

Fibre – insights and perspectives from a clinical researcher

Mark Daly
Consultant endocrinologist,
Exeter

This talk

- A confused public
- Lessons learnt from the pharmaceutical industry (or what makes us cynical about data)
- Implications for fibre data
- Helpful friends – fibre's associations
- Current recommendations set against evolving areas of research
- How might industry help public health advisors and clinicians

A typical week....

- “There’s no point eating healthily – what’s bad for you this week will be life-saving next”
- “It can’t be to do with my diet – I only eat healthy food and I still can’t lose weight!” (at 185kg)
- “This diet’s not working – despite my £150 food bill”
- (50 yr old builder, after eating pkt bacon, 6 eggs breakfast, 8 chops lunch and 6 chicken breasts evening - “Atkin’s Diet”)

Learning from the Drug industry's successes and failures

Changes over time

1997

Observational studies have suggested that oestrogen-replacement therapy may reduce a woman's risk of stroke, heart attack and death

1998

*the HERS investigators conclude that until results from other ongoing randomized trials of HRT are available, oestrogen should **not** be started in women with CHD to prevent heart attacks*

2005

HRT increases the risk of
strokes by as much as
29%.....

Implications for Fibre data

- Habitual intake data, even in the context of a prospective study does not enable firm conclusions
- The more healthy eating is promoted, the more this applies
- Large, long RCTs are needed for hard endpoints

"Soft" versus "Hard" endpoints

- Cholesterol, glucose, insulin, stool markers, stool frequency are "soft" endpoints
- (AKA surrogate markers)
- Cancer, Heart attacks, strokes and death can all be seen as "Hard" endpoints

1995

Widespread use of fibrates (effective in lowering of cholesterol and triglycerides) – First line

Reduced use of statins (powerful lowering of cholesterol, not much effect on triglycerides) – Second line

2005

Widespread use of statins

Minimal use of fibrates

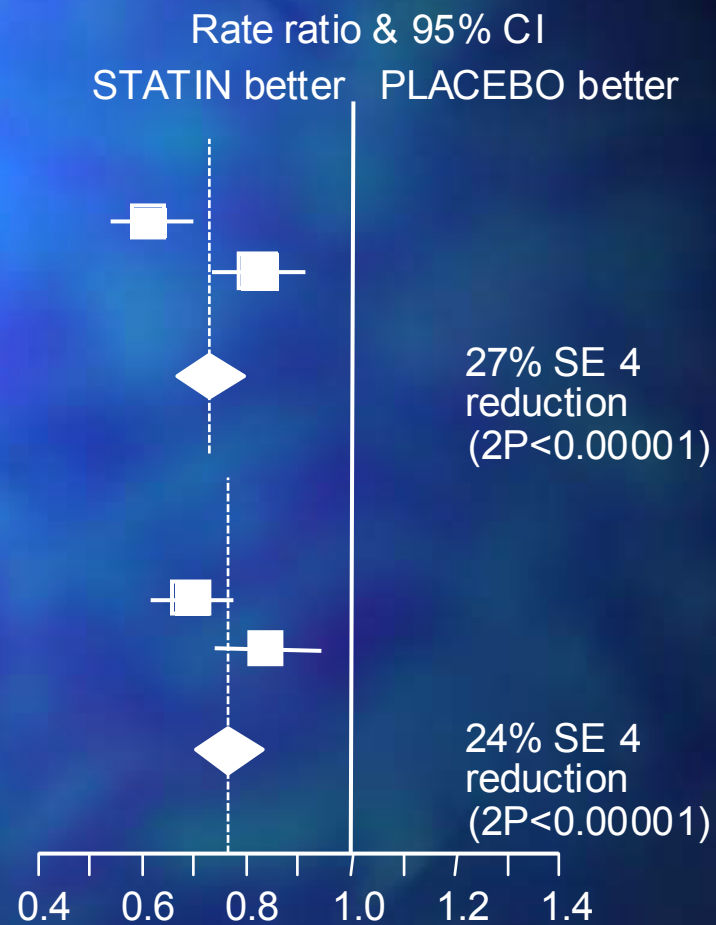
WHY?

2002 – Heart Protection Study

- 10269 v 10267, intervention v placebo with simvastatin

SIMVASTATIN: CORONARY EVENTS & REVASCULARISATION

	SIMVASTATIN (10269)	PLACEBO (10267)
Major coronary event		
Non-fatal MI	357	574
Coronary death	587	707
CORONARY EVENTS	898 (8.7%)	1212 (11.8%)
Revascularisation		
Coronary	513	725
Non-coronary	450	532
REVASCULARISATIONS	939 (9.1%)	1205 (11.7%)



Conclusion

- Surrogate/"soft" endpoints can be misleading in determining real-life events
- Claims cannot be extrapolated from surrogate endpoints

Compliance and contamination in nutritional interventions

Or why it's so difficult –
back to the HPS

STATIN USE: Compliance with study simvastatin or use of non-study statin

Years of follow-up	Approx. no. of patients	SIMVASTATIN allocated	PLACEBO allocated
1	20,000	89%	4%
2	20,000	85%	9%
3	19,000	84%	17%
4	18,500	83%	24%
5	14,500	82%	32%
STUDY AVERAGE		85%	17%

