30 March 2021| Live via Teams

Introduction to Clinical Research

Planning research data management and biostatistical analysis

via Teams

Facilitated by Professor Janet Davies
MNHHS Office of Research
MNHHS-Research@health.qld.gov.au

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Agenda

Topics covered:

- Review of principles and tools for research data management and biostatistical analysis
- Considerations for efficiently collecting and analysing clinical research data
- Deconstruction of the process with clinical research examples

Emma Ballard
Senior Biostatistician
QIMR Berghofer

Thuy Frakking
Research Coordinator
Caboolture Hospital,
MNHHS Clinician
Research Fellow

Kylie Burke
Principal Research Fellow
Metro North Mental Health

Panel Discussion (10 min)

What's next & session close

Please do not mention any confidential details of patients or research.

Teams Virtual session,

Facilitated by Prof Janet Davies, MNHHS Office of Research MNHHS-Research@health.qld.gov.au

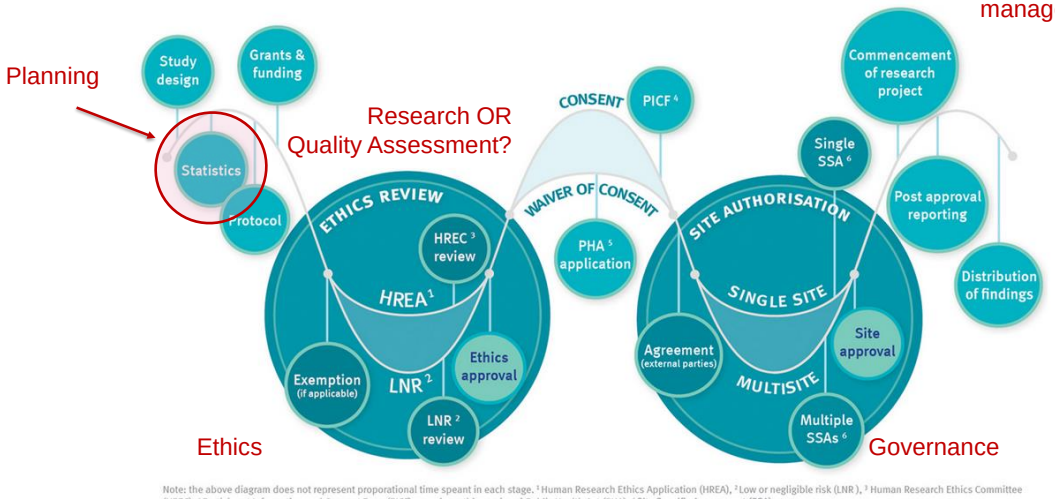
Research process

Key steps in the research approval process are shown in the diagram below.

Research Project execution and management

Planning

Research OR Quality Assessment?



Ethics

Governance

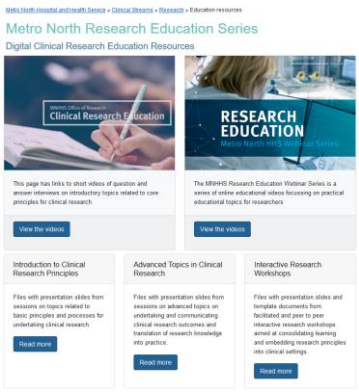
Note: the above diagram does not represent proporational time speant in each stage. [1] Human Research Ethics Application (HREA), [2] Low or negligible risk (LNR), [3] Human Research Ethics Committee (HREC), [4] Participant Information and Consent Form (PICF) - requires ethics review, [5] Public Health Act (PHA), [6] Site Specific Assessment (SSA).

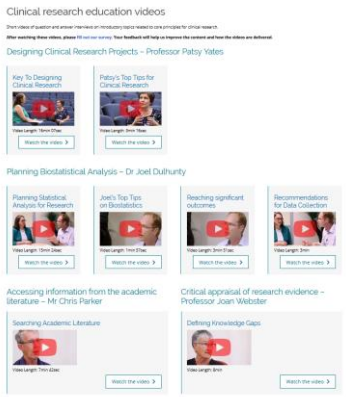
https://metronorth.health.qld.gov.au/research/ethics-and-governance

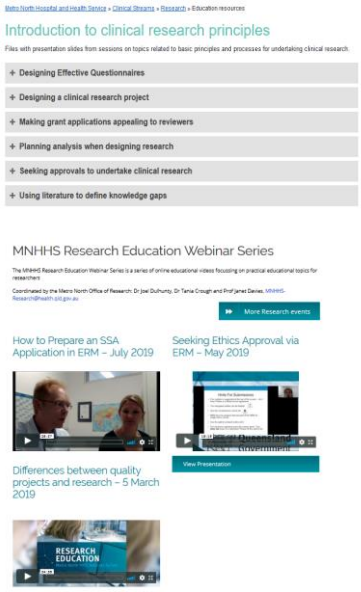
Clinical research education resources and tools

https://metronorth.health.qld.gov.au/research

https://qheps.health.qld.gov.au/metronorth/research/education-resources







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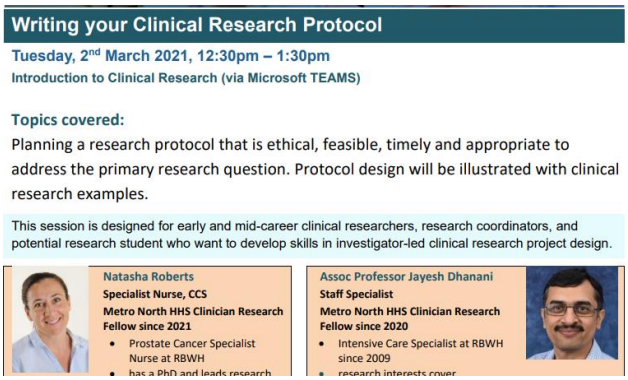

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Emma Ballard

Senior Biostatistician

QIMR Berghofer

- The Statistics Unit conducts collaborative research and provides a statistical consultancy service to Metro North
- Diverse background in medical and agricultural research as a researcher and biostatistician

Expert reviewer for the Human Research Ethics Committees at the Royal Brisbane and Women's Hospital and The Prince Charles Hospital

Key components of a research project

- Research question
- Primary and secondary outcomes
- Study population
- Patient recruitment
- Study design

Key components of a research project - Example

- **Research question**
  - Patients with “condition X” undertaking program 1 will have a greater change in pain score as measured by an 11-point numeric rating scale (NRS) at 3 months compared to patients undertaking program 2
- **Primary outcome**
  - Change in pain score between baseline and 3 months
- **Study population**
  - Adult patients with “condition X”
- **Patient recruitment**
  - Patients attending the clinic between date 1 and date 2 with “condition X” are eligible. Typically, we see XX patients per year.
- **Study design**
  - Randomised control trial

How do the key components inform a sample size calculation?

Components

- We are **comparing** program 1 with program 2
- **Primary outcome** is change in pain score between baseline and 3 months
- The **estimates** we have identified in the literature are: SD = 4, ρ = 0.45, δ = 3
- **Statistical test** to be used: Analysis of covariance (ANCOVA) including baseline pain as a covariate

Sample size

Using the ANCOVA sample size formula [REF 1], with a standard deviation of 4 units for the post-measurement, assumed to be the same for both programs, a correlation of 0.45 between baseline and 3 months, 80% power, 5% two-sided significance and anticipated mean difference between program 1 and 2 of 3 units for the change in pain NRS [REF 2], 23 participants per group will be required (46 in total).

