

# A multicentre collaborative trial assessing the effectiveness and cost effectiveness of acupuncture wristbands in the management of chemotherapy-related nausea and vomiting: development, management and preliminary results

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Combining the strengths of UMIST and  
The Victoria University of Manchester



**NCRI Supportive & Palliative  
Care (SuPaC) Research:**

*Cancer experiences: supportive  
and palliative care needs,  
problems and solutions*

# Team:

## Lead Applicant-Chief Investigator

Professor Alex Molassiotis

## Co-applicants

Dr Sarah Brearley, Dr Malcolm Campbell & Dr Margaret Rogers (University of Manchester)

Prof Mari Lloyd-Williams & Dr John Hughes (University of Liverpool),

Prof Tim Eden, Dr Juan Valle & Dr Peter Mackereth (Christie Hospital, Manchester)

Dr Adam Garrow & Dr Claire Hulme (University of Salford)

Dr Janet Richardson (University of Plymouth)

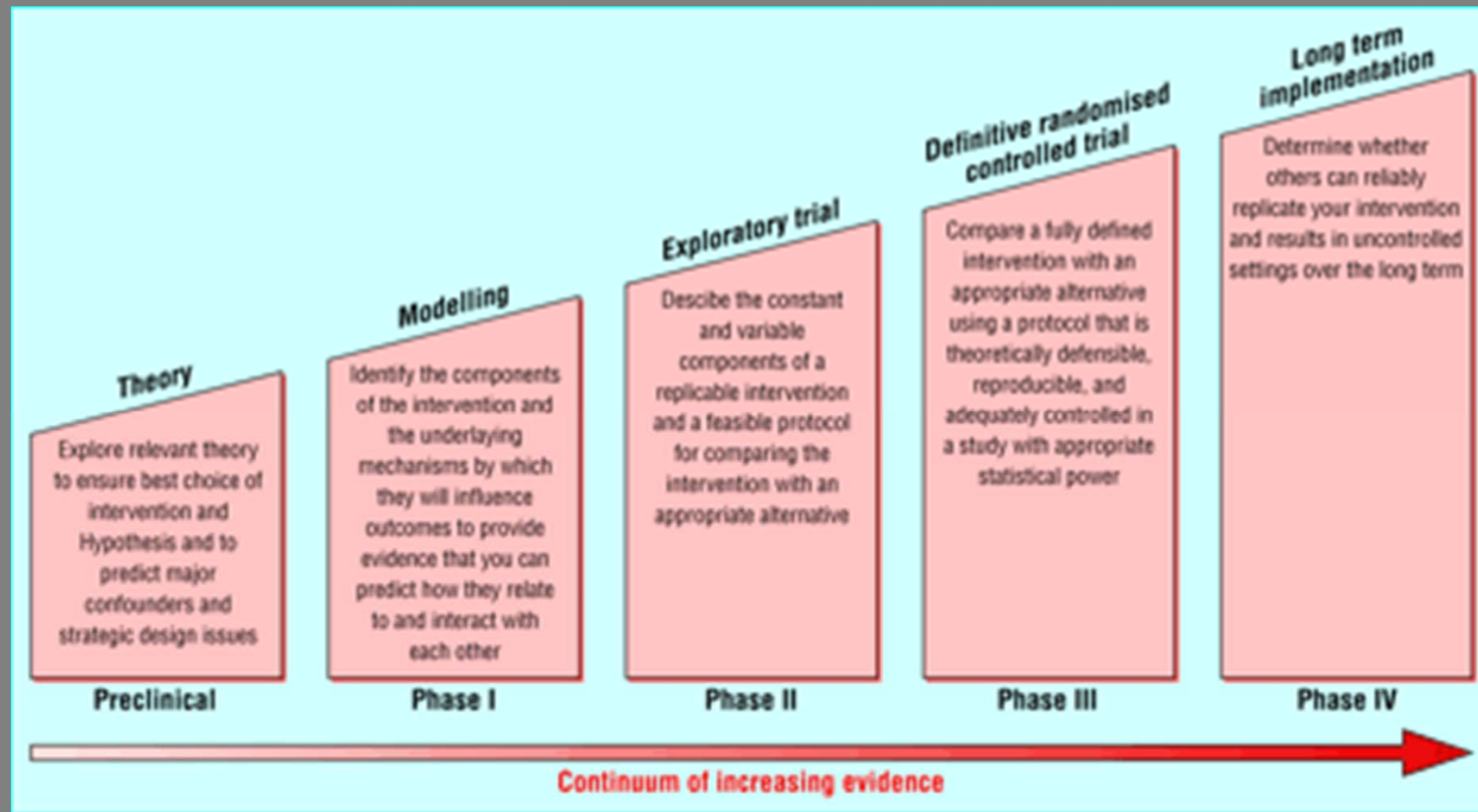
Roger Wilson (CECO & NCRI Consumer Liaison Group)

Trial Manager / Manchester researcher: Dr Wanda Russell

Liverpool researcher: Dr John Hughes

Plymouth researchers: Linnie Price & Matthew Breckons

# Sequential phases of developing trials of complex interventions



# ACUPRESSURE TRIAL, HTA, £500,000

- To assess the effectiveness of self-acupressure using wristbands in addition to standard care in the management of acute and delayed chemotherapy-induced nausea compared to patients receiving standard care with sham acupressure wristbands and standard care alone

