In-situ protection of enamel erosive lesions by fluoride: network meta-analysis

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Conflict of Interest statement

- These studies were funded by **Haleon**, which markets the Sensodyne Pronamel and Aquafresh products tested
- **Jonathan Creeth, Gary Smith** and **Billy Franks** are employees of Haleon
- **Anderson Hara** and **Domenick Zero** are employees of Indiana University, which has received funding from Haleon, and have received consultant income

Introduction

- **Erosive toothwear**: an important 'modern' oral health condition

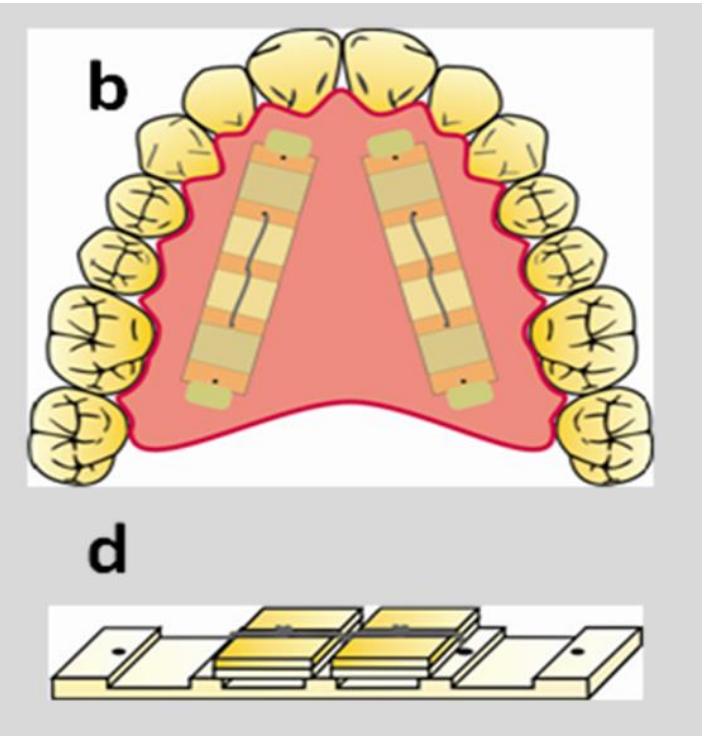
… but difficult to measure

- **In situ clinical methods** are critical to our understanding
- Haleon (ex GSK CH) has run **14 in situ studies / 22 products**
  - Measure **promotion of remineralisation by F** (dose-response)
  - Measure **resistance to demineralisation of F-treated surface**
  - Measure effect of formulation ingredients & vehicle:
    - **F species / Paste vs rinse / polyphosphates / stannous / surfactant**
- **What can we learn across this study set?**

…apply Network Meta-Analysis approach

Methods: *in situ* clinical study protocol

- **Erosive toothwear: an important 'modern' oral health condition**
- Single-centre, **randomized, multi-way crossover*** in situ studies, ethics committee-approved (OHRI) in healthy adults (**N=15-58)**
- Examiner-, subject- and analyst-blind
- **Bovine enamel specimens acid-challenged**:
  - **25 min in grapefruit juice** (citric acid, pH ~3.0).
- **Single use of 1.5 g test dentifrice:**
  - 25 s brushing + 60 s or 95 s swishing + expectorate + rinse
- **4-hour intra-oral remineralisation period**
- **Re-challenge with acid (grapefruit juice)**
- Enamel hardness assessed at each stage via Surface Microhardness (SMH) using a Wilson 2100 indenter