How do the key components inform a statistical analysis plan?

- The **comparison of interest** is between program 1 and program 2

- **Univariate analyses**
  - Summarised as
    - Continuous variables: mean and standard deviation or median and interquartile range if not normally distributed
    - Categorical variables: frequency and percentage
  - Examined using
    - Continuous variables: Student t-test or Mann Whitney U test if not normally distributed
    - Categorical variables: Pearson Chi-squared test or Fisher's exact test if more than 20% of the expected counts are less than 5

- **Modelling**
  - The **change in pain from baseline** will be examined using an ANCOVA with baseline pain as a covariate

How do I decide what data to collect?

- **Patient characteristics**
  - What are the characteristics of your patient population that you would expect to see reported?
  - What characteristics are specific to your study?
  - Create an empty table

Characteristics	Units	Variable type	Statistics
Age	Years	Continuous	mean (SD)
Gender		Categorical	n (%)
BMI	kg/m^2	Continuous or categorical	mean (SD) or n (%) for underweight, normal, overweight and obese

- **Explanatory, confounding and mediating variables**
  - Look at other publications, use your clinical experience
  - e.g. program, number of sessions completed each week, medications, depression, pain catastrophising

- **Secondary outcomes**
  - What other outcomes can you think of that may support your primary outcome?
  - e.g. Quality-of-life, muscle strength

How do I decide what data to collect?

Codebook

Variable No.	Name	Label	Values
1	ID	Unique patient ID	
2	Group	Program	0 = program 1 1 = program 2
3	Age	Age at baseline	years, missing 9999
4	Gender	Gender	0 = male 1 = female
5	Baseline_pain_score	Pain score at baseline	values ranging from 0 to 10, exclude if below 4
6	Month3_pain_score	Pain score at 3 months	values ranging from 0 to 10

Dataset

ID	Group	Age	Gender	Baseline_pain_score	Month3_pain_score
1	1	32	1	7	4
2	1	60	0	8	0
3	0	22	0	6	4
4	1	36	1	7	1
5	1	46	0	7	3
6	0	73	0	7	7
7	0	48	0	10	4
8	1	43	0	6	5

Can I believe these numbers?

- **Data checking**
  - High standards of measurement and data entry
  - Checks on range and logic. Use maximum, minimum, histograms, scatter plots
  - Compatibility with clinical expectations
- **Data summary**
  - Frequency and cross tabulation for categorical data
  - Mean, standard deviation and range for continuous data
  - Simple tables and figures
- **Only the right individuals are included**
  - Satisfy inclusion and exclusion criteria
  - Are the individuals representative of the reference population?
- **Missing data**
  - Reason for missing related to the individual or independent
  - What proportion of data is missing?

Thuy Frakking

Research Coordinator

Caboolture Hospital,

MNHHS Clinician Research Fellow

- Certified practising speech pathologist with 15 years clinical experience in paediatric speech pathology / allied health across tertiary, secondary and community hospital settings
- Active clinical researcher who has attracted >$1.2 million in competitive research funding in the areas of health services research and paediatric feeding disorders

Example 1 – Retrospective Observational Study

QJM: An International Journal of Medicine, 2019, 907–913

doi: 10.1093/qjmed/hcz203
Advance Access Publication Date: 6 August 2019
Original paper

ORIGINAL PAPER

Frailty and hospital outcomes within a low socioeconomic population

S. Clark[1], C. Shaw[1], A. Padayachee[2], S. Howard[3], K. Hay[4] and T.T. Frakking[5,6]

From the [1]Emergency Department, Caboolture Hospital, Queensland Health, McKean St, Caboolture, Queensland 4510, [2]Projects and Service Partnerships, Caboolture Hospital, Queensland Health, McKean St, Caboolture, Queensland 4510, [3]Nursing Informatics, Caboolture Hospital, Queensland Health, McKean St, Caboolture, Queensland 4510, [4]QIMR Berghofer Medical Research Institute, Herston, Queensland 4006, [5]Caboolture Hospital, Research Development Unit, Queensland Health, McKean St, Caboolture, Queensland 4510 and [6]School of Health & Rehabilitation Sciences, The University of Queensland, St Lucia, Queensland 4067, Australia

Address correspondence to Thuy T. Frakking, Research Development Unit, Caboolture Hospital, McKean St, Caboolture, Queensland 4510, Australia. email: t.frakking@uq.edu.au

Summary

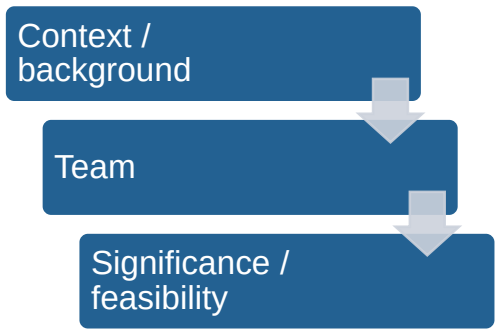
Background: Clinical frailty scales (CFS) predict hospital-related outcomes. Frailty is more common in areas of higher socio-economic disadvantage, but no studies exclusively report on the impact of CFS on hospital-related outcomes in areas of known socioeconomic disadvantage.
Aims: To evaluate the association of the CFS with hospital-related outcomes.
Design: Retrospective observational study in a community hospital within a disadvantaged area in Australia (Social Economic Index for Areas = 0.1%).
Methods: The CFS was used in the emergency department (ED) for people aged ≥ 75 years. Frailty was defined as a score of ≥4. Associations between the CFS and mortality, admission rates, ED presentations and length of stay (LOS) were analysed using regression analyses.
Results: Between 11 July 2017 and 31 March 2018, there were 5151 ED presentations involving 3258 patients aged ≥ 75 years. Frail persons were significantly more likely to be older, represent to the ED and have delirium compared with non-frail persons. CFS was independently associated with 28-day mortality, with odds of mortality increasing by 1.5 times per unit increase in CFS (95% CI: 1.3–1.7). Frail persons with CFS 4–6 were more likely to be admitted (OR: 1.2; 95% CI: 1.0–1.5), have higher geometric mean LOS (1.43; 95% CI 1.15–1.77 days) and higher rates of ED presentations (IRR: 1.12; 95% CI 1.04–1.21) compared with non-frail persons.
Conclusions: The CFS predicts community hospital-related outcomes in frail persons within a socioeconomic disadvantage area. Future intervention and allocation of resources could consider focusing on CFS 4–6 as a priority for frail persons within a community hospital setting.

Key components

- **Research question**
  - What is the association of the Clinical Frailty Score on hospital related outcomes?
- **Primary outcome**
  - 28 day mortality
- **Secondary outcomes**
  - In hospital mortality, admission, LOS, number of ED presentations, falls, delirium, pressure injury
- **Study population**
  - Adults ≥75 years presenting to ED at Caboolture (area of low socioeconomic index for area)
- **Patient recruitment**
  - Already completed.
- **Study design**
  - Observational retrospective.

- **Research question**
  - What is the association of the Clinical Frailty Score on hospital related outcomes?

