

**Centre for High-Value Nutrition** 

HIGH-VALUE NUTRITION

> Ko Ngā Kai Whai Painga

# The effect of Zespri Green Kiwifruit on digestive and gut health functions

# A multi-country, randomised, cross-over clinical intervention study

Dr Richard Gearry Professor of Medicine and Gastroenterology University of Otago, Christchurch

Host Institution











## **Project Team**

- Principal Investigators
  - Professor Richard Gearry (NZ)
  - Professor Giovanni Barbara (Italy)
  - Professor Shin Fukudo (Japan)
- Project Manager
  - Lynley Drummond (Drummond Food Science Advisory Ltd)
- Project Leader
  - Dr Juliet Ansell (Innovation Leader [Health and Nutrition], Zespri)



## **Project Team**

• Research Team

 Plant and Food Research Ltd (Christchurch and Palmerston North) Sarah Eady, Alison Wallace, Dr Chrissy Butts, Hannah Dinnan, Philippa Wadsworth

• Statistics

- Dr Barbara Kuhn-Sherlock (BKS Consulting)



## Relevant disclosures

- Richard Gearry
  - Zespri advisory board member, funding for research
- Lynley Drummond
  - Zespri advisory board member, funding for research
- Giovanni Barbara, Shin Fukado
  - Zespri advisory board member, funding for research
- Juliet Ansell
  - Zespri employee
- Plant and Food Research Staff, Barbara Kuhn-Sherlock
  - Contractors to Zespri for research services



# Background (Constipation)

- Constipation affects 15% of adults in western countries
  - May occur alone (functional constipation)
  - May occur with abdominal pain (Irritable Bowel Syndrome-Constipation predominant)
- Significant effect on physical and mental quality of life
- Significant impact on school and work
- Improvement of quality of life in adults with effective therapy



### Background (Gastrointestinal discomfort)

- Gastrointestinal discomfort
  - less well studied and defined
  - may include pain, bloating, borbourigmi
  - may be related to constipation in some indivduals
  - significant impact on quality of life
  - significant impact on school and work



#### What do we know about kiwifruit and the gut?

Authors	Country	Participants	Study Design	Ν	Findings
Rush et al	NZ	>60 years Constipated	Randomised, crossover, no control	38	<ul> <li>↑ stool frequency</li> <li>↑ ease of passing BM</li> <li>↑ Bulkier, softer stool</li> </ul>
Chang et al	Taiwan	Adult IBS - constipated	Randomised study with capsule control	41	<ul> <li>stool frequency</li> <li>colonic transit time</li> </ul>
Chan et al	Hong Kong	Constipated adults	Prospective observational study (no control)	53	<ul> <li>stool frequency</li> <li>bowel habit satisfaction</li> <li>laxative use</li> </ul>
Hiele (unpubli shed)	Belgium	Adult IBS - constipated	Prospective observational study (no control)	38	<ul> <li>↑ stool frequency</li> <li>↑ ease of passing BM</li> <li>↓ abdominal bloating</li> </ul>



# Why is it important to demonstrate kiwifruit efficacy for bowel frequency and comfort?

- For consumers
  - to confirm what many people suspect is true
  - to provide high quality trusted efficacy and safety information
- For Health care providers
  - expectation of high quality research
  - develops a deeper understanding of the effects of kiwifruit on gut health
- For Zespri
  - Important as a responsible corporate citizen
  - accurate, independent data concerning benefits of consuming kiwifruit
  - as part of a validated health claim, enables marketing direct to consumers



#### How can Zespri Health Science be communicated?



# The effect of Zespri Green Kiwifruit on digestive and gut health functions

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## Hypotheses

- That consumption of two Zespri green kiwifruit (Actinidia deliciosa var Hayward) daily improves bowel motion frequency in constipated individuals by >1.5 complete spontaneous bowel motions / week
- That consumption of two Zespri green kiwifruit (Actinidia deliciosa var Hayward) daily improves gastrointestinal discomfort in constipated people
- That two Zespri green kiwifruit (Actinidia deliciosa var Hayward) are well tolerated by constipated individuals and healthy controls



## Study design

- Randomised single-blinded cross-over design
- Powered to show an increase of 1.5 CSBM per week 90% power, 5% significance



# Inclusion / exclusion criteria

#### Inclusion

- 18-65 years of age
- BMI 18-35
- Functional constipation (20)
- IBS-C (20)
- Healthy (20)

#### Exclusion

- GI alarm symptoms
- Significant chronic medical conditions
- Fasting glucose >7.2mmol/L
- Drugs affecting GI motility
- Pregnant / breastfeeding women
- Known kiwifruit or latex allergy
- Not prepared to stop other laxatives



#### Schedule of Assessments



## Clinical assessments

- Primary outcome
  - Daily bowel habit diary (CSBM, BM, CBM, SBM)
- Secondary outcomes
  - Daily bowel habit diary (ease of defaecation / straining, stool form)
  - Weekly Gastrointestinal Symptom Rating Scale
    - 7-grade scale, 5 domains (reflux, abdominal pain, indigestion, bowel dysfunction)
  - IBS-Quality of Life Questionnaire
  - Colonic transit measured by SmartPill in a subgroup
  - Profile of mood score (POMS)
  - Food diaries (to ensure no changes to habitual diet)
  - Faecal microflora / vitamin C



