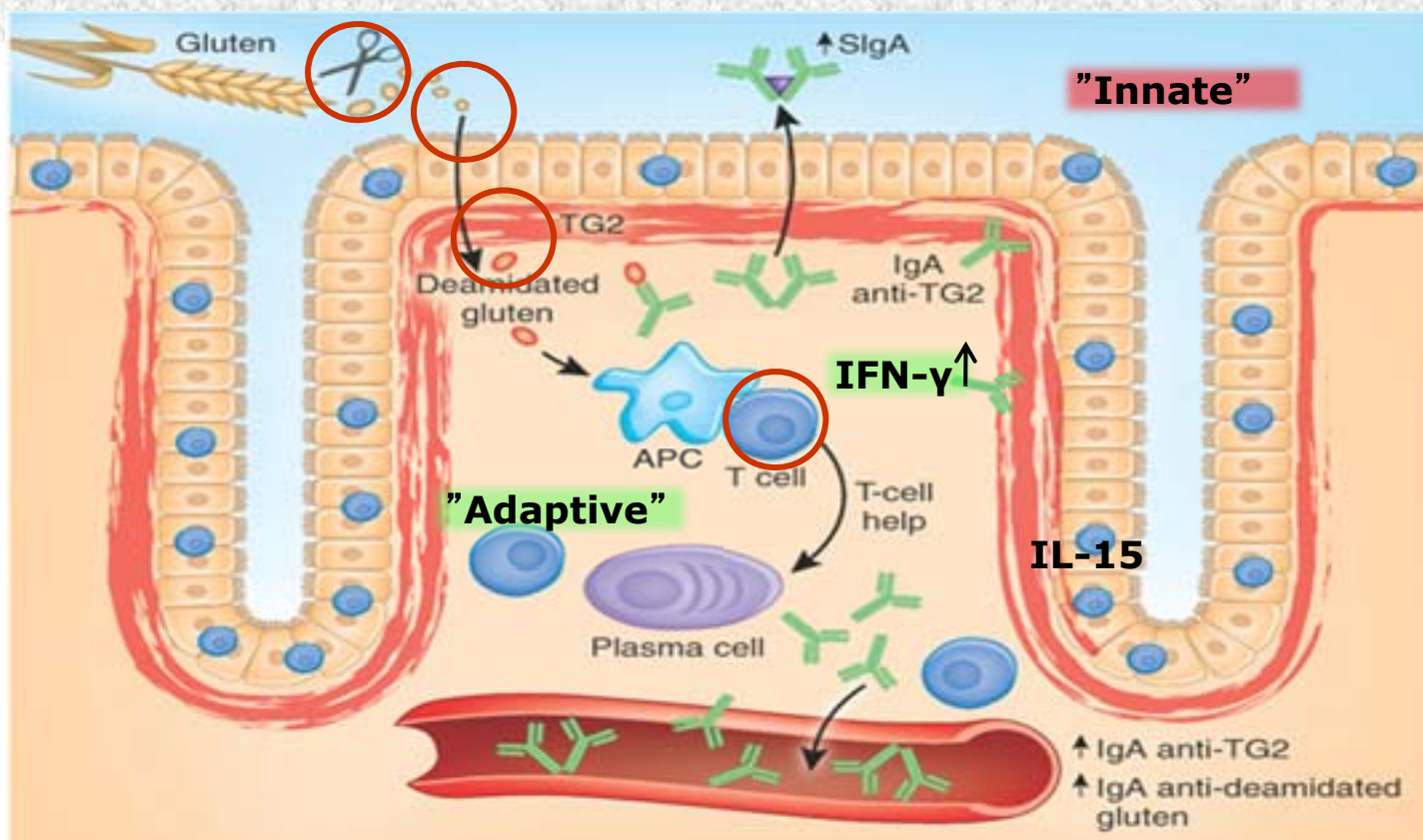
- Unknown to all humans who do not ingest wheat and related cereals.
- Depends on a genetic trait present among very many Caucasoids.
- Possible evolutionary advantage?
- Bottleneck effect?

Kittelsen T: Mom – there is an old woman coming

Describing the plague that killed 50-60 % of Europeans 1347-1351



Immunreaksjon ved cøliaki



Sollid/Lundin, Mucosal Immunology 2009, modified



Hvorfor får noen cøliaki?

- Ca 25 % av norske befolkning har genet for cøliaki (HLA-DQ2)
- “Bare” 1-2 % (av alle) får sykdommen
- Årsaker?
 - Stort sett ukjent
 - Andre gener (40 kjente gener bidrar)
 - Uflaks? (ikke helt usannsynlig)
 - Infeksjoner/stress
 - Lever vi for sterilt?



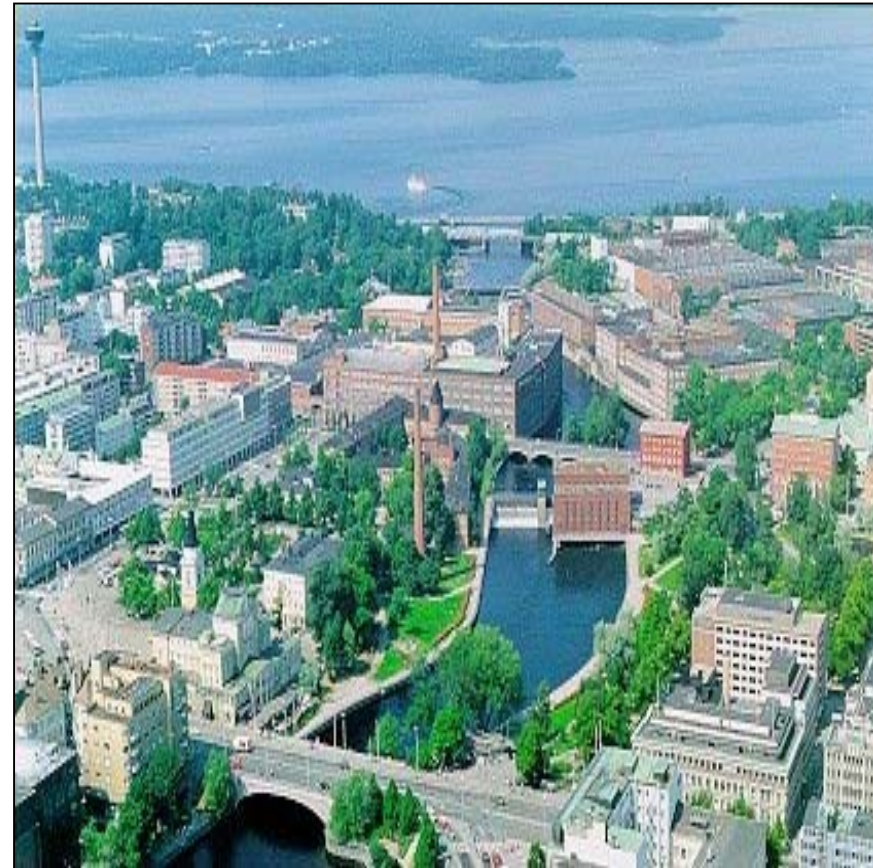
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Increasing prevalence of coeliac disease

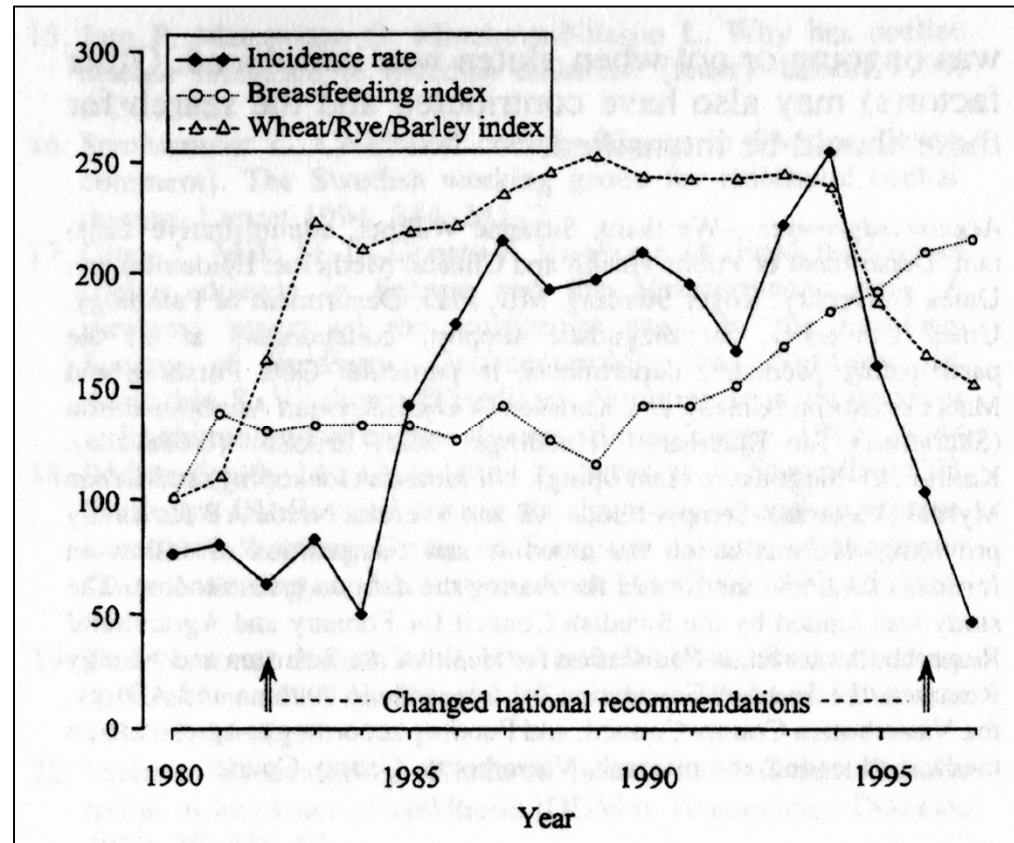
- "Everybody" knows someone with CD
- Active search will find the coeliacs
 - Tampere in Finland:
 - 250 000 inhabitants
 - 0,75 % with CD diagnosis