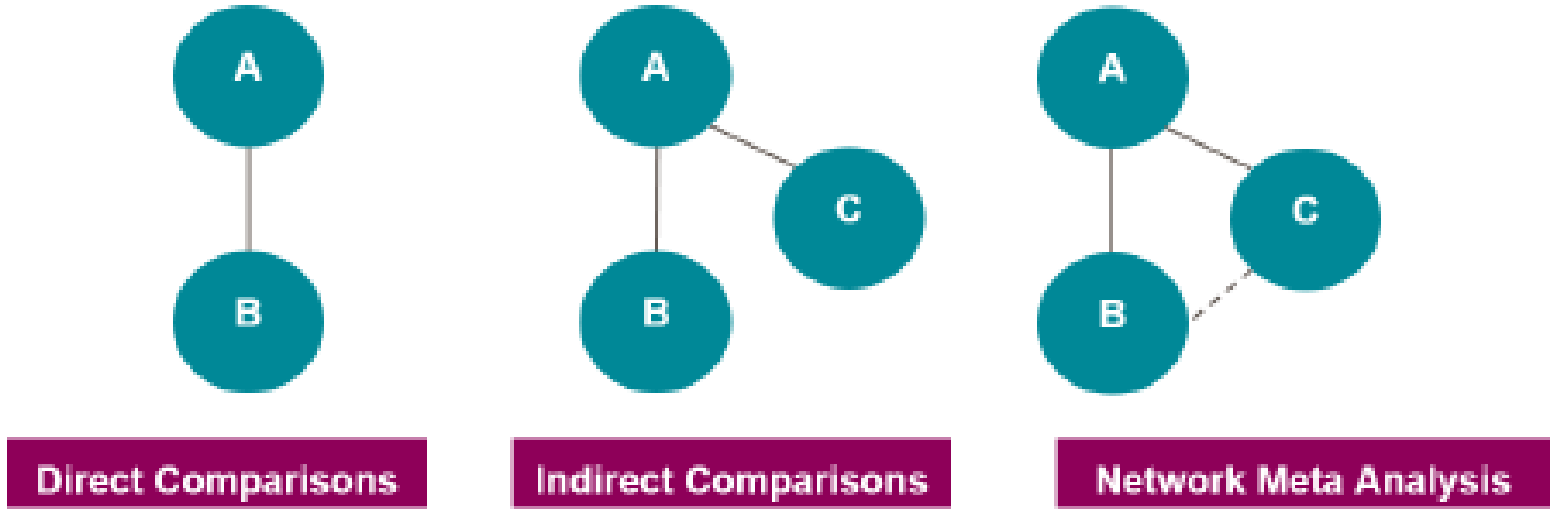
Study measures

After initial demineralisation challenge…

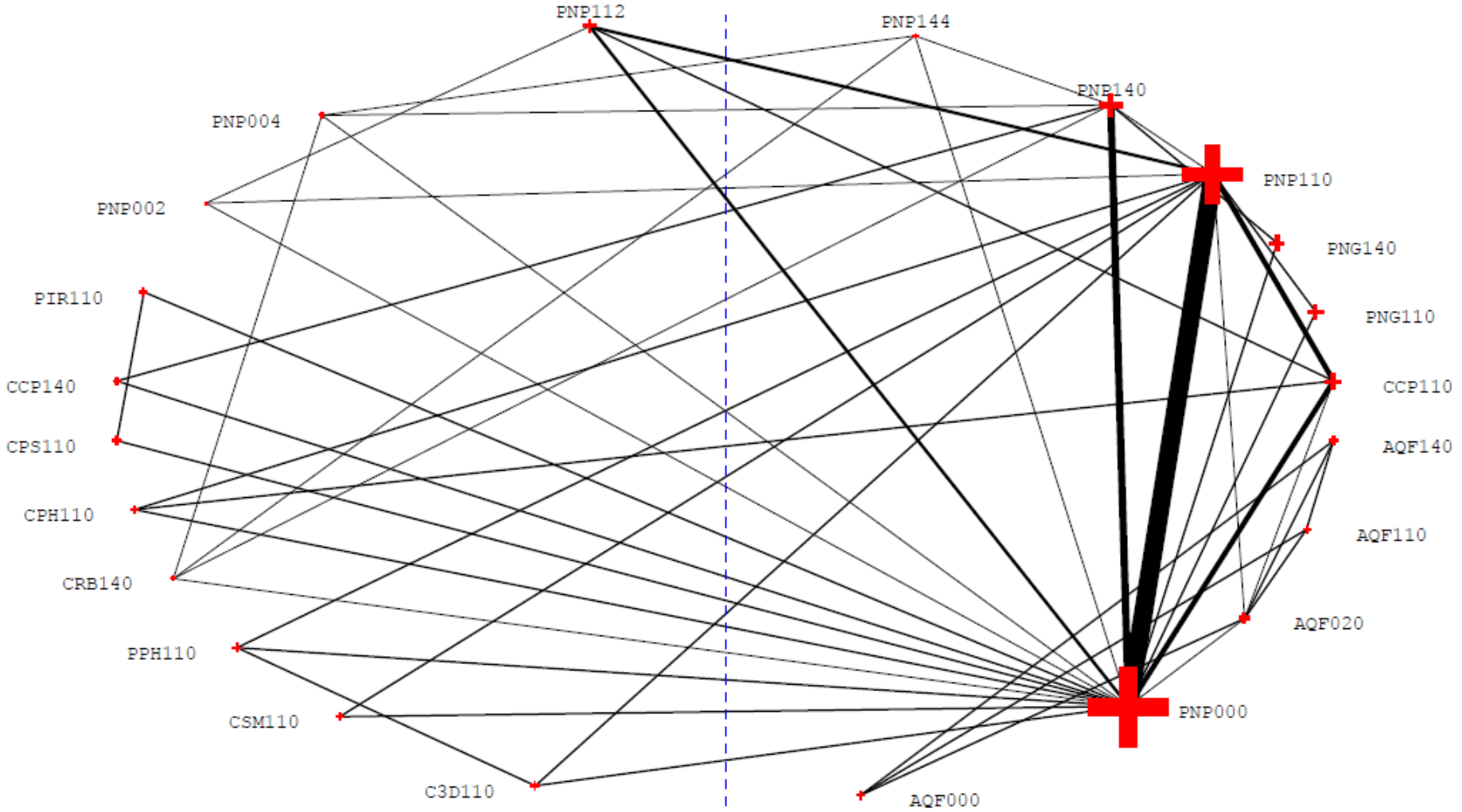
- **Remineralisation:**
  - *Surface Micro-Hardness Recovery*: amount of 'lost' hardness recovered due to treatment
- **Acid Resistance:**
  - *Acid Resistance Ratio*: Effect of 2nd demin challenge relative to 1st
- **Overall protection vs dietary acid:**
  - *Relative Erosion Resistance*: Overall hardness change across cycle of remin & demin