Also aim to assess:

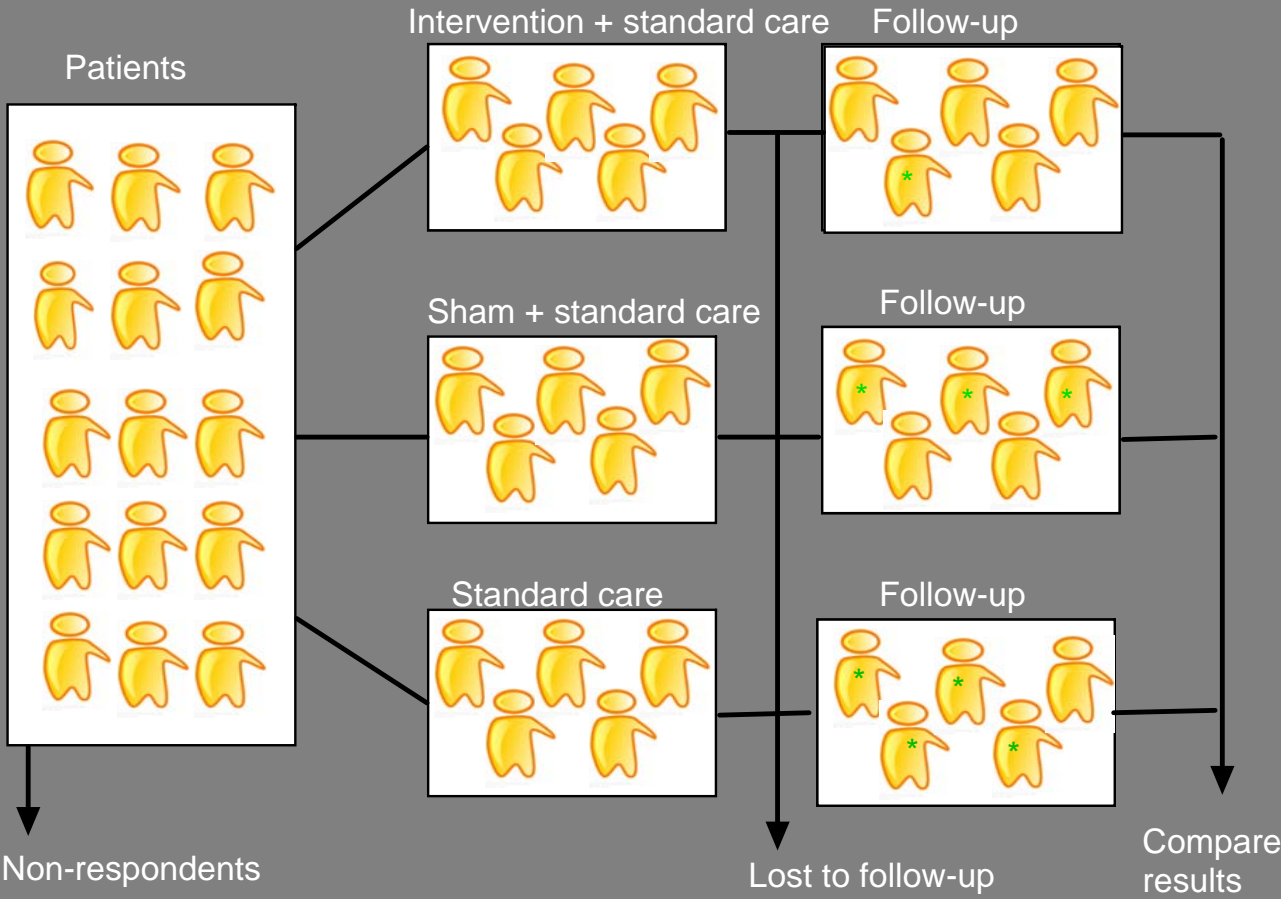
- Effectiveness in management of chemotherapy-induced (acute/delayed) vomiting
- Cost effectiveness and extent of use of usual care
- Level of quality of life
- For which chemotherapy regimens acupressure is more/less effective
- Gender-related difference in effectiveness
- Age-related difference in effectiveness

## Definitive randomised controlled trial

Compare a fully defined intervention with an appropriate alternative using a protocol that is theoretically defensible, reproducible, and adequately controlled in a study with appropriate statistical power

**Phase III**

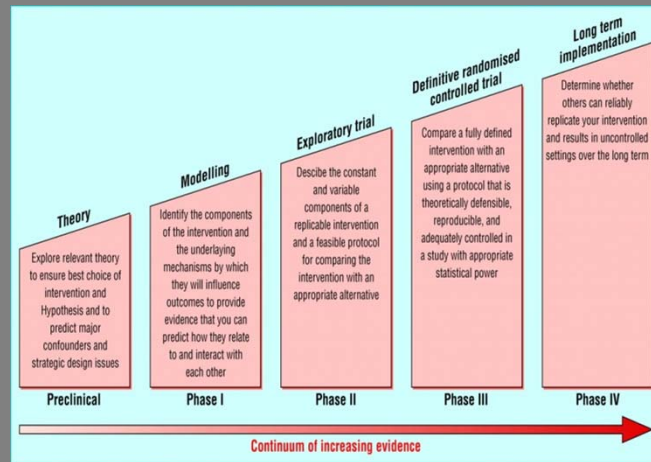
# Method: RCT, multicentre, 500 patients, 4 cycles follow up



# THEORY DEVELOPMENT

- Support Care Cancer. 2008 Feb;16(2):201-8. A prospective observational study of chemotherapy-related nausea and vomiting in routine practice in a UK cancer centre.