Points for consideration:



- **Primary outcome**
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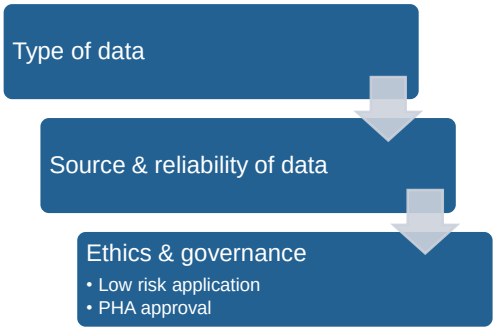

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- **Study population**
  - Adults ≥75 years presenting to ED at Caboolture (area of low socioeconomic index for area)

- **Patient recruitment**
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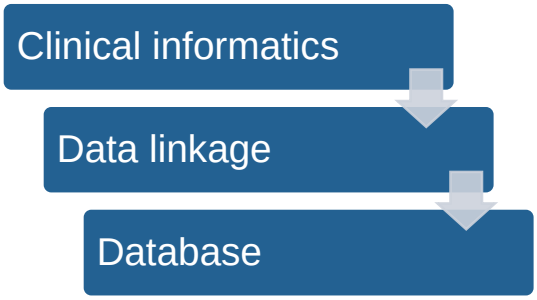
- **Study design**
  - Observational retrospective.

Points for consideration:



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	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U	V	W	X
1	Age	Sex	DxDC	ED Diagnosis ICD10	ED Diagnosis Group	PostCode	Charlson score	Frailty Score	Frailty Score Completed	Required CGAs	Had CGA	Represent No	Readmission within 28 days	Admitted	In hosp mortality	Inpt LOS Hrs	Referral ACP	Referral AHDT	Referral AHOT	Referral AHPT	Referral AHSP
2	81	0	ONATRAEMIA	E87.1	METABOLI	4510	0	6666	0	9999	0		0	0	0	9999	0	0	0	0	0
3	76	0	YPERTENSION	I10	CARDIOVA	4510	0	2	1	9999	0		0	0	0	9999	0	0	0	0	0
4	75	1	CT INFECTION	N39.0	INFECTIOU	4510	0	6666	0	9999	0		0	0	0	9999	0	0	0	0	0
5	78	1	RDIAC FAILURE	I50.0	CARDIOVA	4510	0	3	1	9999	0		0	0	0	9999	0	0	0	0	0
6	91	1	DID NOT WAIT	Z53.2	MISCELLAN	4510	0	4	1	1	0		0	0	0	9999	0	0	0	0	0
7	83	1	AGEAL REFLUX	K21.9	GASTROIN	4510	0	5	1	1	0		0	0	0	9999	0	0	0	0	0
8	83	0	AC CHEST PAIN	I20.0	CARDIOVA	4505	4	5	1	1	0		0	1	0	9	0	0	0	0	0
9	80	1	OBSTRUCTION	K56.6	GASTROIN	4507	0	3	1	9999	0		0	1	0	64	0	0	0	0	0
10	79	0	- UNSPECIFIED	I63.9	NEUROLOC	4511	4	3	1	9999	0		0	1	1	61	0	1	0	1	1
11	76	0	ATAXIA	R27	NEUROLOC	4507	2	4	1	1	0		0	0	0	9999	0	0	0	0	0
12	76	0	FIBRILLATION	I48	CARDIOVA	4505	3	6666	0	9999	0		1	0	0	9999	0	0	0	0	0
13	83	1	RY INFECTION	J22	RESPIRATC	4511	0	3	1	9999	0		0	0	0	9999	0	0	0	0	0
14	93	0	PANCREATITIS	K85.9	GASTROIN	4516	0	6666	0	9999	0		0	1	0	69	0	0	0	1	0
15	87	0	COMPRESSION	G95.2	NEUROLOC	4465	0	6666	0	9999	0		0	0	0	9999	0	0	0	0	0
16	91	1	CT INFECTION	N39.0	INFECTIOU	4506	0	6	1	1	0		0	1	0	57	0	0	0	0	0
17	87	1	W LIMITATION	J44.9	RESPIRATC	4506	1	6	1	1	0		1	1	0	317	0	0	0	1	1
18	75	0	DIZZINESS	R42	NEUROLOC	4104	0	6666	0	9999	0		0	0	0	9999	0	0	0	0	0
19	77	1	TROENTERITIS	A09	GASTROIN	4507	0	6666	0	9999	0		0	0	0	9999	0	0	0	0	0
20	84	0	- UNSPECIFIED	J18.9	RESPIRATC	4507	1	6666	0	9999	0		0	0	0	9999	0	0	0	0	0
21	78	0	AEMORRHAGE	T81.0	ENT & MO	4506	0	3	1	9999	0		0	0	0	9999	0	0	0	0	0
22	83	1	/ITH DELIRIUM	F05.1	NEUROLOC	4507	1	5	1	1	0		1	1	0	515	0	1	0	1	0
23	75	0	AL ADMISSION	Z60.9	MISCELLAN	4510	5	6	1	1	0		0	1	0	334	0	0	1	1	0
24	89	0	LUNG DISEASE	J84.9	RESPIRATC	4514	0	4	1	1	0		0	1	1	221	0	1	1	1	1
25	81	1	ERGLYCAEMIA	R73.0	ENDOCRIN	4510	1	4	1	1	0		0	0	0	99	0	0	0	0	0
26	87	1	YPERTENSION	I10	CARDIOVA	4507	0	3	1	9999	0		0	0	0	9999	0	0	0	0	0
27	76	0	MBOPHLEBITIS	I80.9	CARDIOVA	4510	0	6666	0	9999	0		0	0	0	9999	0	0	0	0	0
28	89	0	AKER FAILURE	T82.1	CARDIOVA	4505	1	6666	0	9999	0		0	1	0	29	0	0	0	1	0
29	75	1	IN RECURRENT	R10.4	GASTROIN	4507	0	6666	0	9999	0		0	0	0	9999	0	0	0	0	0
30	91	1	ND VOMITING	R11	GASTROIN	4507	0	6	1	1	0		0	0	0	9999	0	0	0	0	0
31	76	0	INFLUENZA	J11.1	INFECTIOU	4505	0	6666	0	9999	0		0	0	0	9999	0	0	0	0	0
32	90	1	L PAIN - ACUTE	R10.0	PAEDIATRI	4507	1	6666	0	9999	0		0	1	1	11	0	0	0	0	0

	A	B	C
1	Charlson ICD 10 Codes	Code	Points
2	Myocardial Infarction	I21.x	1
3		I22.x	
4		I25.2	
5			
6	Congestive Heart Failure	I09.9	1
7		I11.0	
8		I13.0	
9		I13.2	
10		I25.5	
11		I42.0	
12		I42.5-I42.9	
13		I43x	
14		I50x	
15		P29.0	
16			
17	Peripheral Vascular disease	I70x	1
18		I71x	
19		I73.1	
20		I73.8	
21		I73.9	
22		I77.1	
23		I79.0	
24		I79.2	
25		K55.1	
26		K55.8	
27		K55.9	
28		Z95.8	
29		Z95.9	
30			
31	Cerebrovascular disease	G45x	1
32		G46x	
33		H34.0	
34		I60x-I69x	
35			