Methods: Network Meta-Analysis approach

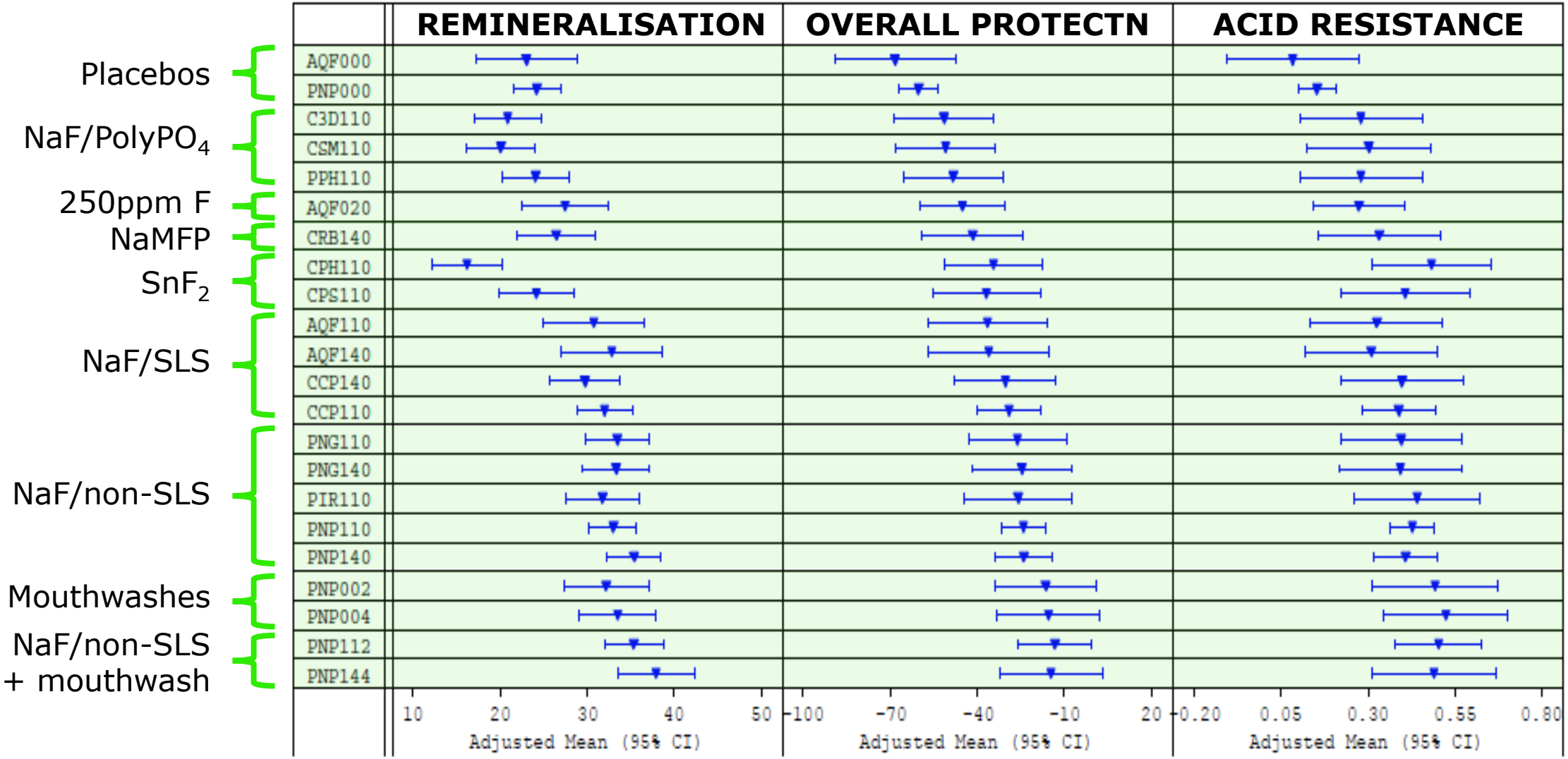
- **Principle of NMA:**
  - Determines a treatment effect as mean value adjusted across a set of studies with (near-) identical protocol
  - Allows comparisons between treatments not tested in same study