A. Molassiotis, M. P. Saunders, J. Valle, G. Wilson, P. Lorigan, A. Wardley, E. Levine, R. Cowan, J. Lancaster and C. Rittenberg

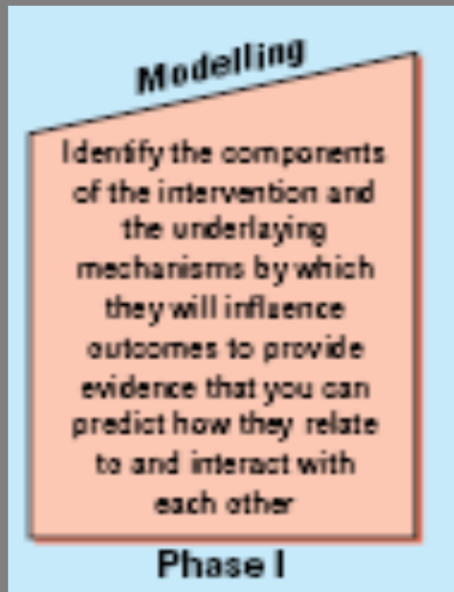


## Key issues:

- Despite recent advances in antiemetic therapy (5-HT<sub>3</sub> receptor antagonists, NK-1 receptor antagonists) patients still suffer from nausea
- 56.1 % and 43.9% experienced acute and delayed nausea respectively, at cycle 4
- Data highlighted inappropriate use of antiemetics and high cost (£17,534/100 patients over 4 cycles)

# Modeling & Theory

Molassiotis A, Stricker CT, et al. Understanding the patient experience of chemotherapy-related nausea and vomiting. European Journal of Cancer care (2009).



## Key findings:

Qualitative study about the experience of chemotherapy-related nausea found that self-management techniques (dietary, distraction) were common but acupuncture was not used

Self management was key patient strategy

Preliminary evidence that nausea forms part of a cluster of symptoms

## Cochrane Systematic review:

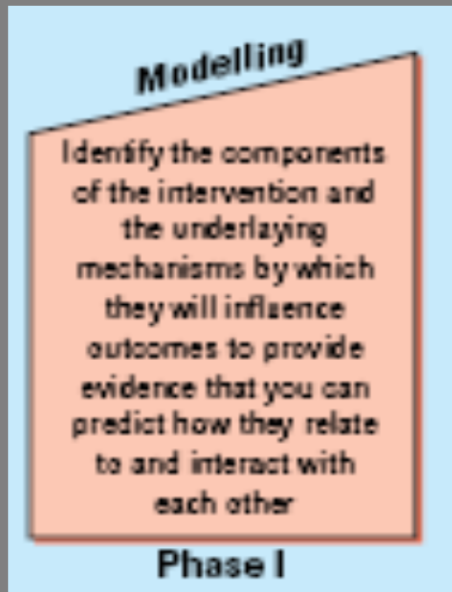
- Cochrane review from pooled trial data showed P6 stimulation to be superior to antiemetic medication for nausea (Ezzo et al, 2006) but focus was primarily on acupuncture
- Acupressure worthy of further testing (Ezzo et al, 2006)

# Modeling

**Molassiotis A, Yam, BM, Yung H, Chan FY, Mok TS.**

Pretreatment factors predicting the development of postchemotherapy nausea and vomiting in Chinese breast cancer patients.

Support Care Cancer. 2002 Mar;10(2):139-45.



Key factors:

Identification of predisposing/risk factors for the development of nausea and vomiting during chemotherapy, including gender, age, vestibular dysfunction, chemotherapy protocol, anxiety and stage of disease.

Other literature:

Confirmatory similar information from other studies over the past 10 years.

# THEORY DEVELOPMENT: ASSESSMENT

Molassiotis A, Coventry PA, Stricker CT, Clements C, Eaby B, Velders L, Rittenberg C, Gralla RJ.

Validation and psychometric assessment of a short clinical scale to measure chemotherapy-induced nausea and vomiting: the MASCC antiemesis tool.

- J Pain Symptom Manage. 2007; 34(2):148-59.

Support Care Cancer  
DOI 10.1007/s00520-008-0428-y

REVIEW ARTICLE

## A review of patient self-report tools for chemotherapy-induced nausea and vomiting

Sarah G. Brearley · Caroline V. Clements · Alex Molassiotis

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### Abstract

*Goals of work* The assessment of chemotherapy-induced nausea, vomiting and retching (CINVR) is important and to date, no review has comprehensively assessed available

(nausea and vomiting); two phases (acute and delayed); measuring the aspects of occurrence, frequency, intensity alongside duration and functional interference; and antiemetic use and adverse events should be developed. Poor

# THEORY DEVELOPMENT: SYSTEMATIC REVIEWS

## [Molassiotis A.](#)

Managing nausea and vomiting after cancer treatments: patients still suffer unnecessarily.

[Eur J Oncol Nurs.](#) 2005 Mar;9(1):4-5.

[Aapro MS, Molassiotis A, Olver I.](#) Anticipatory nausea and vomiting.