Feeding habits influence

- Sweden 1982: Delay gluten intro to age of 6 months
- Same time: Less breast feeding
- 1984: Dramatic increase in CD



Public reactions!



Boycot wheat slurry!



Prevention of CD – still search for a strategy

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Randomized Feeding Intervention in Infants at High Risk for Celiac Disease

S.L. Vriezinga, R. Auricchio, E. Bravi, G. Cast
P. Crespo Escobar, S. Kolaček, S. Koletzko, I.R. Ko
I. Polanco, H. Putter, C. Ribes-Koninckx, R. Shamir,
L. Greco, J. Gyimesi, C. Hartman, C. Hogen Esch
T. Koltai, F. Koning, E. Martinez-Ojinaga, C. te Marvel
E. Stoopman, V. Villanacci, C. Wijmenga, R. Tr

The NEW ENGLAND JOURNAL of MEDICINE

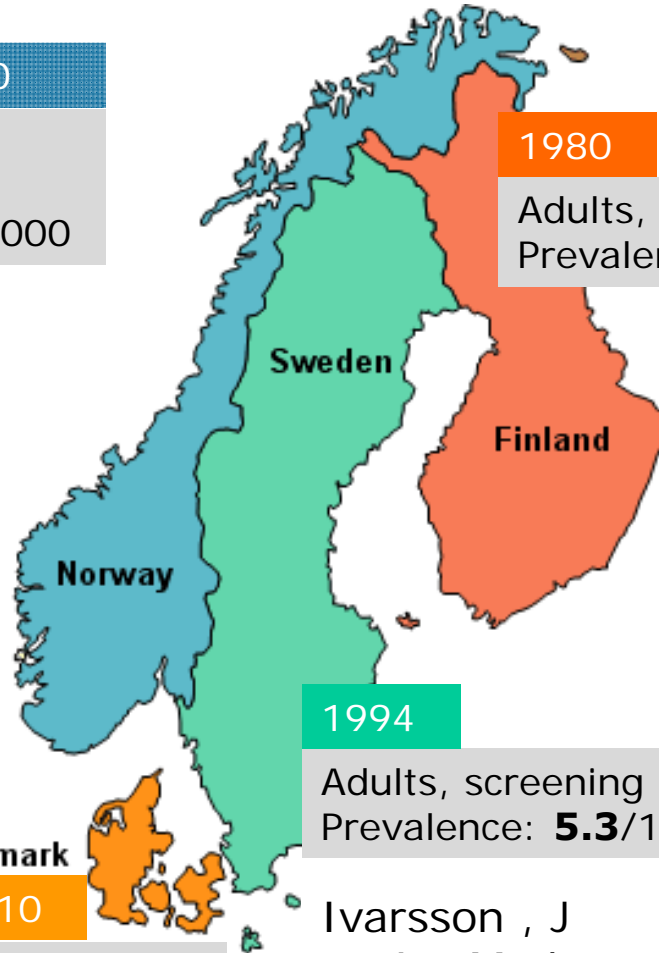
ORIGINAL ARTICLE

Introduction of Gluten, HLA Status, and the Risk of Celiac Disease in Children

Elena Lionetti, M.D., Stefania Castellaneta, M.D., Ruggiero Francavilla, M.D., Ph.D.,
Alfredo Pulvirenti, Ph.D., Elio Tonutti, M.D., Sergio Amarri, M.D., Maria Barbato, M.D.,
Cristiana Barbera, M.D., Graziano Barera, M.D., Antonella Bellantoni, M.D.,
Emanuela Castellano, M.D., Graziella Guariso, M.D., Maria Giovanna Limongelli, M.D.,
Salvatore Pellegrino, M.D., Carlo Polloni, M.D., Claudio Ughi, M.D.,
Giovanna Zuin, M.D., Alessio Fasano, M.D., and Carlo Catassi, M.D., M.P.H.,
for the SIGENP (Italian Society of Pediatric Gastroenterology, Hepatology,
and Nutrition) Working Group on Weaning and CD Risk



Cøliaki øker i Skandinavia



2000-2002	2008-2010
Children Incidence 16.2/100.000	41.7/ 100.000

Beitnes & Størdal et al, unpublished 2012

1980	2001
Adults, screening Prevalence: 10.5/1000	19.9/1000

Lohi , Aliment Pharmacol Ther, 2007

Myleus, J Pediatr Gastroenterol Nutr. 2009

1994	2006
Adults, screening Prevalence: 5.3/1000	Children, born 1993, screening "epidemic" Prevalence: 29/1000

Dydensborg , Acta Pæd 2011

1996	2010
Children, register Prevalence 0.43/1000 Incidence : 0.8/100.000	0.84/1000 6.9/100.000

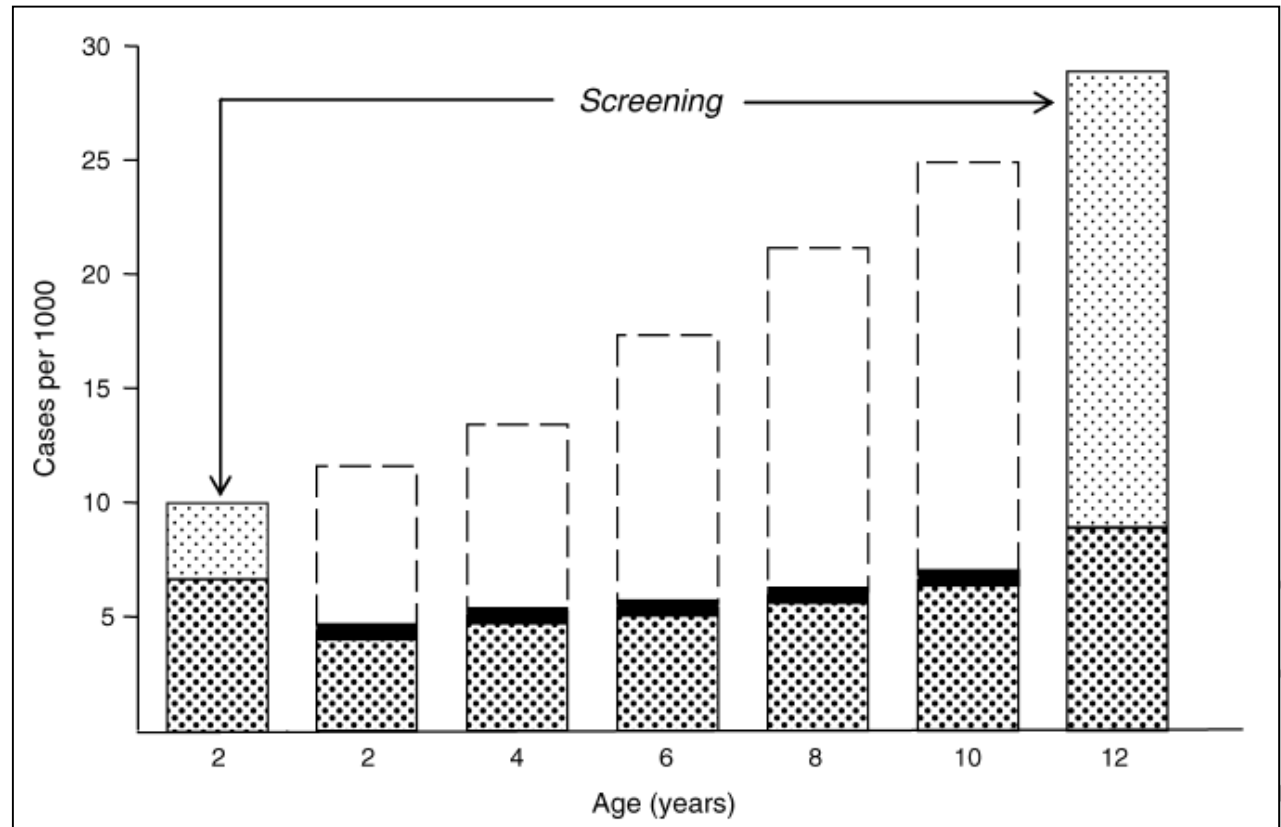
Ivarsson , J Int Med 1999

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Celiac Disease Revealed in 3% of Swedish 12-year-olds Born During an Epidemic

*Anna Myléus, *Anneli Ivarsson, †Charlotta Webb, ‡Lars Danielsson, §Olle Hernell,
||Lotta Högberg, ¶Eva Karlsson, §Carina Lagerqvist, *Fredrik Norström,
*#Anna Rosén, §Olof Sandström, ||**Lars Stenhammar, *Hans Stenlund,
*Stig Wall, and †Annelie Carlsson



4-2014

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Can an Increase in Celiac Disease Be Attributed to an Increase in the Gluten Content of Wheat as a Consequence of Wheat Breeding?