Importance of a codebook

	A	B	C
1	**Code**	Meaning	Notes/Source
2	ED Presentation date	"XX/XX/XXXX"	
3	UR No	"000000"	
4	Age	Continuous number ≥75 years +	
5	Sex	0=Male, 1=Female	EDIS
6	DXICD10 group	Cardiovacular	
7		Dermatology	
8		Endocrine	
9		Ent & Mouth	
10		Environmental Conditions	
11		Gastrointestinal	
12		Haematology	
13		Iatrogenic Conditions	
14		Immunological	
15		Infectious	
16		Metabolic Disorders	
17		Miscellaneous Conditions	
18		Neoplasia	
19		Neurological	
20		Obstetric & Gynae	
21		Ophthalmology	
22		Orthopaedic Conditions	
23		Paediatric Conditions	
24		Psychiatric	
25		Renal	
26		Respiratory	
27		Symptom codes - No Diagnosis	
28		Toxicology	
29		Trauma	
30		Urology	
31	Charlson Comorbidity Index	0 to 37	See Charlson tab for ICD10 codes
32	Frailty Score	6666=not done, 0 to 9	
33	Frailty Score completed	1=Yes, 0=No	
	Required a CGA	Had a FR score > 4, 1=Yes, 9999=N/A if score less than 4	If CGA was completed on the next dat it is not included
34			
35	CGA	1=Yes, 0=No	Any item maked as a risk equals a 1 for a heading if any item was marked as a risk eg CGA1 is Commu

Practical tips

- Sending of de-identified information only to those listed in original PHA application
- Know variables and how it will be used by your biostatistician
- CHECK, CHECK and Re-CHECK format of database including drop down options
- Different team members have different strengths, use this!
  - Biostatistician: data linkage, statistical planning and analyses, missing data, data summary, checking assumptions and violations
  - Clinicians: content experts of what is clinically acceptable, feasibility, translation
  - Research Coordinator / Fellow: network and guidance on steps in research
  - Executive sponsor/lead: escalation of barriers, facilitation of dissemination

Example 2 – Prospective multi-centre randomised control trial

Frakking et al. BMC Pediatrics (2018) 18:72
https://doi.org/10.1186/s12887-018-1034-x

BMC Pediatrics

STUDY PROTOCOL Open Access

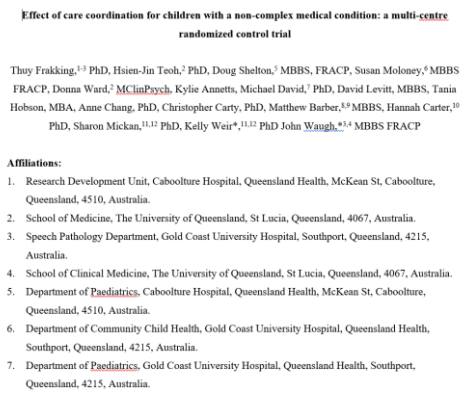
Integrated children's clinic care (ICCC) versus a self-directed care pathway for children with a chronic health condition: a multi-centre randomised controlled trial study protocol

Thuy Thanh Frakking[1,2*], John Waugh[3,4], Hsien-Jin Teoh[2], Doug Shelton[5], Susan Moloney[6], Donna Ward[2], Michael David[7], Matthew Barber[8,9], Hannah Carter[10], Sharon Mickan[11,12] and Kelly Weir[11,12]

Abstract

Background: Children with chronic health conditions have better health-related outcomes when their care is managed in a personalised and coordinated way. However, increased demand on Australian ambulatory care hospital services has led to longer waitlist times to access specialists and appropriate intervention services; placing vulnerable children at increased risk of poorer short-term (e.g. social difficulties) and long-term (e.g. convictions) health and social outcomes. Traditional approaches to increasing frequency and service of delivery are expensive and can have minimal impact on caregiver burden. A community based service-integration approach, rather than self-directed care is proposed as increased service linkages are more likely to occur and improve the health outcomes of children with a chronic health condition.

Methods: An open, unblinded, multi-centre randomised controlled trial in two Australian public hospitals. 112 children (0–16 years) fulfilling the inclusion criteria will be randomised to one of two clinical pathways for management of their chronic health condition: (1) integrated children's care clinic (ICCC) or (2) self-directed care pathway. All children and



Effect of care coordination for children with a non-complex medical condition: a multi-centre randomized control trial

Thuy Frakking,[1-3] PhD, Hsien-Jin Teoh,[2] PhD, Doug Shelton,[5] MBBS, FRACP, Susan Moloney,[6] MBBS FRACP, Donna Ward,[2] MClinPsych, Kylie Annetts, Michael David,[7] PhD, David Levitt, MBBS, Tania Hobson, MBA, Anne Chang, PhD, Christopher Carty, PhD, Matthew Barber,[8,9] MBBS, Hannah Carter,[10] PhD, Sharon Mickan,[11,12] PhD, Kelly Weir*,[11,12] PhD John Waugh,*[3,4] MBBS FRACP

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3. Speech Pathology Department, Gold Coast University Hospital, Southport, Queensland, 4215, Australia.
4. School of Clinical Medicine, The University of Queensland, St Lucia, Queensland, 4067, Australia.
5. Department of Paediatrics, Caboolture Hospital, Queensland Health, McKean St, Caboolture, Queensland, 4510, Australia.
6. Department of Community Child Health, Gold Coast University Hospital, Queensland Health, Southport, Queensland, 4215, Australia.
7. Department of Paediatrics, Gold Coast University Hospital, Queensland Health, Southport, Queensland, 4215, Australia.

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Key components

- **Research question**
  - Does integrated care coordination improve quality of life outcomes for children with a newly diagnosed chronic non-complex medical condition?
- **Primary outcome**
  - Paediatric Quality of Life; Family Quality of Life
- **Secondary outcomes**
  - School absences; number of primary care, specialists and admissions
- **Study population**
  - Children 0 to 18 years with a chronic non-complex medical condition
- **Patient recruitment**
  - Prospective, unblinded, N=81
- **Study design**
  - RCT

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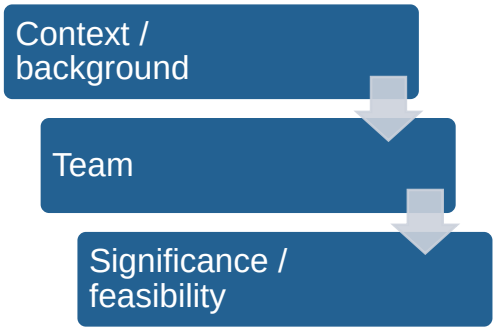
- **Research question**
  - Does integrated care coordination improve quality of life outcomes for children with a newly diagnosed chronic non-complex medical condition?

Points for consideration:



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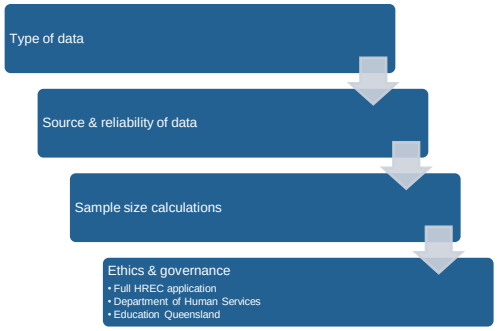
- **Primary outcome**
  - Paediatric Quality of Life; Family Quality of Life

- **Secondary outcomes**
  - School absences; number of primary care, specialists and admissions

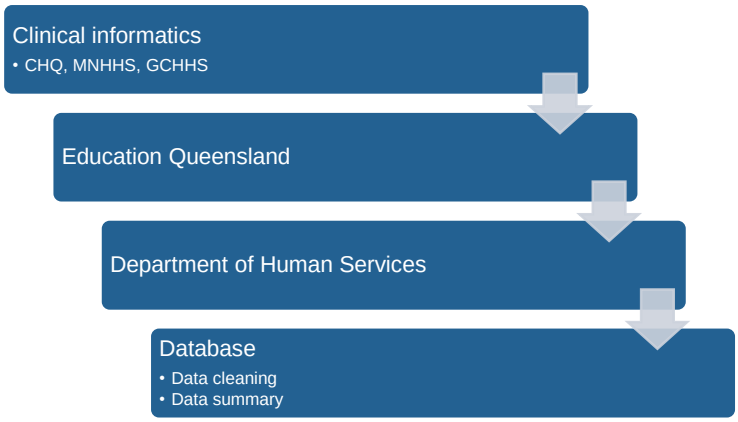
Points for consideration:



28

- **Study population**
  - Children 0 to 18 years with a chronic non-complex medical condition
- **Patient recruitment**
  - Prospective, unblinded, N=81
- **Study design**
  - RCT

Points for consideration:



29

29

	A	B	C	D	E	F	G	H	I	
1	Participant number	Site	Date consent signed	Group	Sex	D.O.B	Caregiver 1_relationship	Education level_1	Employment_1	Employm
2	1	1	30/10/2017	1	0	9/06/2003	0	3	0	
3	2	1	6/11/2017	0	0	2/08/2008	0	3	1	
4	3	1	13/11/2017	0	0	2/02/2006	0	2	0	
5	4	1	27/11/2017	0	0	21/05/2011	0	2	0	
6	5	0	21/11/2017	0	0	6/01/2012	0	2	0	
7	6	1	27/11/2017	1	1	11/09/2009	0	3	0	
8	7	1	27/11/2017	1	1	24/11/2003	0	2	1	
9	8	1	4/12/2017	1	1	10/03/2011	0	3	0	
10	9	1	4/12/2017	1	1	2/05/2010	0	2	1	
11	10	0	12/01/2018	1	0	2/07/2009	0	2	0	
12	11	1	11/12/2017	0	0	24/05/2012	0	3	1	
13	12	0	18/01/2018	1	0	23/12/2015	0	3	0	
14	13	0	24/01/2018	0	1	8/08/2013	0	1	0	
15	14	0	24/01/2018	0	1	27/04/2011	0	3	0	
16	15	1	12/02/2018	1	1	24/11/2009	0	1	0	
17	16	0	15/02/2018	1	0	14/03/2012	0	2	0	
18	17	0	2/03/2018	1	0	18/05/2011	0	1	0	
19	18	0	2/03/2018	0	0	29/11/2004	0	4	1	
20	19	0	9/03/2018	0	0	1/08/2013	0	3	0	
21	20	1	12/03/2018	0	1	10/12/2005	0	3	1	
22	21	0	22/05/2018	0	0	30/09/2014	0	2	0	
23	22	0	28/03/2018	1	0	10/09/2004	0	3	0	
24	23	0	28/03/2018	1	1	28/03/2012	1	2	1	
25	24	0	6/04/2018	1	1	27/05/2010	0	3	1	
26	25	0	20/05/2018	0	0	10/11/2011	0	4	1	
27	26	0	17/05/2018	1	0	5/09/2008	0	2	0	
28	27	0	20/05/2018	1	1	27/11/2008	0	1	1	
29	28	0	25/05/2018	0	0	19/12/2012	0			
30	29	1	12/06/2018	0	1	14/03/2014	0	2	1	
31	30	0	13/06/2018	0	0	19/03/2008	0	2	0	
32	31	0	15/06/2018	0	1	22/06/2004	0	3	1	
33	32	0	22/06/2018	1	0	2/08/2007	1	2	1	
34	33	0	20/06/2018	1	0	17/03/2005	0	3	1	
35	34	0	21/06/2018	0	0	17/09/2004	1	3	0	

30

30

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O
1	Participant number	Site	Group	B.QOLoverall	B.QOLphy	B.QOLPsycho	B.QOLfam	B.QOLpar	B.QOLfunc	B.SUDS	B.Rot	B.Pedi_care_raw	B.Pedi_care_stand	B.Pedi_mob_raw	B.Pedi_mob_stand
2				1 WEEK POST											
3	1	1	1	62	50	68.3	80.6	81.3	75	10	4	9999	9999	9999	9999
4	2	1	0	68.5	78.1	63.3	57.6	61.3	43.8	15	9	9999	9999	9999	9999
5	3	1	0	56.5	68.8	50	63.2	71.3	43.8	10	9	9999	9999	9999	9999
6	4	1	0	68.5	78.1	63.3	63.9	62.5	43.8	50	8	60	69.1	58	94.2
7	5	0	0	65.2	81.3	56.7	76.4	77.5	78.1	10	10	56	30.6	58	39.7
8	6	1	1	55.4	50	58.3	60.4	71.3	50	15	5	6666	6666	6666	6666
9	7	1	1	58.7	62.5	56.7	40.3	57.5	21.9	50	6	6666	6666	6666	6666
10	8	1	1	51.1	68.8	41.7	61.1	57.5	65.6	10	4	73	62.3	59	53.9
11	9	1	1	32.6	43.8	26.7	45.8	50	59.4	50	7	72	43.8	59	54.7
12	10	0	1	71.7	68.8	73.3	47.9	57.5	59.4	10	4	6666	6666	6666	6666
13	11	1	0	62	71.9	51.7	29.2	18.8	53.1	60	7	71	50.5	59	54.3
14	12	0	1	54.8	71.9	44.2	40.2	38.8	53.1	40	2	25	35.6	34	24
15	13	0	0	35.7	50	26.9	18.1	22.5	12.5	50	10	35	52.4	51	73.3
16	14	0	0	43.5	68.8	30	26.4	28.8	34.4	30	5	62	30.9	56	10
17	15	1	1	21.7	28.1	18.3	31.3	30	40.6	80	14	6666	6666	6666	6666
18	16	0	1	73.9	68.8	76.7	43.8	40	40.6	20	6	69	44.2	58	39.7
19	17	0	1	8888	8888	8888	8888	8888	8888	8888	8888	8888	8888	8888	8888
20	18	0	0	44.6	40.6	46.7	47.9	48.8	43.8	70	6	6666	6666	6666	6666
21	19	0	0	39.3	62.5	25	22.2	20	28.1	90	15	59	33.5	56	37.5
22	20	1	0	73.9	84.4	68.3	83.3	87.5	93.8	10	8	6666	6666	6666	6666
23	21	0	0	67.9	90.6	53.9	81.3	77.5	87.5	0	10	11	10	53	38.9
24	22	0	1	21.7	21.8	21.7	10.4	15	3.1	80	5	6666	6666	6666	6666
25	23	0	1	38	46.9	33.3	19.4	28.8	12.5	90	5	62	19.5	51	10
26	24	0	1	44.6	50	41.7	44.4	45	46.9	40	6	72	43.8	59	54.7
27	25	0	0	50	56.3	46.7	59.7	72.5	43.8	50	6666	6666	6666	6666	6666
28	26	0	1	46.7	56.3	53.3	27.8	22.5	28.1	20	10	6666	6666	6666	6666
29	27	0	1	37	6.3	50	43.1	41.3	62.5	60	8	6666	6666	6666	6666
30	28	0	0	8888	8888	8888	8888	8888	8888	8888	8888	8888	8888	8888	8888
31	29	1	0	57.1	84.4	40.4	26.4	32.5	21.9	20	6	65	48	59	63.8
32	30	0	0	16.3	12.5	18.3	20.8	30	18.8	70	13	6666	6666	6666	6666
33	31	0	0	42.4	59.4	33.3	22.9	17.5	15.6	80	5	6666	6666	6666	6666
34	32	0	1	61.9	78.1	53.3	40.3	50	31.3	50	9	6666	6666	6666	6666
35	33	0	1	44.6	100	15	29.9	36.3	12.5	20	9	6666	6666	6666	6666