[Support Care Cancer.](#) 2005 Feb;13(2):117-21.

[Feyer PCh, Maranzano E, Molassiotis A, Clark-Snow RA, Roila F, Warr D, Olver I.](#)

Radiotherapy-induced nausea and vomiting (RINV): antiemetic guidelines.

[Support Care Cancer.](#) 2005 Feb;13(2):122-8.

[Maranzano E, Feyer PCh, Molassiotis A, Rossi R, Clark-Snow RA, Olver I, Warr D, Schiavone C, Roila F;](#)

Evidence-based recommendations for the use of antiemetics in radiotherapy.

[Radiother Oncol.](#) 2005 Sep;76(3):227-33.

**\*\*MASCC/ASCO ANTIEMETIC GUIDELINES WORKING GROUP\*\***

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### Exploratory trial

Describe the constant and variable components of a replicable intervention and a feasible protocol for comparing the intervention with an appropriate alternative

### Phase II

## Acupressure for Nausea: P6 Acu-point

- Focus on the stimulation of the P6 acu-point
- Located between the tendons, approx 3 finger widths up from crease of wrist



## Pilot Study using Acupressure Wristband

[Molassiotis A, Helin AM, Dabbour R, Hummerston S.](#)

The effects of P6 acupressure in the prophylaxis of chemotherapy-related nausea and vomiting in breast cancer patients.

[Complement Ther Med.](#) 2007 Mar;15(1):3-12.

- 2-arm pilot study of 36 breast cancer patients using acupressure wristbands
- Key finding suggests acupressure improved the nausea experience
- Nausea and vomiting occurrence and distress improved across first 5 days of chemotherapy
- Mean percentage of improvement was 44.5% in experimental subjects over the control subjects
- Limited study, needing a larger randomised controlled trial (RCT) to test the intervention, based on the methods of the pilot study and using an adequately

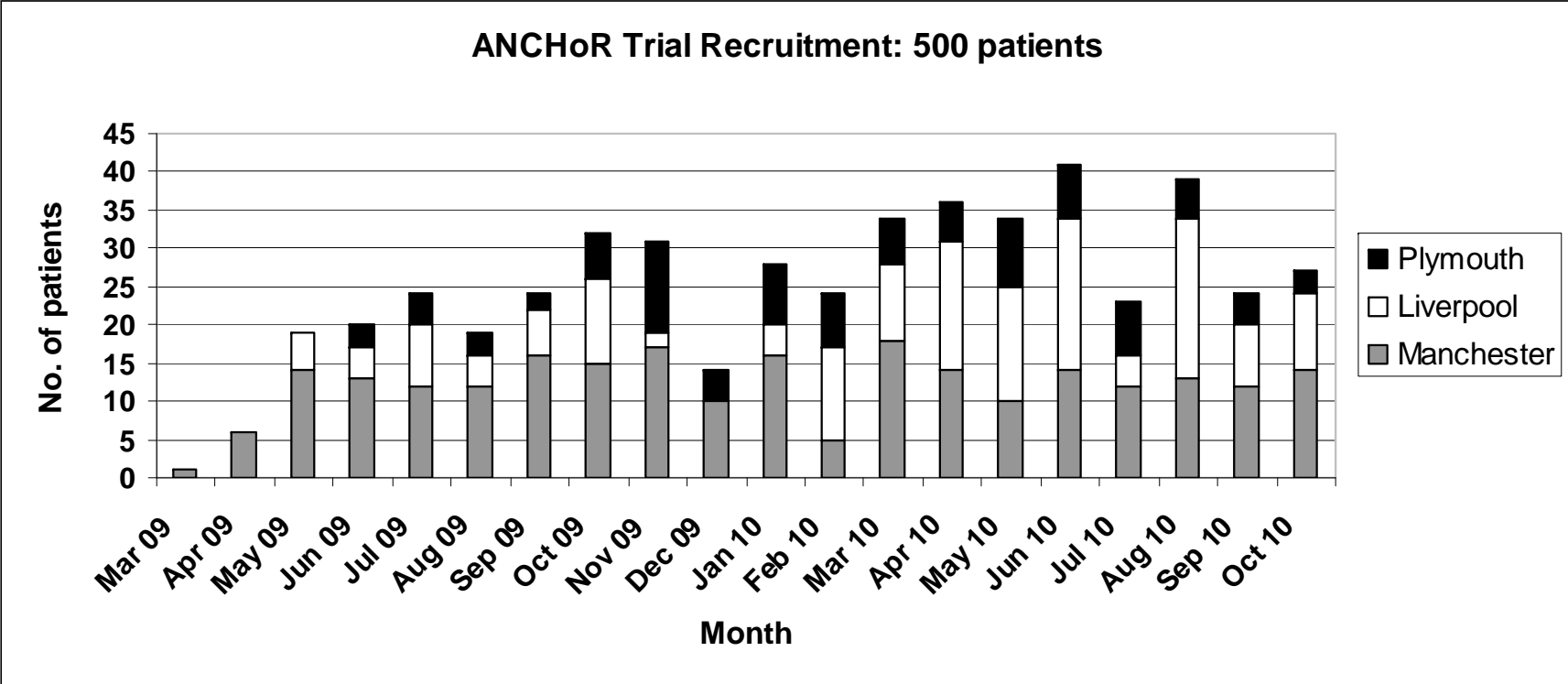


## ....back to the HTA trial

### Data Collection:

- Screening data: eligibility criteria, and cancer, chemo and antiemetic data
- Sociodemographic data: Baseline
- Patient Expectations of Nausea & Vomiting, and complementary therapy: Baseline
- Rhodes Index of Nausea & Vomiting (Rhodes & McDaniel, 1999) (nausea component): Day -1 to day 7 (primary outcome data)
- MASCC antiemesis tool (MAT) (Molassiotis et al, 2007)): Acute & Delayed (24hrs & day 4)
- FACT G (Fairclough & Cella, 1996) (functional assessment): Baseline & day 10
- HADS (Zigmond & Snaith, 1983) (anxiety component): Baseline & day 10
  