Donald D. Kasarda

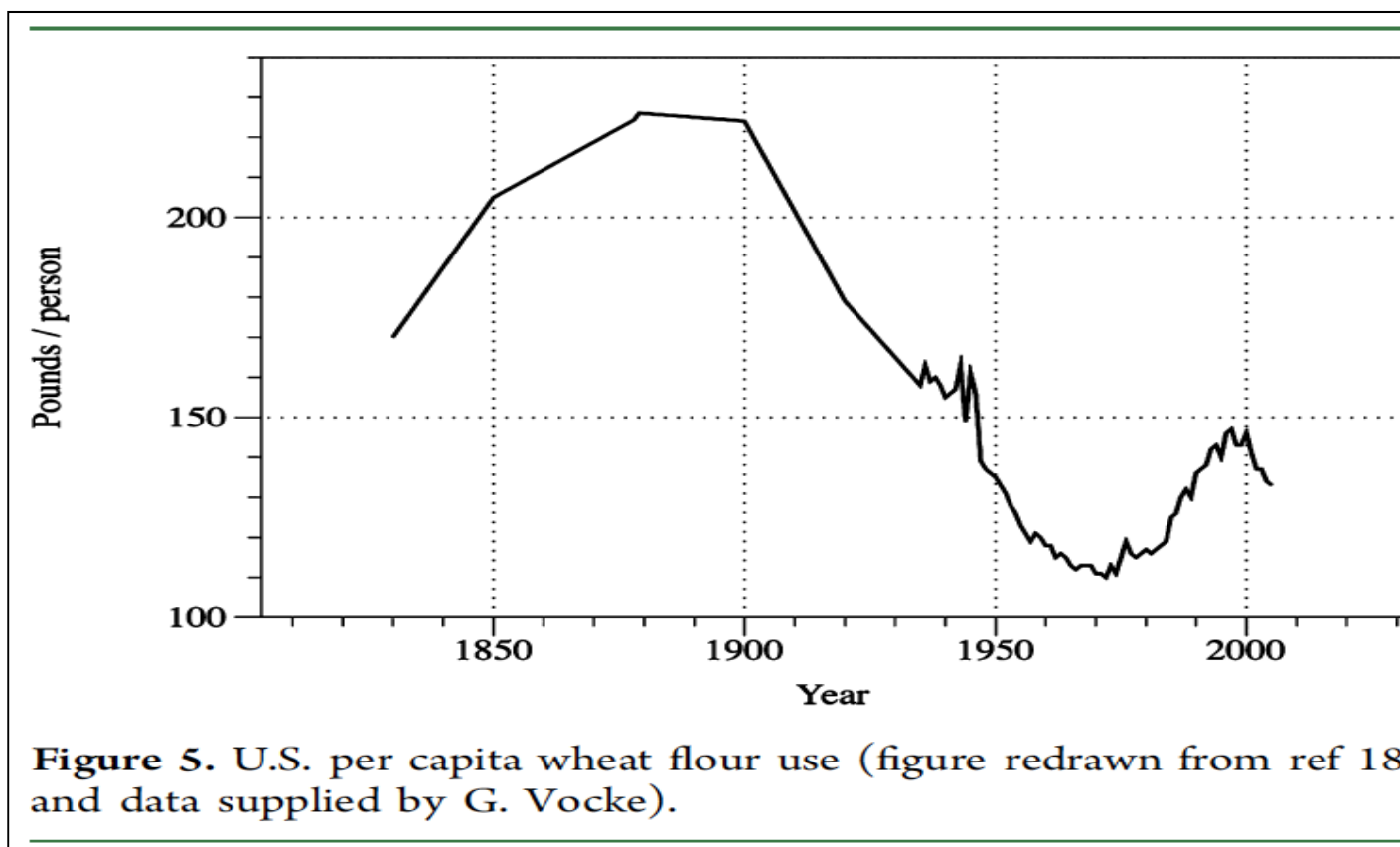
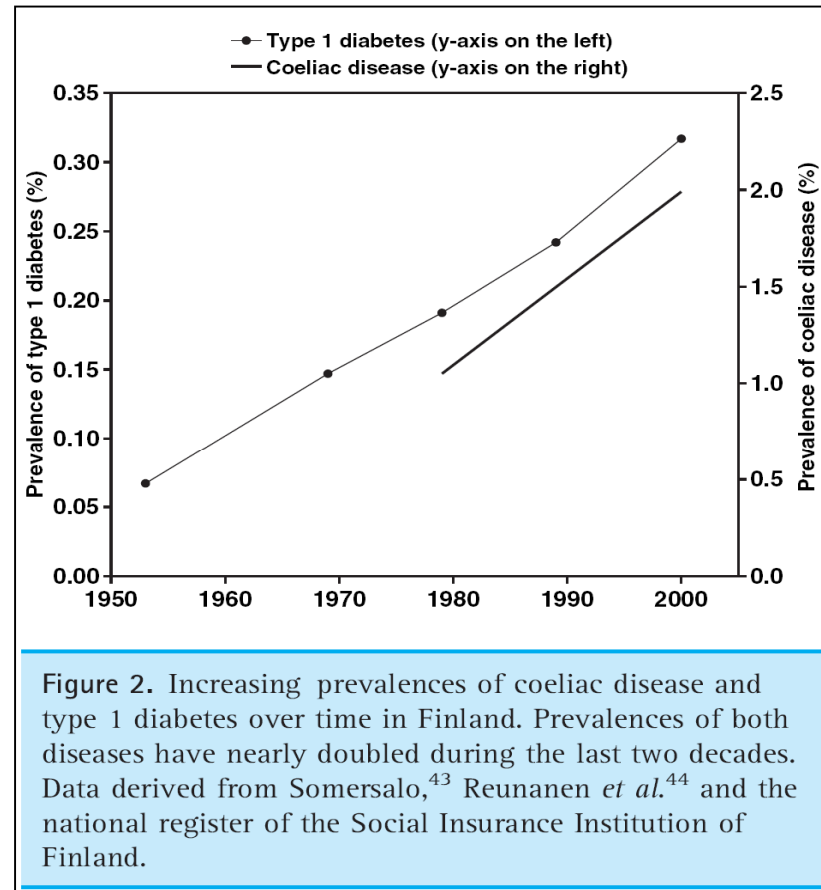
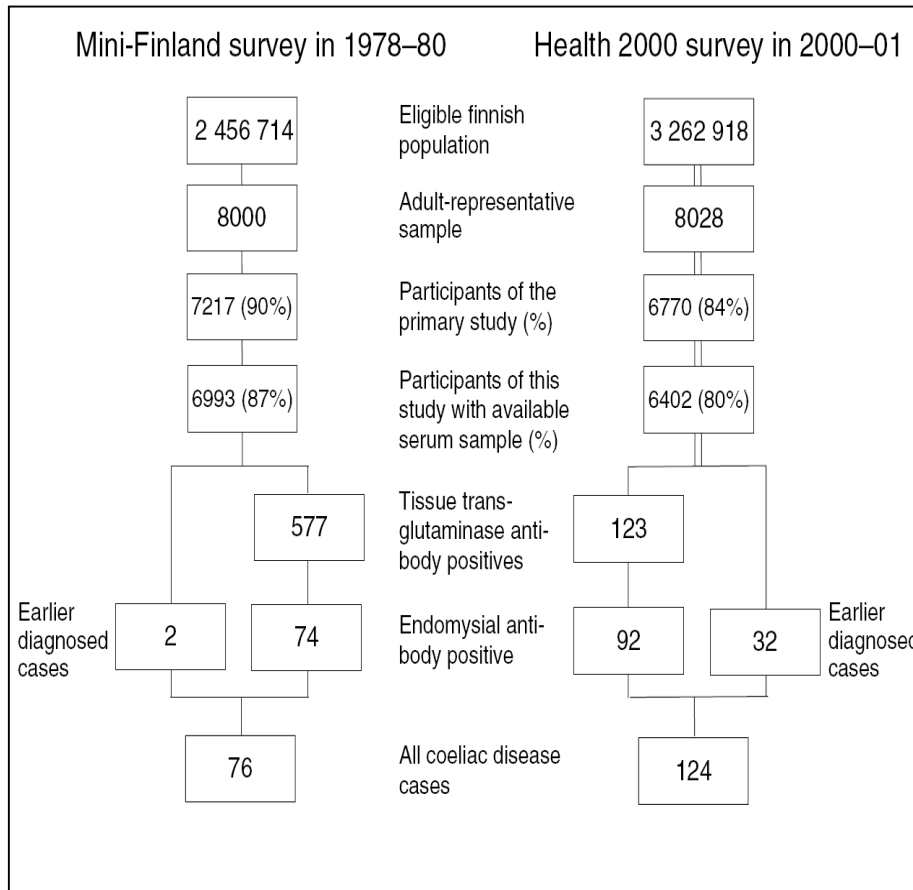


Figure 5. U.S. per capita wheat flour use (figure redrawn from ref 18 and data supplied by G. Vocke).