Importance of a codebook

	A	B	C
1	Code	Meaning	
2	Consent signed	0=no, 1=yes	
3	Group	0=self-directed care; 1=ICCC	
4	Sex	0=male; 1=female	
5	Child name_first	Free text	
6	Child name_surname	Free text	
7	D.O.B	Dates must be between 29/08/00 to 29/08/2017	
8	Caregiver 1_name	Free text	
9	Caregiver 1_relationship	0=mother; 1=father; 2=grandma; 3=grandpa; 4=foster carer; 5=other	
10	Education level_1	0=none; 1=primary school; 2=high school; 3=tafe; 4=university; 99= not asked	
11	Employment_1	0=no; 1=yes; 99=not asked	
12	Employment_1 detail	0=full-time; 1=part-time; 2=casual; 3=centrelink; 4=studying; 5=combination; 6=full-time carer; 7=other; 99 =not asked	
13	Mental health_1	0=no; 1=yes; 99=not asked	
14	Address_1	Free text	
15	Contact number_1	Free numerical	
16	Caregiver 2_name	Free text	
17	Caregiver 2_relationship	0=mother; 1=father; 2=grandma; 3=grandpa; 4=foster carer; 5=other	
18	Education level_2	0=none; 1=primary school; 2=high school; 3=tafe; 4=university	
19	Employment_2	0=no; 1=yes	
20	Employment_2 detail	0=full-time; 1=part-time; 2=casual; 3=centrelink; 4=studying; 5=combination; 6=other	
21	Mental health_2	0=no; 1=yes	
22	Address_2	Free text	
23	Contact number_1	Free numerical	
24	School	Free text	
25	Yr level	0=prep; 1 to 12 equivalent; 13=childcare; 77=N/A , 99 = not asked	
26	GP Practice	Free text	
27	GP_name	Free text	
28	Medicare number	Free numerical	
29	Site	0=Caboolture; 1=GCUH; 2=QCH	
30			

Practical tips

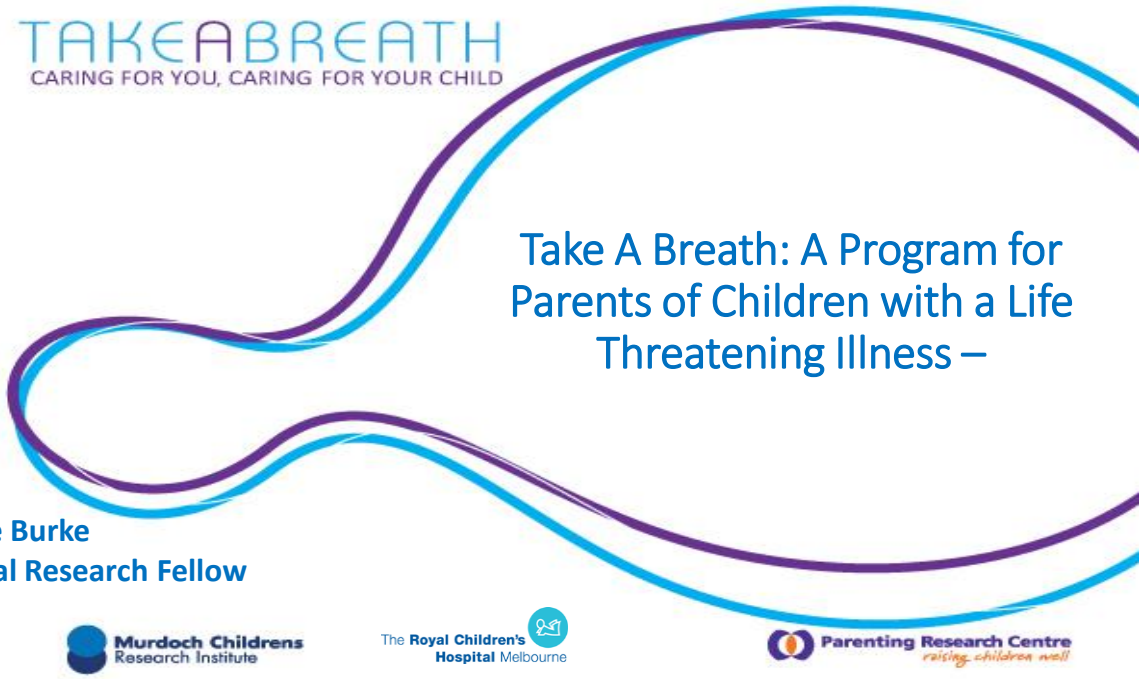
- Sending of de-identified information only to those listed in original approved HREC applications
  - Different organisation may charge fees for data extraction, check!
- Know variables and how it will be used by your biostatistician
- CHECK, CHECK and Re-CHECK format of database including drop down options
  - Do this at the beginning. Send to health economist, biostatistician
- Different team members have different strengths, use this!
  - Biostatistician: statistical planning and analyses, missing data, data summary, checking assumptions and violations
  - Health economist: variables required for formal economic evaluation, methods are different to stats
  - Clinicians: content experts of what is clinically acceptable, feasibility, translation
  - Research Coordinator / Fellow: network and guidance on steps in research
  - Executive sponsor/lead: escalation of barriers, facilitation of dissemination
- RESPECT for confidentiality of all participants in our study. The need for further permissions if wanting to share individual patient stories

Kylie Burke

Principal Research Fellow

Metro North Mental Health

- Responsibility for building research capacity within Mental Health
- Psychologist and researcher whose work has focused on supporting parents and children experiencing adversity, including adolescence, children with life-threatening illnesses and the intergenerational effects of social disadvantage



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Identifying the Problem, Topic or Solution

"I dream about being on a train with my daughter. Then we are hanging off the back whilst it goes out of control. I can't hold onto her – she is slipping away from me. I wake up feeling sick to the stomach, scared and completely wiped out"

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What do we know?

- The most distressed parents do not always have a child with the worst diagnosis/prognosis
- The event/s are not necessarily the trigger for a trauma response
- Cognitions (i.e. subjective appraisal) are the key

- Other things to consider:
  - Timing
  - Tailoring according to risk

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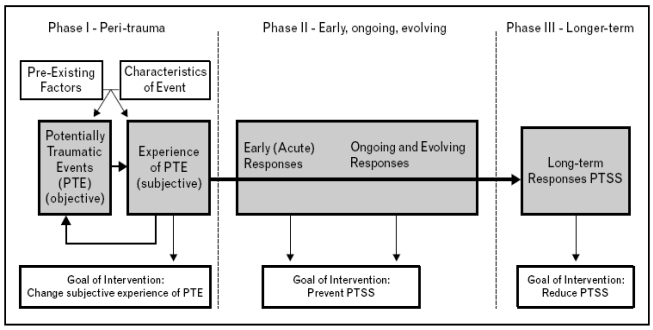
Figure 1 Model of medical traumatic stress for pediatric patients and their families



Source: Kazak AE, Kassam-Adams N, Schneider S, Zelikovsky N, Alderfer M, Rourke M. An integrative model of pediatric medical traumatic stress. J Pediatr Psychol 2006; 31: 343–355.