- Health Economics data: Baseline & post cycles 1, 2, 3 & 4

# Recruitment

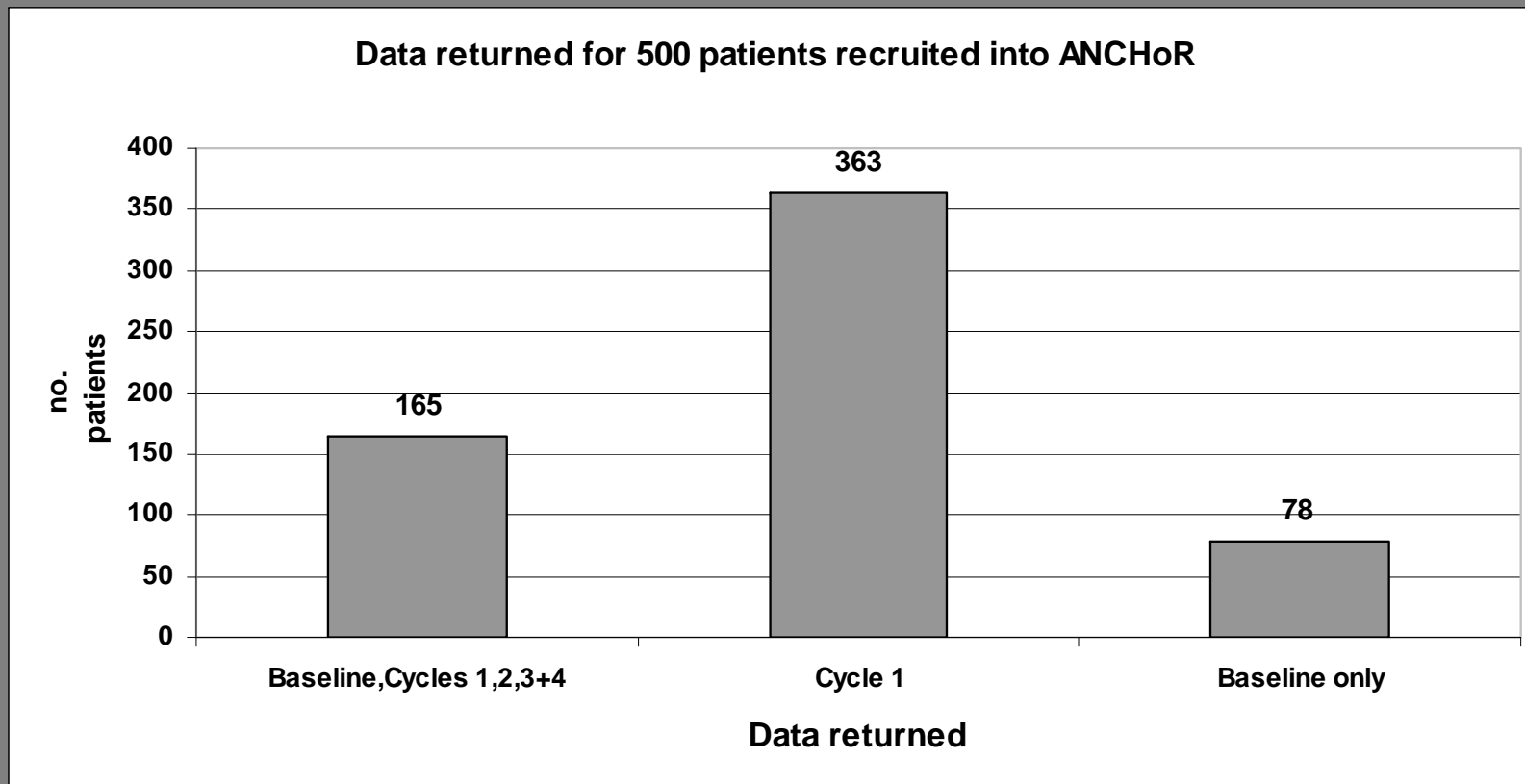


## Recruitment profile

500 patients randomised:

- 168 acupressure, 168 sham acupressure, 164 no acupressure
- 136 high emetogenicity, 327 moderate, 37 low
- 339 in  $\geq 51$  years old age group, 161 in 16-50 group
- 385 females, 115 males