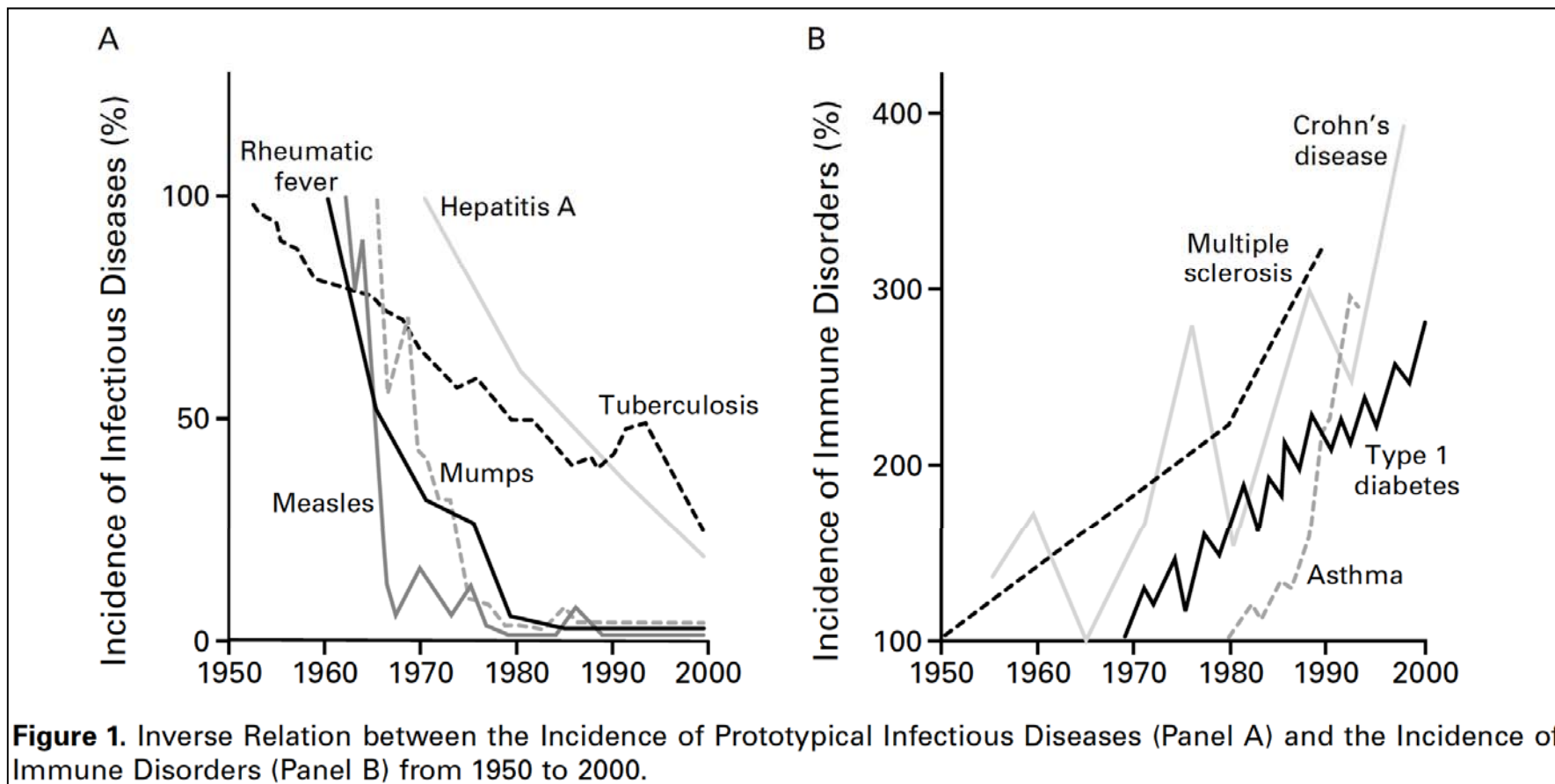
Increasing prevalence of coeliac disease over time

S. LOHI*, K. MUSTALAHTI*, K. KAUKINEN*,†, K. LAURILA*, P. COLLIN†, H. RISSANEN‡, O. LOHI*,§, E. BRAVI¶, M. GASPARIN¶, A. REUNANEN‡ & M. MÄKI*,§





Økning av alle immunsykdommer!



Bach JF. New Eng J Med 2002



Our new health threat

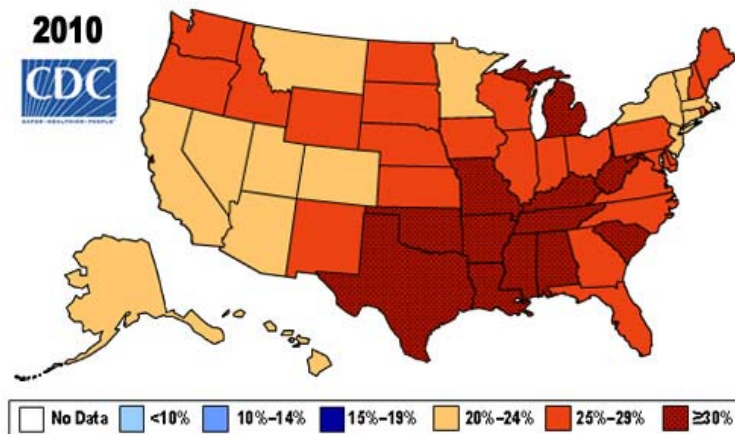
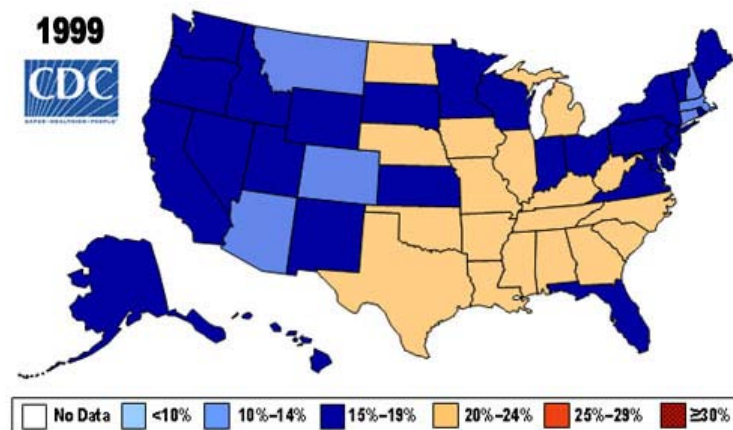
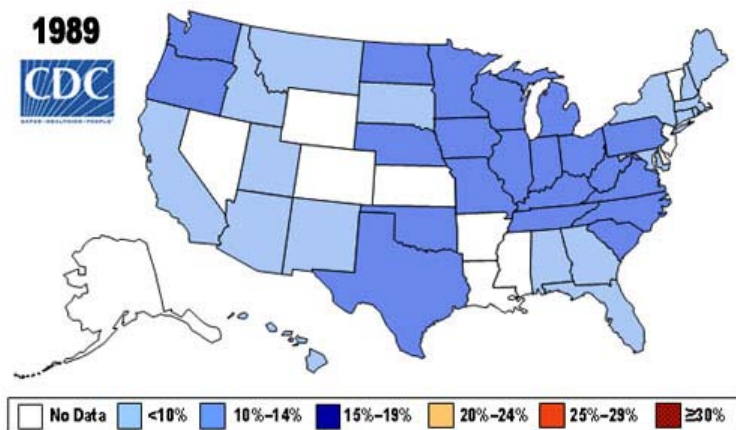


Knut E. A. Lundin

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Obesity development



35.7% of adults BMI>30





Skyldes økningen av cøliaki øket gluten inntak?