Conclusion

- Compliance will always be less and contamination greater in a nutritional intervention
- If it takes 20000 to show an hard endpoint outcome with a pill, it will take many more with a dietary change

The state of play in some key areas

Cancer, Diabetes, CVD

Cancer

- The Polyp Prevention Study
 - People can change their diets!
- The Wheat-Bran Fibre Study
- Whole grain rye & wheat food 4 wk intervention
 - Improved markers of bowel health (at 32g/d)
 - (huge improvements in insulin responses)
- But case control > cohort
- “Modest support”
- “Other factors associated with whole grain intake may play a role”

Cardiovascular Disease

- Fibre intake v total energy intake
- Energy intake reflects expenditure (at a population level)
- Strong inverse associations in cross-sectional and cohort studies
- Disappointing small scale effect on lipids (eg 2.1% reduction v 30% for a statin)
- But some suggestion for protection of viscous fibre and pectin against atherosclerosis prevention

Diabetes

- It's more people than you think and they're getting bigger (and more numerous)
- ~50% of Americans over 50 have some form of impaired glucose tolerance
- The diagnostic hurdle is getting ever lower.....

Diabetes

- Strongest data of the three
- GI, GL, total fibre intake, whole-grain
 - All associated with incidence of T2D in cohorts
 - Inc fibre a main aim in large, successful RCTs !!

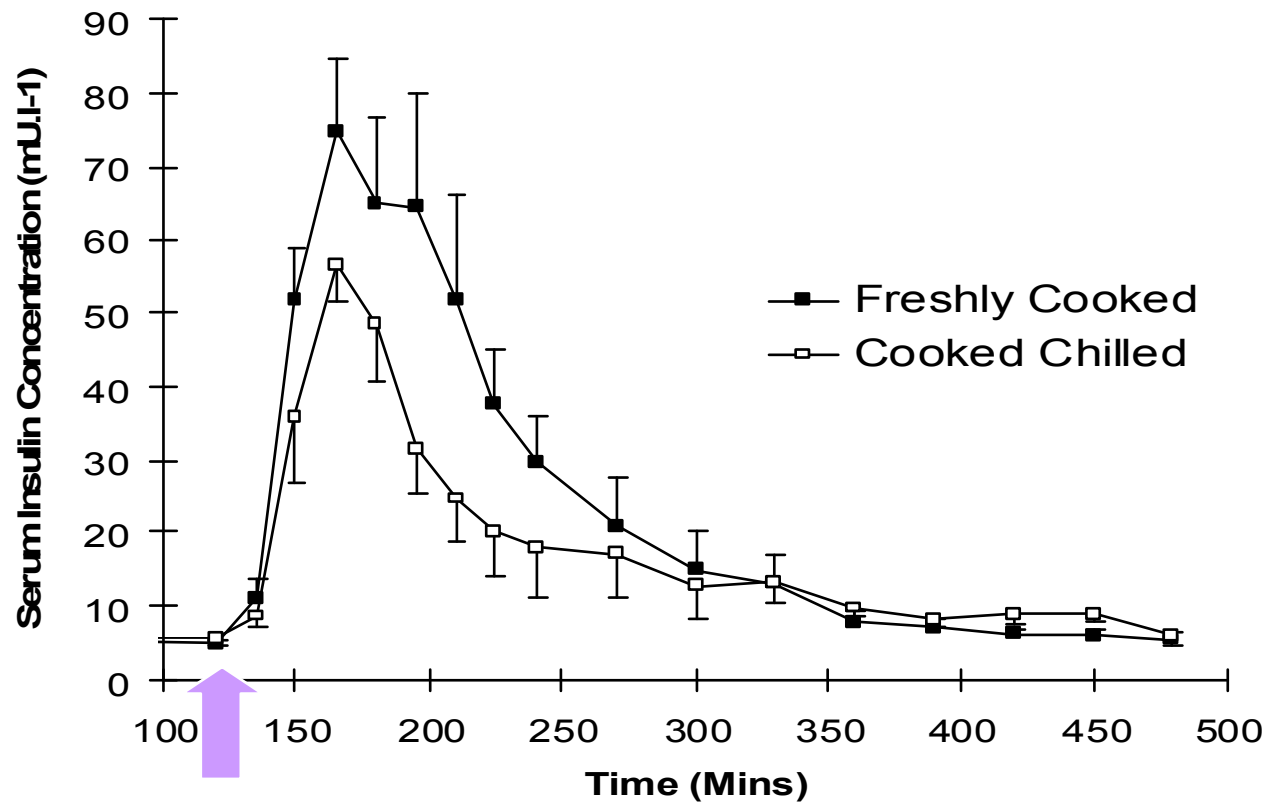
So where does that
leave us?