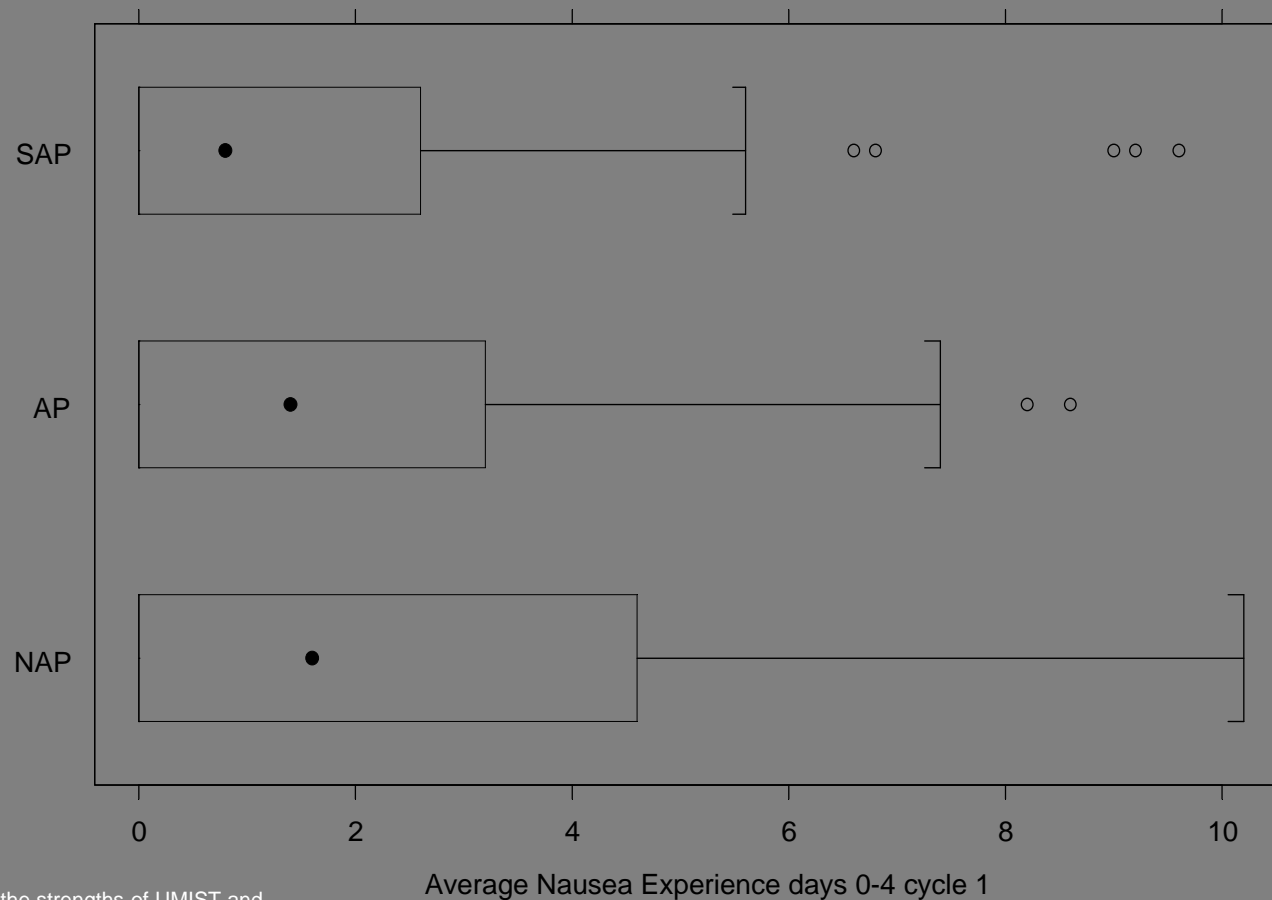
# Trial data



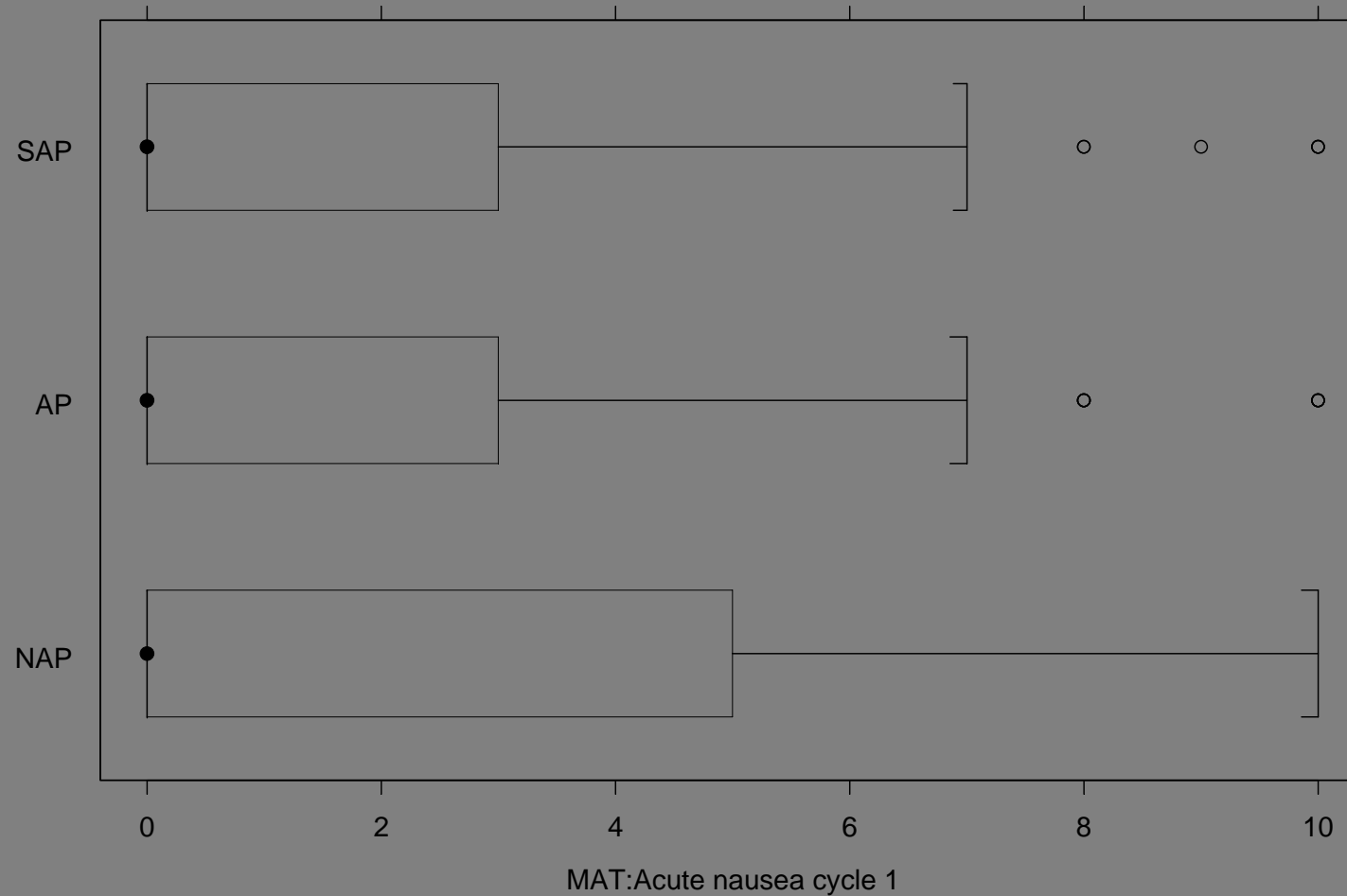
- **HEALTH WARNING.....**

# Preliminary findings – primary