- Har bakerne og bøndene “skylden”?
- Mye debattert, spesielt på “sosiale medier”
- Støttes ikke av forskningen



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GFD som trend

- Australia
 - 20 million innbyggere
 - 1 million eller mer på GFD
 - Markedsvekst 15-20 %/år
- New Zealand
 - 5 % av barn gluten-fri
- USA
 - 6 % av befolkningen?
 - USD 5 - 10 000 000 00
 - Markedsvekst > 20 %
- Non-coeliacs på GFD holder dietten strengt
 - Men ikke alltid kontroll på symptomer

The screenshot shows a Newsweek article from December 3, 2008, titled "A New Diet Villain" under the "NUTRITION" category. The article discusses the growing market for gluten-free products, which Americans are spending about \$2 billion a year on. It notes that while advocates claim these products can help with conditions like autism and ADHD, the trend is more about hype than health. The article is by Karen Springen and is a Newsweek Web Exclusive. The article text is partially visible at the bottom of the screenshot.

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Newsweek Search

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LIFE/HEALTH THE WAY WE LIVE AND WHY HEALTH · LIFE · STYLE · HEALTH CARE

NUTRITION ADVERTISEMENT

A New Diet Villain

Americans are spending about \$2 billion a year on gluten-free products, which advocates claim can help with everything from autism to ADHD, but is the trend more about hype than health?

By [Karen Springen](#) | Newsweek Web Exclusive
Dec 3, 2008

Share: [Facebook](#) [Digg](#) [Tweet](#) [LinkedIn](#) [Buzz up!](#) [Print](#) [Email](#)

Tools: [52 Post Your Comment](#) [Print](#) [Email](#)

About six years ago, Diane and Jim McConnell and their son, James Jr., 11, embarked on a dramatic diet change. They decided to give up foods containing gluten, a protein found in wheat, rye and barley. Sticking to the regimen is no easy feat—gluten is ubiquitous in the American diet, as well as in other nonfood products. Not only is it in almost every kind of commercially baked good and pasta, it's even in medications, lipsticks and Play-Doh.

Why take such a life-changing step? It all started when James Jr. began suffering from chronic constipation. "Sometimes I couldn't play with my friends because I was hurting so bad," he says. His condition baffled doctors, who initially prescribed laxatives. He stopped growing and started losing



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To pasienter

•Kvinne f 1952

- 8-9 år mageplager
- Gastroskopi
- Blodprøve med tanke på cøliaki normal
 - IgA-TG2 0,2 U/ml
- Gluten fri kost med godt resultat
- Provokasjon med gluten – nye plager

•Mann f 1978

- 4-5 år mageplager
- Mistanke om sur reflux
- Blodprøve med tanke på cøliaki normal
 - IgA-TG2 0,5 U/ml
- Gastroskopi 2006: Reflux
- Startet GFD m godt resultat

Mye betennelse i

Dagens

STIL

om for allergikermat

tror de har matallergi – få har det. Side 24-25

plagg
Side
26-35
D2

Nordens
design-
topper
Side
36-39
D2

21/2-14

DAG Tøyer strikken

D2 hver fredag!

Hver tredje unge
droppet korn ifjor:

Gluten- skrekk

ONDSKAPENS AKS: Markedet for glutenfri kost har eksplodert. Én av seks nordmenn forsøkte glutenfri diett i 2013. Gluten er gift, mener kritikerne. Ingen dokumentasjon, svarer eksperter.

«Hysteri» og «vrøvl», ifølge forskere

D2
Side 10-20

NYHET!

TØFT BORD FRA NAVER COLLECTION

BLANK SPISEBORD

Øket fokus

År	Cøliaki	NCGS	Forhold NCGS/CD
1970-1979	2632	6	1:438
1980-1989	4915	118	1:43
1990-1999	9498	733	1:13
2000-2013	2014	188	1:10

Publiserte artikler i vitenskapelige tidsskrifter



Prøvd gluten fri mat eller diett i 2013?

	Percentage
Alle	17 %
Kvinner	21 %
Menn	14 %
15-24 år	32 %
25-45 år	17 %
46 + år	14 %

Hvete forbruk



Kg pr person og år - Norge

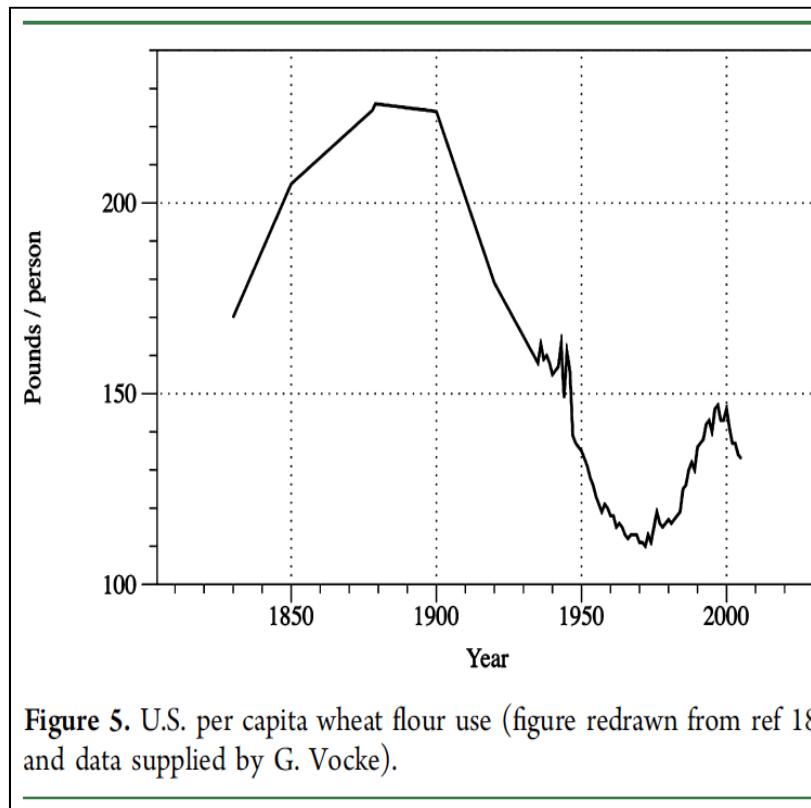


Figure 5. U.S. per capita wheat flour use (figure redrawn from ref 18 and data supplied by G. Vocke).

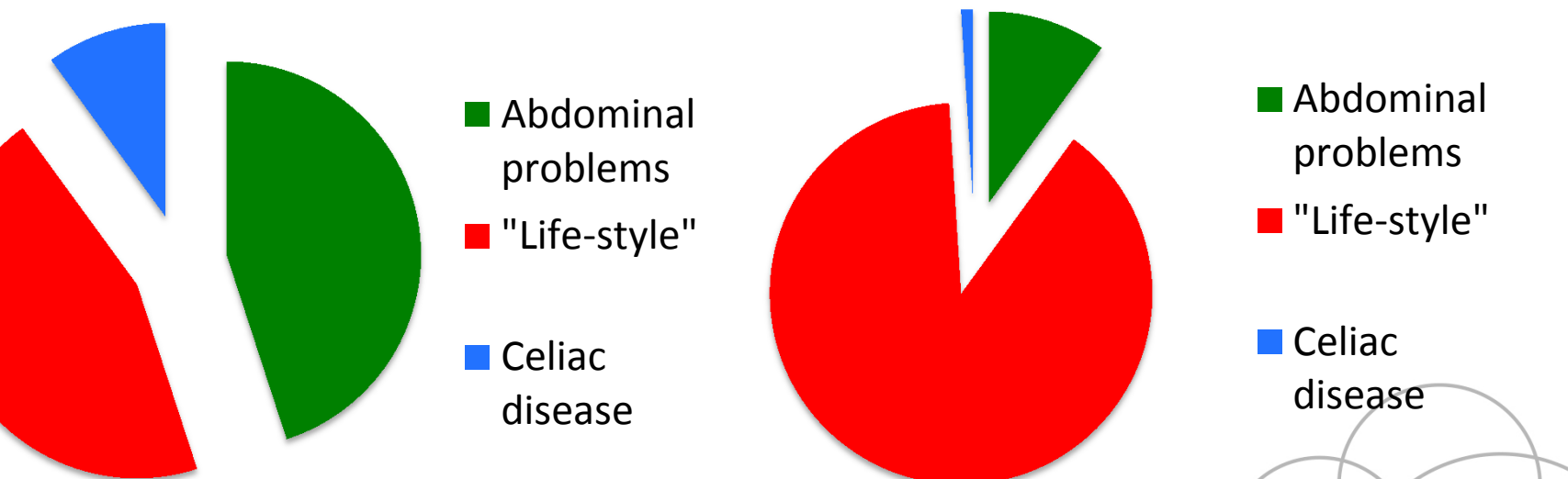
Kasarda 2013. J Agric Food Chem

Generell befolkning - Norge

	2006	2012
prøver å få en slankere opp	55 %	77 %
unngår mat med mye sukker og fett	64 %	81%
er ikke så opptatt av åpen min	24 %	10 %
tenker lite over hva jeg er	20 %	14 %