The *in situ* erosion study Meta-Analysis Network

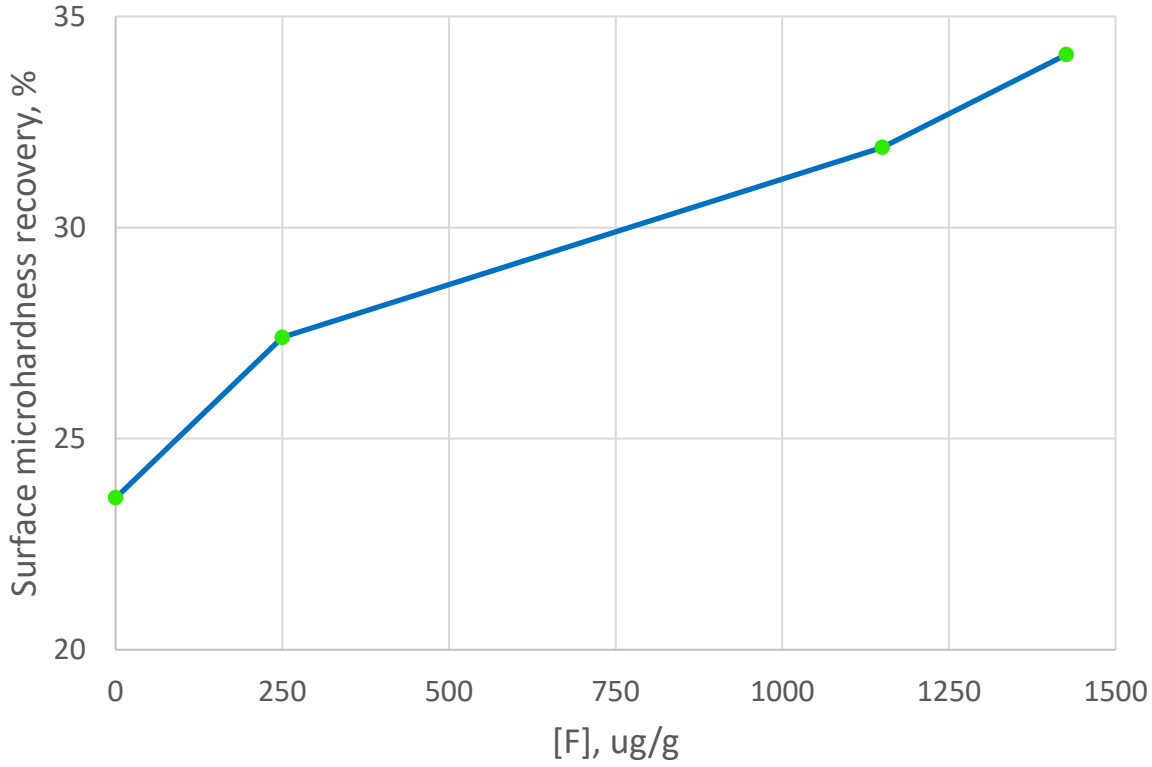


Results: Forest plot of Network Meta-Analysis

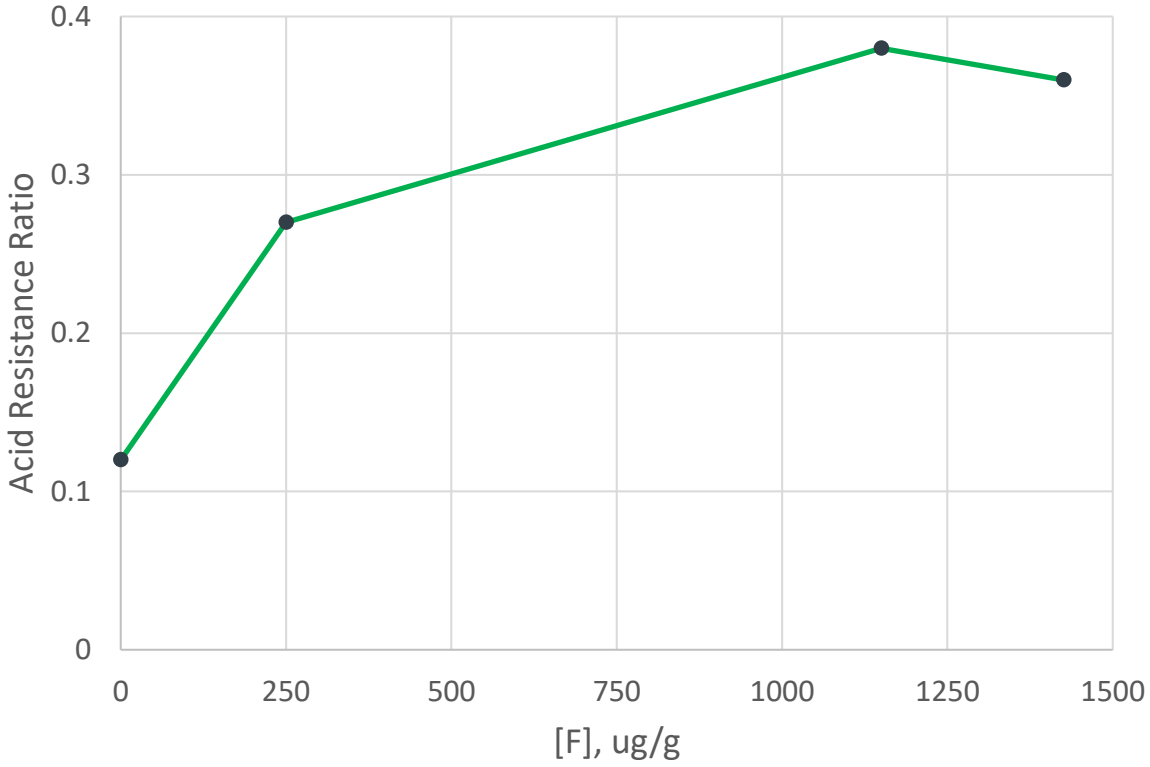


Fluoride dose-response

Remineralisation promotion (Surface microhardness recovery)



Demineralisation reduction (Acid resistance ratio)



Key ingredient effects on remineralisation (SMHR)

Ingredient effect	Specifics	P-value	Products compared
Surfactant	**Tegobetain > SLS**	p=0.006	Pronamel vs Crest Cavity Protection (1100 & 1450ppm F)
Fluoride type	**F^- > FPO_3^-**	p<0.001	Colgate Cavity Protection vs. Pronamel or Aquafresh(p=0.065)
Rinse	**paste+rinse > paste**	p=0.043	Pronamel toothpaste +/- Pronamel mouthwash
Sn^{2+}	**no Sn^{2+} > Sn^{2+}**	P=0.001	Crest Pro-Health 'Smooth' vs Pronamel or Aquafresh(p=0.053)
Phytate	**no phytate > phytate**	p<0.001	Pronamel-Phytate vs Pronamel
Pyrophosphate	**no pyro > pyro**	p<0.001	Crest 3D White vs Pronamel or Aquafresh(p=0.004)
HMP/Sn^{2+}	**no HMP/Sn^{2+} > HMP/Sn^{2+}**	p<0.001	Crest Pro-Health vs Pronamel or Aquafresh

Conclusions

NMA approach:

- Effective approach to understand/compare efficacy across a body of studies

  …linked by products-in-common

This NMA: 14 studies/22 products/consistent in-situu erosion model:

- F^- ion is key to remineralisation, and important to demineralisation resistance
- F rinses work well, and can add to F toothpaste benefits
- Stannous ions can reduce remin
  - but can enhance demin resistance
- Polyphosphates can reduce remin
  - but don't enhance demin resistance in this model (for those tested)
- Choice of surfactant can influence remineralisation

F effects on enamel remin & demin are highly formulation-dependent