outcome data

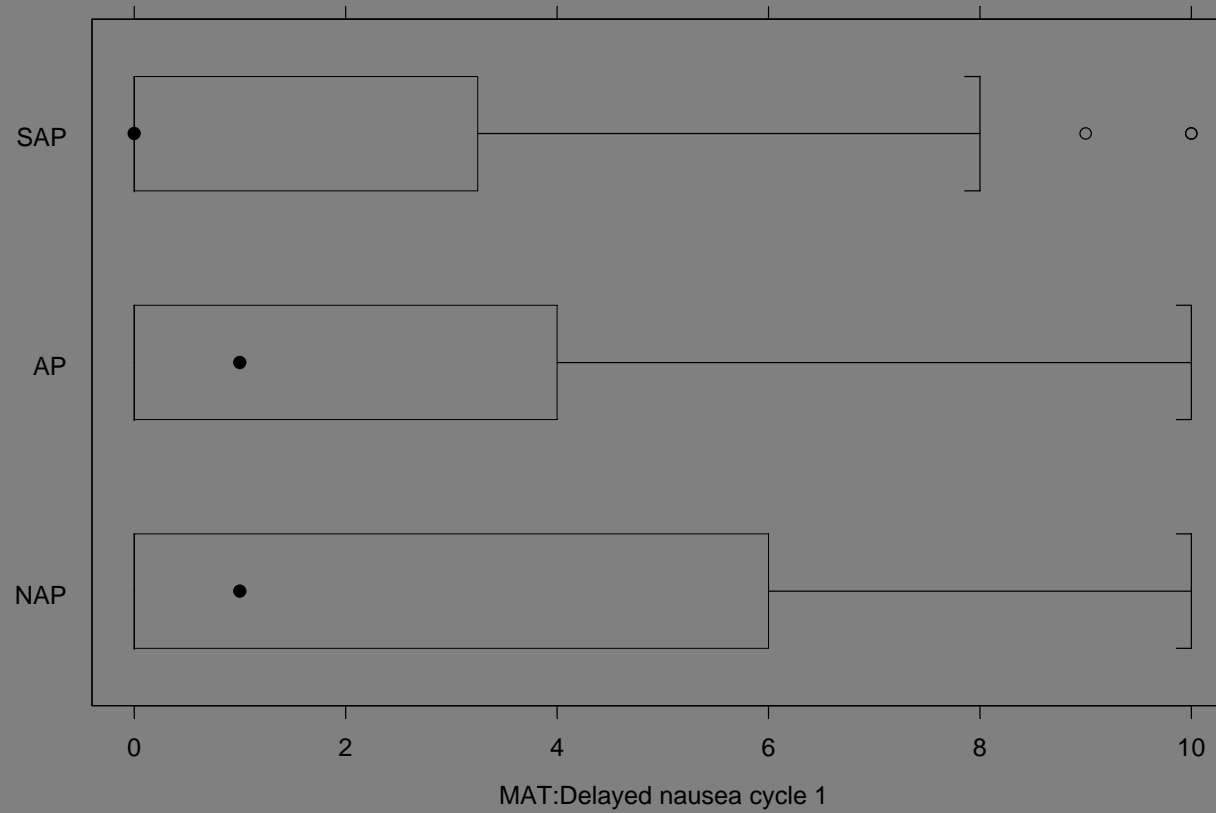
Box and whisker plot of mean nausea experience score by trial arm (n=320)-Rhodes Index of Nausea