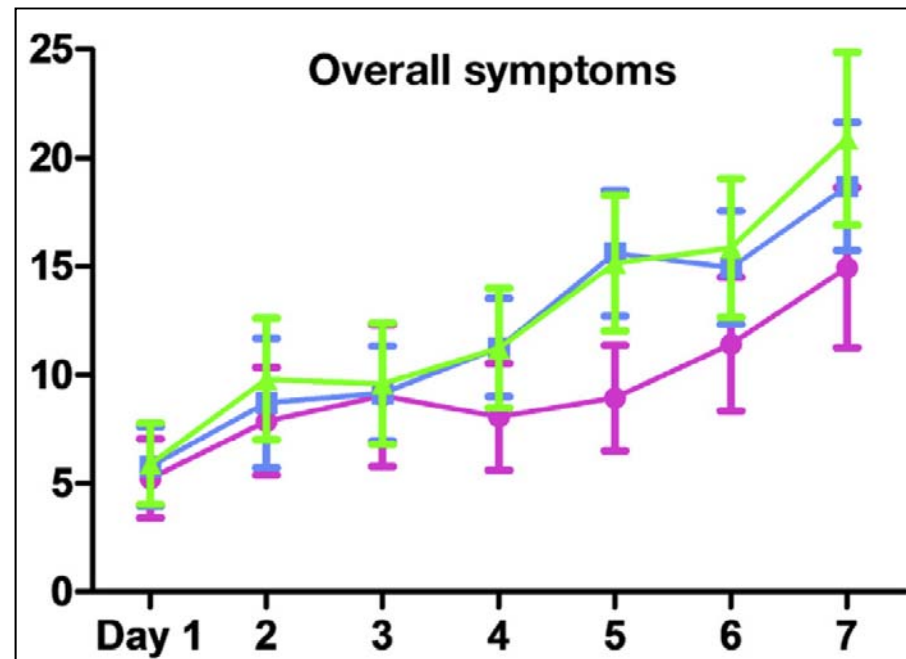
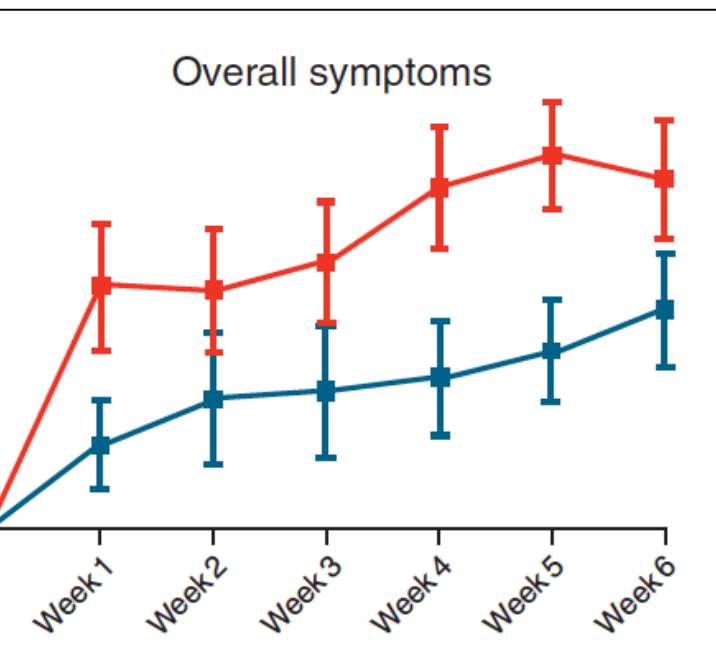
Gluten-free market Europe and US

Europe USA
scientific evidence basis?



consumption of gluten free food USD 5-10 000 000 000

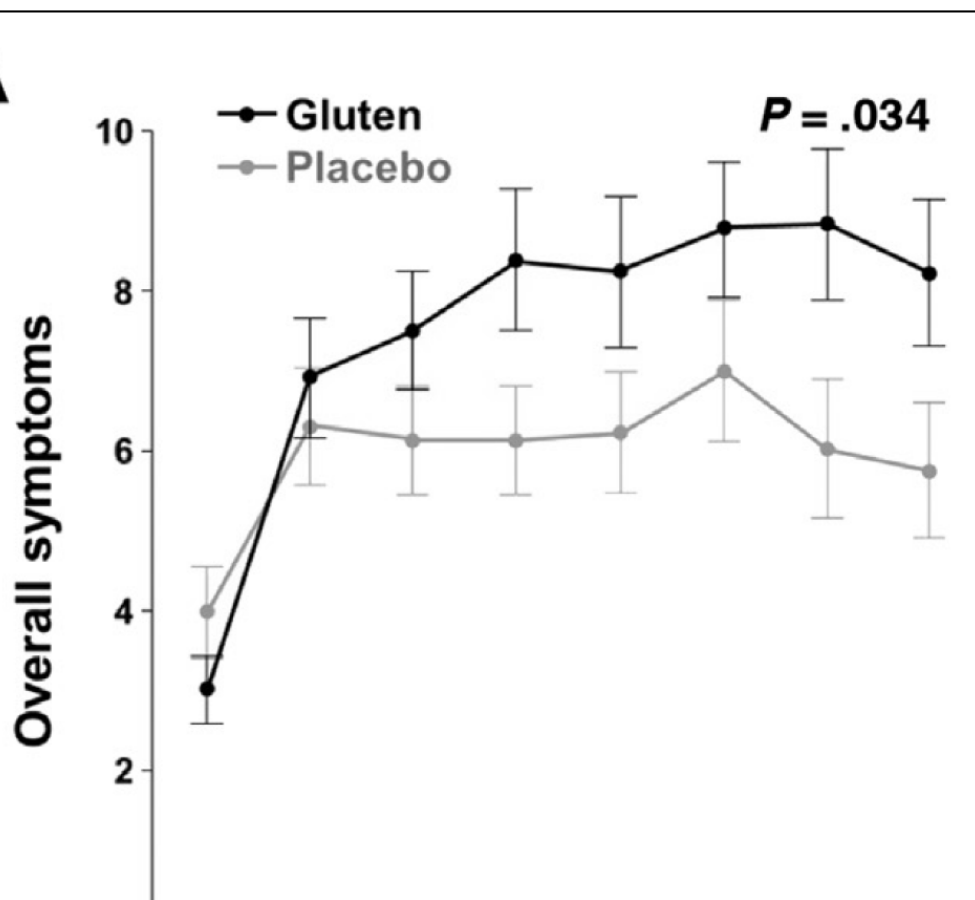
Gluten challenge



Gluten
Placebo
S Score: 0 = None 100 = Worst



Gluten challenge



- 61 voksne uten CD eller hvete allergi
- 4,375 g “gluten” eller ris stivelse i kapsler
 - Di Sabatino et al 2015
Clin Gastro Hepatol

Forskjellige syn

NCGS skyldes en
spesifikk reaksjon mot
proteiner i gluten

- NCGS skyldes en
reaksjon mot vanskelig
fordøyelige
karbohydrater
(FODMAP)



Frivillige til glutenfri kosthold?

Glutenfritt ikke alltid
velsmakende!

- Men kan være godt!



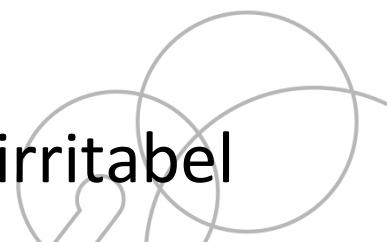


fermentable Oligo-, Di-, Monosaccharides And Polyols
(FODMAP)

uskelig nedbrytbare karbohydrater etc

duksjon av FODMAP beste behandling for "irritabel

ms syndrom"



semantisk spørsmål

Snakker vi om

- Irritabelt tarm syndrom (IBS) med reaksjon mot mat
 - ICD-10 K58.0
- Matvareintoleranse (gluten) med IBS liknende symptomer
 - ICD-10 K52.2
- Cøliaki (incl “lettere varianter”)
 - ICD-10 K90.0

Uttrykket “IBS” er ganske problematisk

Glutensensitive norske “pasienter” kan ha rett til

gruppnet med fra NAV



Provokasjon - placebo problemet



- NAV krever provokasjon hos spesialist for stønad
- Tradisjonell placebo
 - Kapsler med mel eller narrekapsler
 - Vanskelig, gjøres ikke
 - Lundin and Alaedini 2012
- Quinoa basert müsli bars med og uten gluten
 - studie i Oslo



Konklusjon

- Glutenfri kost
 - Antatt store proporsjoner
 - NCGS mangler diagnostiske kriterier
 - Placebo-kontrollert blindet eller åpen provokasjon?
 - Har vi et godt placebo produkt?
 - Terskel for diagnose?
 - Biomarkører av begrenset nytte (men brukes mye)
- Ingen “harde endepunkter” for NCGS
- Stort press blant publikum – sykdom? Grunnstønad?

va med ”harde endepunkter”?