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Aims, Research Questions and Hypotheses

- Aims
  - broad statement of problem, topic or solution
  - Terms like: assess, build knowledge, understand, identify, evaluate
- Research Question/s
  - Can be 1 or multiple
  - Linked to aim
  - Primary and Secondary
  - Phrased as a question
  - More specific than aim
- Hypotheses
  - Relate to a specific research question
  - A research question can have multiple or multi-part hypotheses
  - Statement of expected outcome

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Project Aims

- The project sought to advance capacity to both screen and treat at risk families by extending previous work in the area of childhood cancer to other life-threatening illnesses (LTIs) and by development and evaluation of an intervention targeting parent distress following a traumatic experience. The overall aims of the project are to:
- **Identify the psychosocial risk factors in families with a child with a serious childhood illness/injury (cardiac disease, acquired brain injury or having been admitted to the Paediatric Intensive Care Unit).**
- Assess if a parenting intervention leads to improvements in psychosocial distress for parents of children with cancer.

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Aims

1. **To investigate** the prevalence of parent psychosocial distress in four illness groups: Pediatric diagnosis of cancer, a cardiac or neurological condition or admission to Pediatric Intensive Care Unit (PICU).
2. **To determine** the trajectory of parent psychosocial distress symptoms over an 18 month period from the child's initial diagnosis of cancer, a cardiac or neurological condition or admission to PICU.
3. **To identify** the demographic, psychosocial and illness related predictors of parent psychosocial distress and to investigate whether these vary at different timepoints after the child's initial diagnosis.
4. **To examine** the relationship between parent psychosocial distress and child psychological wellbeing from 4 to 19 months after the child's initial diagnosis.

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Research Questions

The **Primary research questions** were:

- **What** factors identified at 4 weeks post diagnosis reliably predict psychosocial recovery in parents and children when a child is diagnosed with a SCII?

(Psychosocial recovery was defined as improvement in reports of quality of life, the impact of the SCII and symptoms of post traumatic stress)

The **Secondary research questions** were:

- **Does** the PAT 2.0 reliably predict:
  - families at risk for psychopathology, including depression, anxiety, PTSD symptoms;
  - quality of life at 4, 7 and 24 months post-diagnosis?
- **What** is the prevalence rate of depression, anxiety and PTSD symptoms of children with SCII, and their parents, acutely and over the 24 months post-diagnosis?
- **What** are the risk factors, and their associations for depression, anxiety and PTSD symptoms in children with SCII and their parents?

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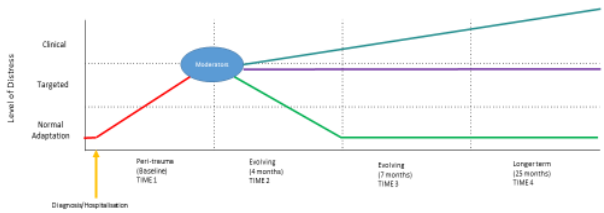
Design

Conceptual Model: Hypothesised Psychosocial Trajectories for Families of Children with LTI

- A **prospective longitudinal design** (see Figure) to track the developmental trajectory of trauma for families across 4 time points.



Participants completed **a survey** on a maximum of **four separate** occasions:

- Time 1 administered within four weeks of diagnosis during the Peri-Trauma phase;
- Time 2 at 3 months following Time 1 (4 months; Evolving Phase);
- Time 3 completed 3 months from Time 2 (7 months; Evolving Phase);
- Time 4 completed 18 months from Time 3 (25 months) during the Long term trauma phase of the PMTSM model.

Participant data was included if returned no later than two weeks from dissemination.

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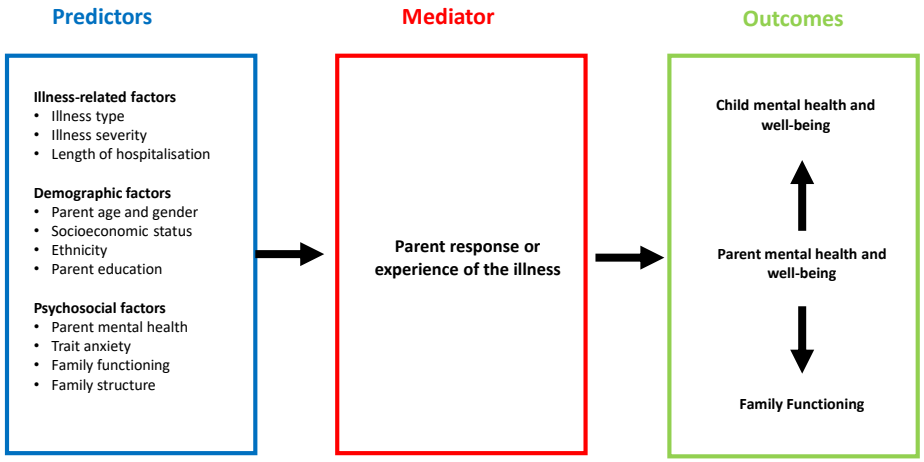

Project Logic Model

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Participants

Inclusion criteria

Eligible parents were:

- those who were caregivers of children aged 0-to 18-years admitted to the RCH for the first time for cardiac surgery in the first month of life (Cardiology),
- a new cancer diagnosis of any type (Oncology), a stroke or moderate-to-severe head injury (Neurology), or admission to PICU for longer than 48 h and their first admission for that illness (PICU).
- Ill children who were aged 7-to 18-years were invited to participate in data collection during time-points 2, 3 and 4 of the project. They were not involved in timepoint 1.
- Parents were still able to participate even if their child did not.

Exclusion criteria

Parents were excluded if:

- they were aged below 18-years of age,
- had experienced a major trauma in the 2 months prior to their child's diagnosis (such as the death or serious injury of another immediate family member),
- or had insufficient English to complete the questionnaires.
- Parents of children not expected to live longer than 6 months were identified by the clinical team and were not approached for participation.

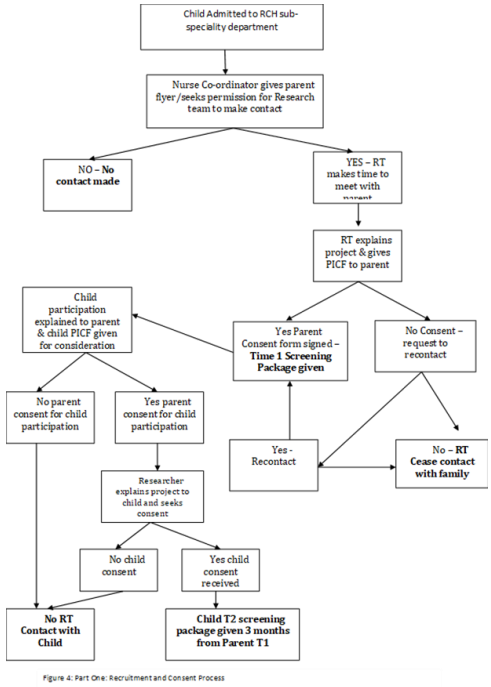

Figure 4: Part One: Recruitment and Consent Process

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Recruitment, Consent and Participant Tracking

- CONSORT – RCTs

Moher, D., Hopewell, S., Schulz, K., Montori, V., Gøtzsche, P., Devereaux, P., Elbourne, D., Egger, M., & Altman, D. (2010). for the CONSORT Group. CONSORT 2010 Explanation and Elaboration: updated guidelines for reporting parallel group randomised trial. J Clin Epi.

- STROBE – Observational studies

von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies.

- PRISMA – Systematic reviews

Rethlefsen ML, Kirtley S, Waffenschmidt S, Ayala AP, Moher D, Page MJ, Koffel JB; PRISMA-S Group. PRISMA-S: an extension to the PRISMA Statement for Reporting Literature Searches in Systematic Reviews. Syst Rev. 2021;10(1):39.