# Preliminary findings – MASCC Antiemesis Tool (MAT): Acute Nausea



# Preliminary findings – MASCC Antiemesis Tool (MAT): Delayed Nausea



# Health Care utilisation

Services	Returned questionnaires across 4 cycles		
	Acupuncture (n=86)	No Acupuncture (n=88)	Sham Acupuncture (n=98)
GP surgery visit	5	6	5
GP home visit	3	4	3
District nurse,	4	11	17
Contact with oncology hotline for advice	6	11	9
Contact with hospital oncology nurse clinician for advice	9	9	6
Contact with hospital oncology clinic for advice	5	8	7
Hospital inpatient stay	4	1	4
Hospital accident and emergency department	3	1	2
Hospital general outpatient clinic	1	0	2
Other services	3	1	1
<b>Total</b>	<b>43</b>	<b>52</b>	<b>56</b>
<b>% of returned questionnaires</b>	<b>50%</b>	<b>59%</b>	<b>57%</b>

# Nested qualitative evaluation

## Objectives:

- Outline experiences of using acupuncture wristbands.
- Identify why patients consented to take part in the trial.
- Outline patients' experiences of taking part in the trial.

## Methodology:

- Convenience sample.
  - Semi-structured interviews, tape recorded and transcribed.
  - Transcripts analysed thematically using *Framework analysis*.
- 
- Sample: 26 participants

# Themes

## 4 Emergent themes:

- Reasons for taking part in the trial
- Experience of taking part in the trial
- Experiences of using wristbands
- Views on intervention

## Experience of participation in the trial:

- Most patients had not taken part in research before
- Participation not perceived as onerous – most found questionnaire completion ‘easy’ and not time-consuming
- Participation for some was a positive experience:
  - doing something positive for others
  - gave an element of control over cancer situation
  - useful process to reflect on symptoms
- Participation for others was a negative experience:
  - reminded them of their symptoms
  - questionnaire completion slightly onerous and required commitment whilst feeling unwell

*“It makes you feel better, feeling you’ve contributed.”*

*“Some of the questions actually don’t help you when you’re not feeling well”*

## Experiences of using wristbands:

- Wristbands (acupressure and sham) typically perceived as reducing nausea
- Some adverse effects reported but these deemed minor and acceptable
- Worn correctly
- Good 'compliance' – worn at least constantly for first 7 days per cycle
- A few inhibitions about appearance in social contexts and/or negative responses from others

*“I think they have helped, I really do.”*

*“Can make it red, itchy... [wrist].”*

*“You start pulling your shirt, or sleeves, down so nobody sees them.”*

## Views on intervention:

- Some hadn't considered the differences between the 2 types of wristbands
- Others had expected one type would be a placebo, but some of these patients were unsure how this would work
- All believed the true/sham wristbands were presented in an acceptable way with no 'deception' involved
- Those who didn't receive any wristbands were not disappointed
- Some who received wristbands said they would have been disappointed if they had not been given wristbands

*"I assumed one was a placebo."*

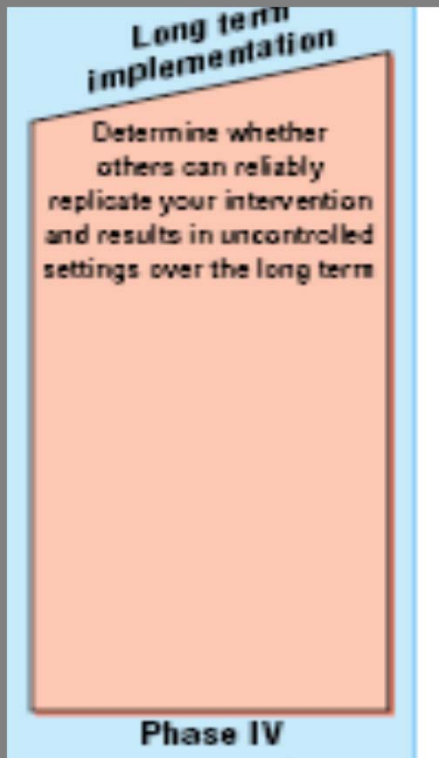
*"Presumed one wouldn't do what it was supposed to do."*

*"If somebody was wearing a wristband with acupuncture then you want to know whether that is actually doing something.... To do it with the other [placebo] will categorically support your research argument."*

# Summary

## Acupressure for nausea in chemotherapy:

- ANCHoR is the second largest study ever conducted worldwide
- the only multi-centre trial of this kind
- the only study to control for antiemetics
- the only study to use sham wristbands
- Initial preliminary results indicate at this stage that acupressure wristbands have a positive effect ...
- ... and a strong placebo effect
- ... an extensive analysis plan of the data is currently in progress and much analysis is still to be done, including:
  - subgroup analyses e.g. by gender and age, emetogenicity of chemotherapy
  - taking account of factors such as wristband compliance, patient expectations, use of antiemetics



- Dissemination
- Long term surveillance studies
- Currently completing observational prospective study (n=1100, 6 countries)
- Practice survey (Support Care Cancer, in press)
- Risk factors model for CINV (in progress) leading to RCT
- PROGRAMME GRANT