- Gunstig effekt av korn hos befolkningen?
- Helse og død hos cøliakere?
- Og hva med ikke-cøliakisk gluten sensitivitet



Current treatment

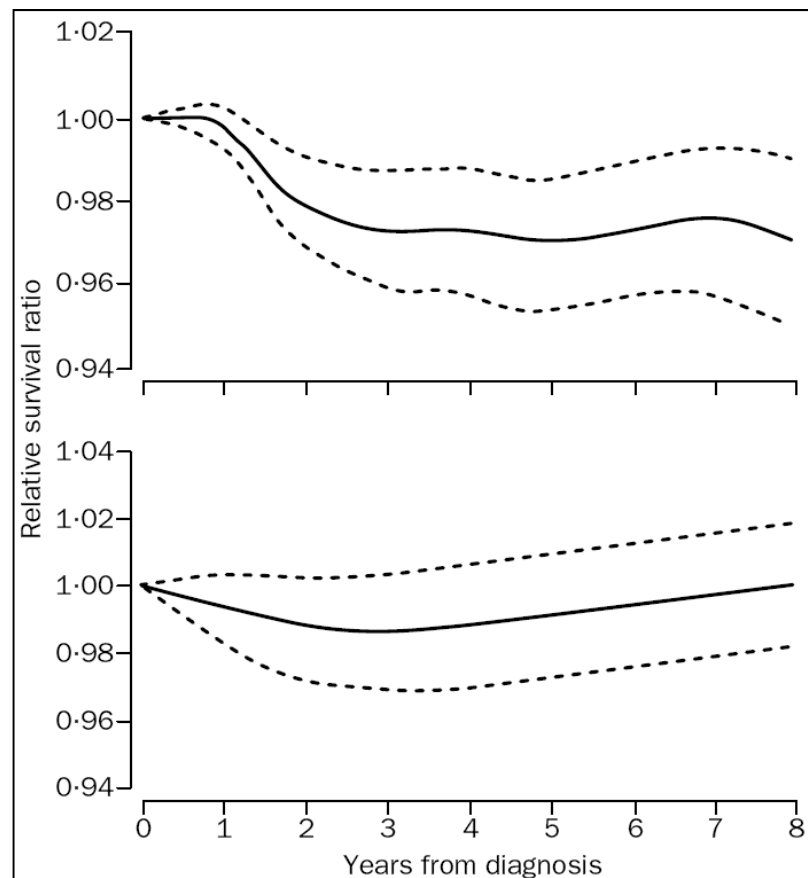
1072 coeliacs and
3384 relatives.

53 coeliacs dead,
expected 25,9.

Non-Hodkins lymfoma.

Protection by GFD.

Selection bias?



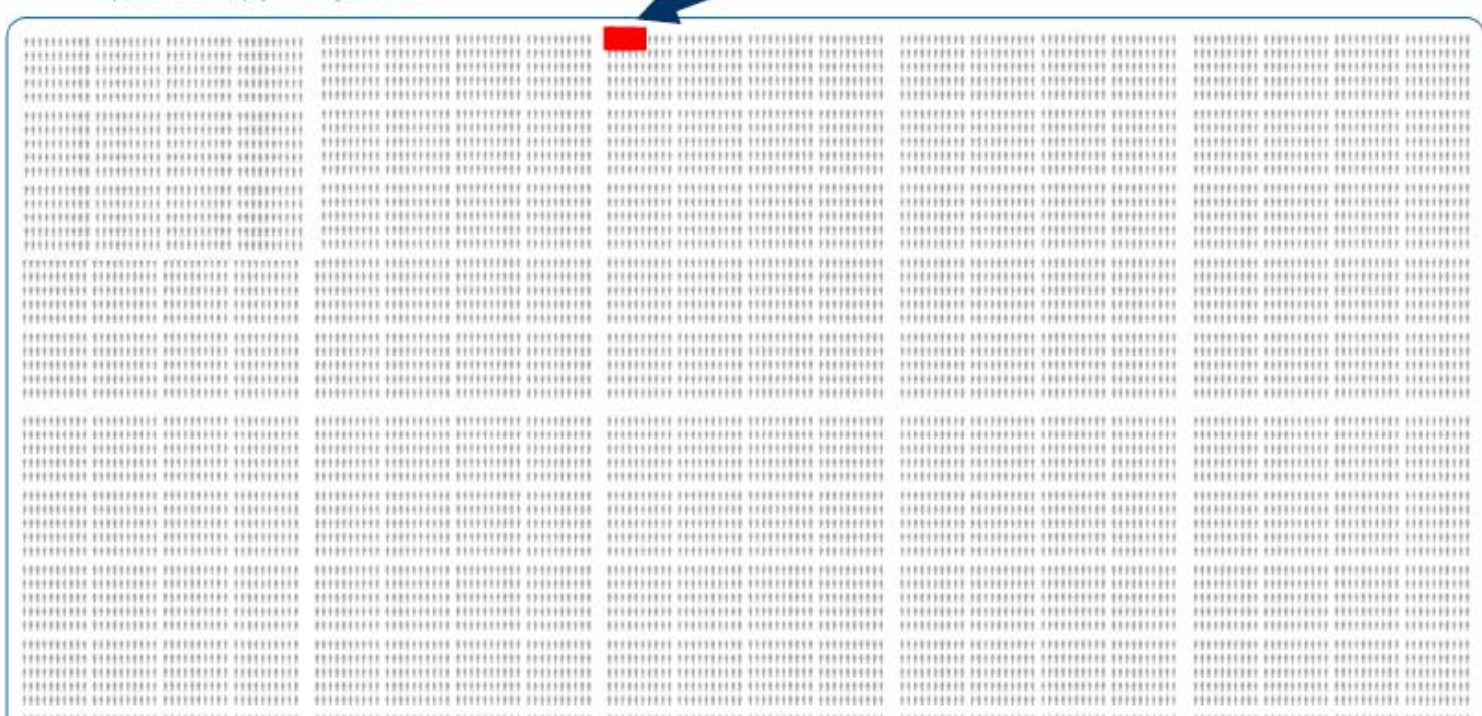
Risk assessment –lessons from IBD

Risk of Developing NH Lymphoma

20 year old male receiving anti-TNF + Immunomodulator Therapy

Ten Thousand People
– pictures to help you see your odds

Risk with combination therapy



Swedish registry studies

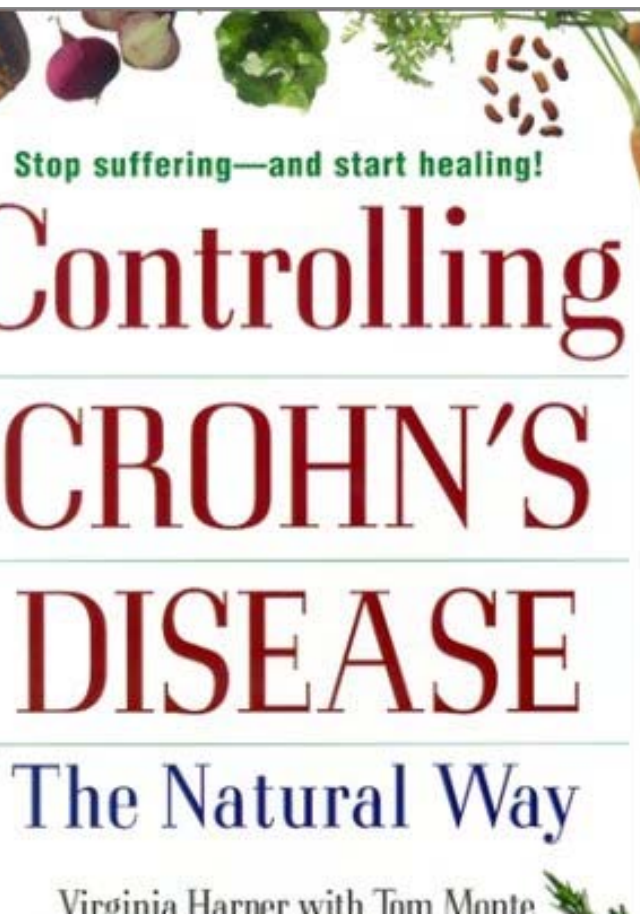
Causes of death:

- 10 032 coeliacs
- Hospitalized
- Follow-up 1965-1994
- 2 fold increased death for coeliacs
- Cancer and immune diseases.
- 1,4 fold increased death risk if CD was only diagnosis

• Cancer types:

- 12 000 coeliacs
- Hospitalized
- Adults (but not children) had 1,3 x cancer risk
- Declining risk
 - After diagnosis
 - With time
- Protection by gluten free diet
 - Askling et al. 2002

Coeliac disease and IBD



- Patients with Crohn and UC:

- Find a diet to get rid of drugs!

- Patients with Coeliac disease:

- Find a drug to get rid of the diet!

- East is east and west is west and never shall the twain



Alvine pharmaceuticals



Celiac Disease occurs
in 1 to 2 out of every
100 people

90% Remain Undiagnosed Even though They
Are Experiencing Symptoms or Complications
of Celiac Disease.