Fibre's friends

Fibre's friends

- Low glycaemic index foods
 - Diabetes, HDL, insulin sensitivity (wt loss)
 - Readily modifiable
- Low glycaemic load
 - High fibre pulses - low GI and lower carb content = Lower GL
 - Readily modifiable
- Wholegrains

Post-prandial insulin



Simple changes in potato cooking radically alter insulinaemia

Current recommendations

- Diabetes UK
- Food and Health Action Plan
- Dietary Guidelines for Americans

Current recommendations

- Dietary Guidelines for Americans
 - Choose fibre-rich fruits, vegetables and whole grains often
 - At least 3-ounce equivalent servings per day of whole grains
 - Aim for 14g per 1000 kcal consumed of fibre (not further qualified)

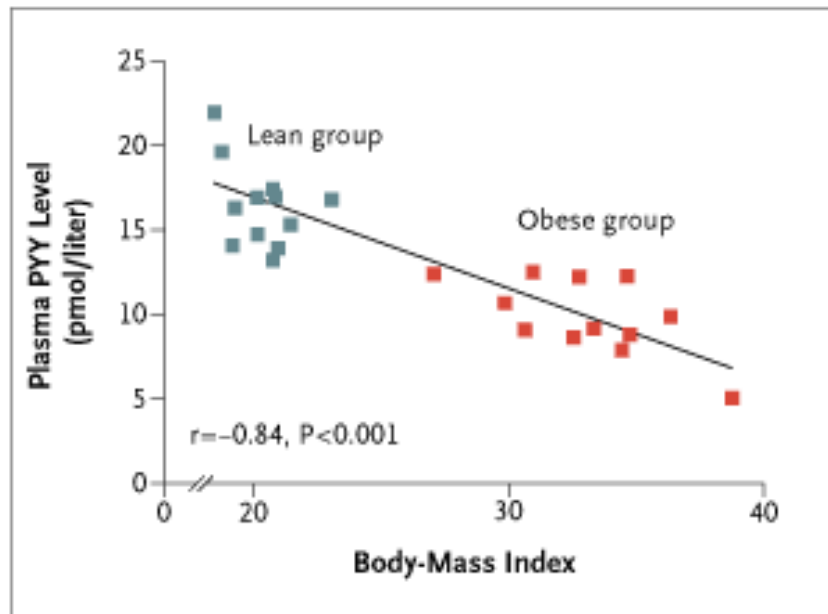
Current Recommendations

- Diabetes UK
 - No quantitative advice
 - Soluble good for glycaemia
 - Low GI good
 - Insoluble good for weight & appetite

Future directions

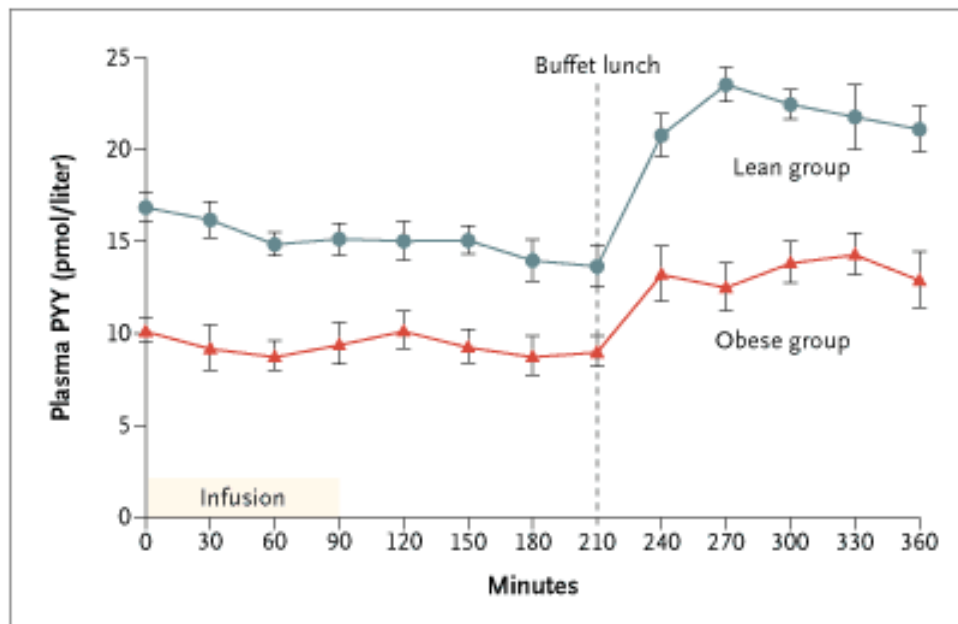
- Surrogate (but marketable endpoint studies) with fibre subtypes
 - GI, GL
 - Functional foods?
- Collaborative research re: changing consumer practice for the benefit of all
- The appetite hormones (PYY, Ghrelin)

PYY and obesity



- Reduces food intake
- Strong correlation with PYY in fasting state for BMI
- Maladaptive response
- Gut hormone, likely to be regulated by food

PYY and the post-prandial state



- Differences between lean and obese are exaggerated after meals
- Any food which promotes PYY secretion may be especially beneficial

Conclusions

- Strongest benefit for fibre is with metabolic benefits
- Such benefits are best proven in association (wholegrains, low GI etc)
- May yet have a role in hormonal regulation of appetite