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#### **GSRS** Domains

Diarrhoea	<ul> <li>Increased passage of stools</li> <li>Urgent need for defeacation</li> </ul>
Indigestion	<ul> <li>Abdominal distension Borbourigmus</li> <li>Eructation Increased flatus</li> </ul>
Constipation	<ul> <li>Decreased passage of stools Hard stools</li> <li>Feeling of incomplete evacuation</li> </ul>
Abdominal Pain	<ul> <li>Abdominal pain</li> <li>Nausea and vomiting</li> </ul>
Reflux	Heartburn     Acid regurgitation     Challenges

#### **Bristol Stool Chart**



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### SmartPill<sup>®</sup> Motility Monitoring System

#### What is SmartPill?

An ingestible capsule utilizing sensor technology to evaluate GI motility, specifically delayed gastric emptying (gastroparesis) and chronic constipation

#### Replaces

- Scintigraphy
- Sitzmarks<sup>®</sup> (ROM)

#### Complements

- Endoscopy
- Antroduodenal Manome





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#### SmartPill<sup>®</sup> Tracing



## Safety

 Rescue therapy with bisacodyl 5g suppositories available and reported

Reactions to kiwifruit and psyllium sought throughout study

All adverse events after consent recorded and potential causality attributed



## Statistics

- Analyses completed by statistician blinded to the treatment allocation
- Analyses completed for four patient groups
  - Healthy controls (HC)
  - Functionally constipated (FC)
  - IBS-C
  - All constipated (FC and IBS-C combined)
- Raw data analysed for least-squares means / 95% confidence intervals
- Appropriately transformed data for generation of p values



# Results



#### CONSORT Diagram showing disposition of participants



### **Baseline characteristics**

	Healthy (20)	Functional Constipation (19)	IBS-C (19)
Female, n (%)	12 (60)	16 (84)	19 (100)
Age, mean (SD)	44.5 (14)	45.5 (15)	47.3 (13)
Pakeha, n (%)	15 (75	16 (84)	15 (79)
BMI, mean (SD)	25.9 (4.7)	25.8 (4.6)	24.5 (3.8)
IBS severity, mean (SD)	49 (39) <sup>c</sup>	115 (56) <sup>b</sup>	191 (64)ª

Means with different superscripts are significantly different (p<0.001)



#### Primary Outcome – Increase in CSBM



Challenges

\*p<0.05, \*\*p<0.01

#### Secondary outcome – constipation (straining)





Scores: 0=No, 1=at least 1 BM, 2=all BM \*p<0.05, \*\*p<0.01, \*\*\*p<0.001



#### Secondary outcome – stool form (Bristol)





National SCIENCE

Challenges

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\*p<0.05, \*\*p<0.01, \*\*\*p<0.001, # p<0.10 (trend)

#### Secondary outcomes – constipation (Rome III)



\*p<0.05, \*\*p<0.01, \*\*\*p<0.001

#### Secondary outcomes – gastrointestinal comfort (GSRS)



#### Secondary outcomes – quality of life



\*p<0.05, \*\*p<0.01, \*\*\*p<0.001

#### Secondary outcomes – colonic transit time



#### Data to follow ...

- Analysis of faecal microbiota
- Profile of Mood Score
- Food diaries
- Vitamin C measurements



## Conclusions

#### **IMPROVED BOWEL MOTION FREQUENCY**

- Consumption of two Zespri green kiwifruit (Actinidia deliciosa var Hayward) daily improves bowel motion frequency in constipated individuals by 2 complete spontaneous bowel motions / week
- FDA recognises an increase of 1CSBM / week to be clinically significant



### Conclusions

#### IMPROVED GASTROINTESTINAL COMFORT

- Consumption of two Zespri green kiwifruit (Actinidia deliciosa var Hayward) daily improves gastrointestinal discomfort in constipated people
- Reduced straining
   Reduced abdominal pain
- Reduced bloating/distension Reduced incomplete evacuation
- Improved quality of life

## Conclusions

#### **NO CONCERNING SAFETY SIGNALS**

- That two Zespri green kiwifruit (Actinidia deliciosa var Hayward) are well tolerated by constipated individuals and healthy controls
- No diarrhoea in healthy controls / symptomatic participants
- No other treatment-related adverse events



## Limitations

- Participants were not blinded to the intervention
   many subjective outcomes
  - very difficult to blind participants to ingestion of a whole food
  - a positive control was used to demonstrate similar efficacy in the same cohort
- Relatively small numbers

   however a consistent effect observed
- Little mechanistic data available



## **Future Directions**

- Awaiting results of Italian and Japanese studies
- May form part of an EFSA application for a validated health claim
- Possibility of echo studies in other Zespri markets to support validated health claims in these regions



### Acknowledgements





# Plant & Food **RESEARCH**

RANGAHAU AHUMARA KAI

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![](_page_37_Picture_6.jpeg)

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