[learn more](#)

celiac disease our science our people

Focused on Celiac Disease and other
autoimmune/inflammatory diseases

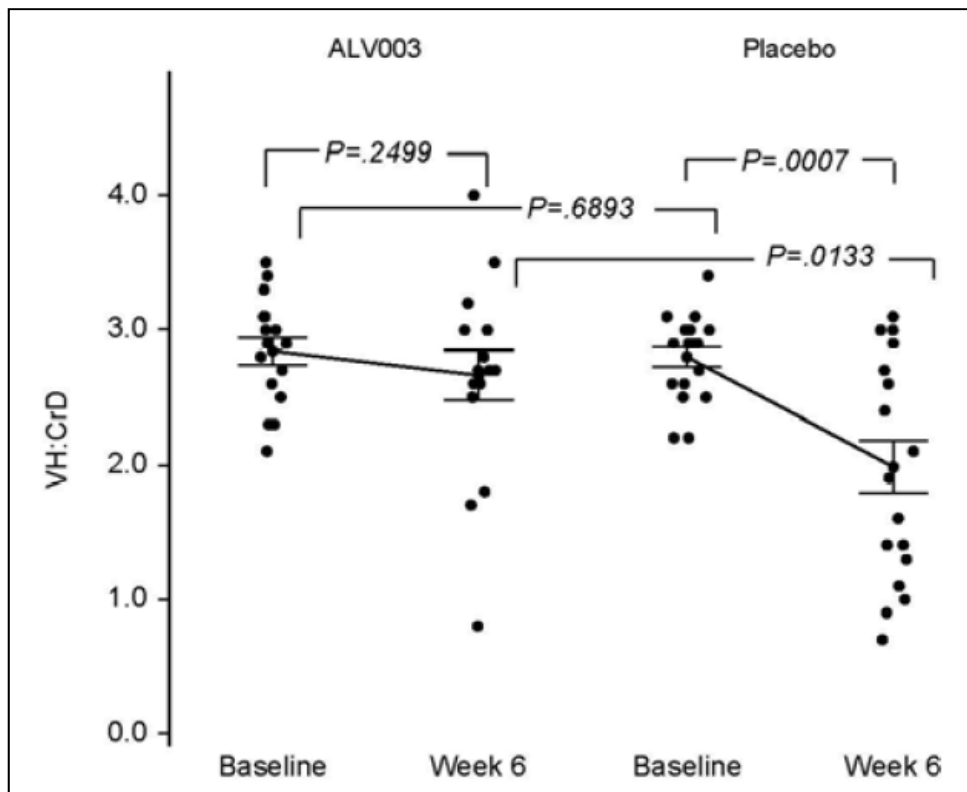
Alvine Pharmaceuticals, Inc., is a privately held, clinical stage
company developing biologics to target
autoimmune/inflammatory diseases. Alvine's lead product



To inquire about participating in the Phase
2b clinical study, email:
info@alvinepharma.com



Alvine Pharma ALV003 beskytter mot 6 ukers gluten provokasjon



Enzympille og cøliaki

- Utviklet av stort amerikansk firma
- Internasjonal multisenter studie på behandlet cøliaki nettopp fullført
 - Vi hadde med 4 av ca 500 pasienter
- Ryktene forteller om “negativt resultat”



Enzyme therapy

Alternativ terapi?

Aktuelt for aksidentiell
eksponering?

Enzymer fra

- Korn
- Bakterier
- Sopp

Aktuelt som
kosttilskudd?

Home Products Contact Us Quality Resources

KIRKMAN Specialty probiotic, ThreeLac™! Use Key Code FB2 at checkout. Limited time offer.

- Home
- Kirkman Products
- Kirkman Kleen Products
- Hypoallergenic
- Products By Function
- About Us
- Kirkman® Ultra Tested®
- Press Room
- Doctors / Wholesale

ULTRA TESTED™
The highest standard of purity testing!

What's New?
Dr. Skip Kingston Praises Kirkman's Ultra Tested®

WATCH THIS!
The case for Ultra Tested®

The KIRKMAN® Difference
We've Been Serving Our Customers Since 1949

KIRKMAN® is the oldest and one of the leading manufacturers of nutritional supplements for individuals with food allergies, special dietary requirements and environmental sensitivities.

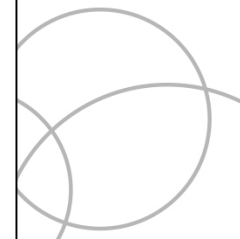
Quick Order

Have You Joined the Kirkman Family yet?

Find Supplements Free of: [Read More](#)

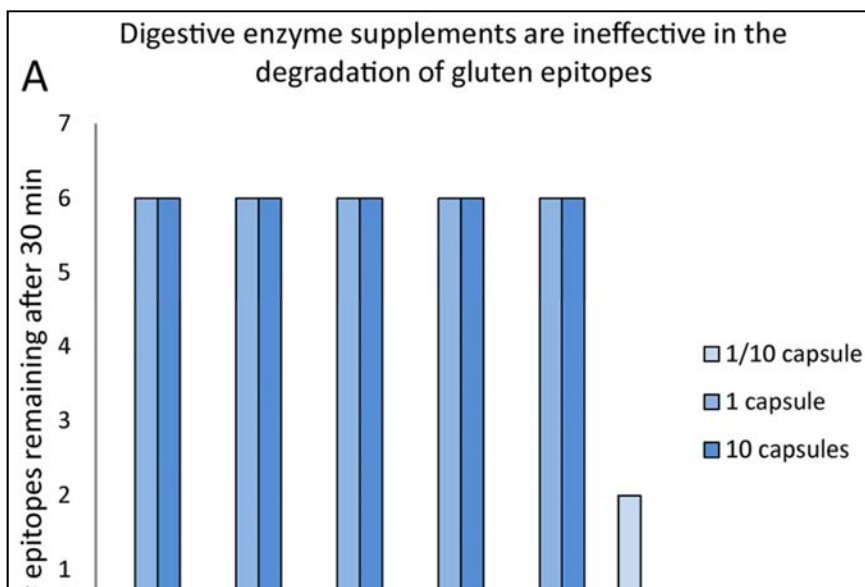
Enzym-Complete/DPP-IV™

Description | Free Of | Warnings | Supp



Ineffective Degradation of Immunogenic Gluten Epitopes by Currently Available Digestive Enzyme Supplements

George Janssen¹, Chantal Christis², Yvonne Kooy-Winkelaar¹, Luppó Edens²,
Drew Smith³, Peter van Veelen¹, Frits Koning¹*

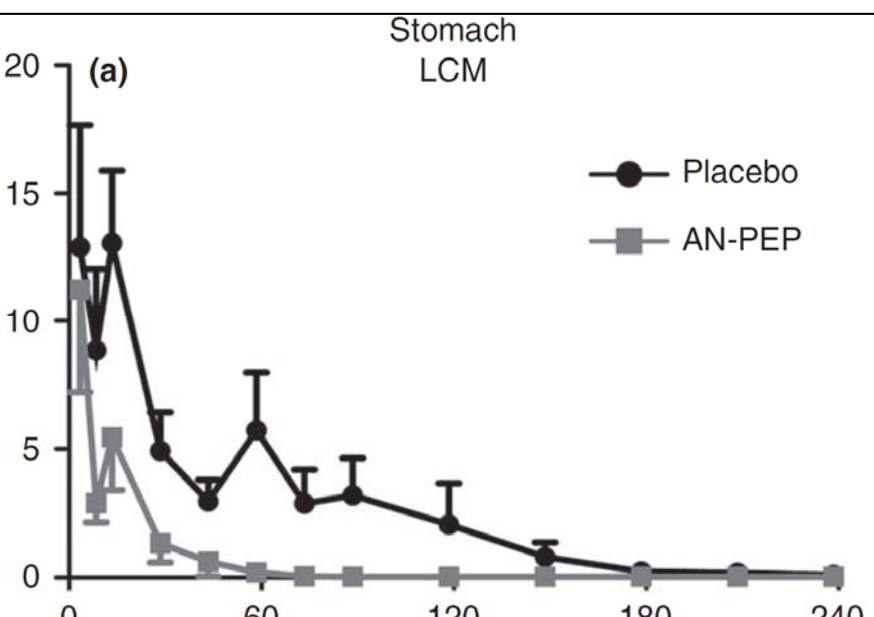


Enzympreparater i handelen bryter ikke ned gluten godt nok!



Randomised clinical study: *Aspergillus niger*-derived enzyme digests gluten in the stomach of healthy volunteers

S. Salden^{*}, V. Monserrat[†], F. J. Troost^{*}, M. J. Bruins[‡], L. Edens[‡], R. Bartholomé[§], G. R. Haenen[§], B. Winkens[¶], J. M. A. M. van Duyn[†] & A. A. Masclee^{*}



- AN-PEP enzym fra DSM
- Bryter ned gluten effektivt
- Ikke testet på cøliakere
- Markedsføres i USA som