For other designs go to: https://www.equator-network.org/reporting-guidelines/

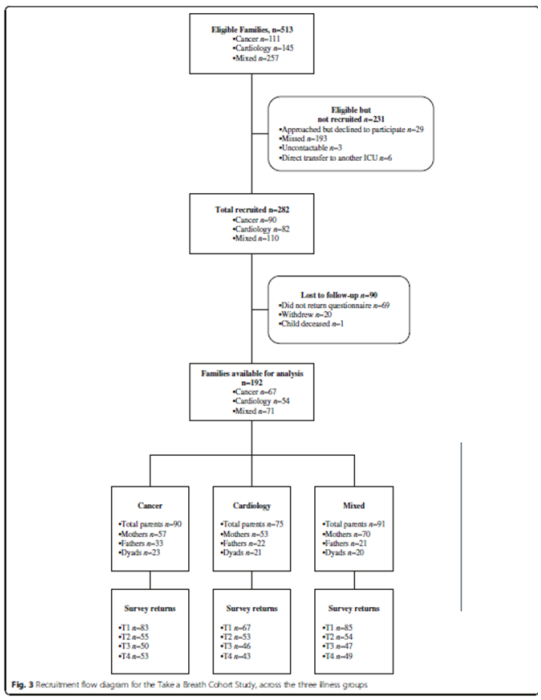

Fig. 3 Recruitment flow diagram for the Take a Breath Cohort Study, across the three illness groups

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Data Analysis and Power

- For Aim 2, Repeated Measures ANOVA will be used to assess temporal changes in parent traumatic stress symptoms, with time since diagnosis as the independent variable and the PCL-S as the outcome measure. Random effects linear regression may also be employed, as it allows for correlations between repeated measures taken from the same participant, and analyses available data (allowing missing timepoints). This procedure will be repeated for the child measures with the CROPS as the outcome measure.
- Power analysis suggests that in order to detect a small-to-medium effect size ($\eta 2 = 0.025$) the target of 240 families (80 in each illness group) is sufficient to conduct the planned analyses (power = 80 %, $\alpha = 0.05$).

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Selecting Measures

Linked to Research Questions and Hypotheses

- What are the constructs you want to measure?
- Do you have a measure for each construct?

Choosing Measures

- Are there already developed and psychometrically sound measures available (are they accessible? Free?)
- Unsure?
  - Ask colleagues
  - Literature Search/Google
- Nothing Available?
  - Develop your own (use clinical knowledge AND literature)

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Measure Selection

AIMS

1. To investigate the prevalence of **parent psychosocial distress** in four illness groups: Pediatric diagnosis of cancer, a cardiac or neurological condition or admission to Pediatric Intensive Care Unit (PICU).
2. To determine the trajectory of **parent psychosocial distress symptoms** over an 18 month period from the child's initial **diagnosis** of cancer, a cardiac or neurological condition or admission to PICU.
3. To identify the **demographic, psychosocial and illness related predictors** of parent psychosocial distress and to investigate whether these vary at different timepoints after the child's initial diagnosis.
4. To examine the relationship between parent psychosocial distress and **child psychological wellbeing** from 4 to 19 months after the child's initial diagnosis.

Table 1 Summary of the measures included in the take a breath cohort study

Construct	Measure	Source	Time-point			
			1	2	3	4
Outcome Measures						
Parent Distress	Posttraumatic Stress Checklist-Specific Version (PCL-S) [40]	P		*	*	*
Post traumatic growth	Post Traumatic Growth Inventory – Short form [41]	P				*
Child psychopathology	The Brief Infant Toddler Social Emotional Assessment [42], or Strengths and Difficulties Questionnaire (SDQ) [43]	P		*	*	*
	Strengths and Difficulties Questionnaire (SDQ) [43]	C		*	*	*
	Parent Report of Posttraumatic Stress Symptoms [44]	P	*	*	*	*
	Child Report of Posttraumatic Stress Symptoms [44]	C		*	*	*
Child wellbeing	PEDS Quality of Life (6 years+) [45] or TNO-AZL Preschool Children Quality of Life (1–5 years) [46]	P		*	*	*
	PEDS Quality of Life [45]	C		*	*	*
Illness Related Factors						
Illness variables	Severity of Illness Scale [47]	MD	*			
Demographic Factors						
Demographics	General questionnaire of parent demographic information (eg. age, years of education, ethnicity)	P	*			
Health Economy	General questionnaire of health economy factors (eg. level of income, services used in the hospital and in the community)	P	*	*	*	*
Psychosocial Factors						
Psychosocial factors	Psychosocial Assessment Tool (PAT 2.0) [48] (assessing psychosocial risk factors such as family structure, family beliefs, access to services and transport)	P	*	*	*	*
	Psychosocial Assessment Tool (PAT-S) [25]	SW	*	*		
Parent distress/ wellbeing	Acute Stress Disorder Scale (ASDS) [49]	P	*			
	Depression Anxiety Stress Scale Short Form (DASS-21) [50]	P	*	*	*	*
	Assessment of QoL (AQOL) [51]	P	*	*	*	*
	State Trait Anxiety Scale [52]	P	*			
Family Functioning	Family Environment Scales [53]	P	*			
Moderators						
Experience of Illness	Parent Experience of Child Illness (PECI) [54]	P		*	*	*
	Family Management Measure [55]	P		*	*	*
	Benefit Burden Scale - Children [56]	C		*	*	*

* = measure administered at this time point, P = Parent reported measures, MD = Doctor reported measures, SW = Social Worker reported measures, C = Child reported measures, Timepoint 1 = acute (within first month since hospitalization/diagnosis), Timepoint 2 = three months after Timepoint 1 (four months since hospitalization/diagnosis), Timepoint 3 = six months after Timepoint 1 (seven months since hospitalization/diagnosis), Timepoint 4 = 18 months after Timepoint 1 (19 months since hospitalization/diagnosis)

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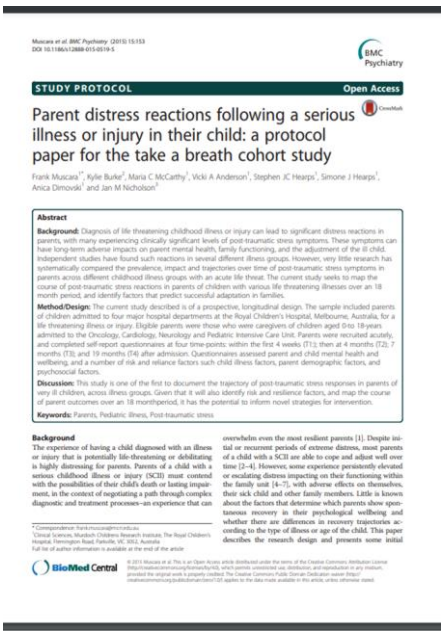
Key Points

- Build a team
- Develop a clear project plan (Protocol)
- Diagrams!
- Codebook

The Protocol

- Developed at the beginning
- Included with ethics
- Ensures you have a well defined plan
- Provides detail for reports, presentations and papers
- Can be a publication



Muscara et al. *BMC Psychiatry* (2015) 15:153
DOI 10.1186/s12888-015-0519-5

BMC Psychiatry

STUDY PROTOCOL Open Access

Parent distress reactions following a serious illness or injury in their child: a protocol paper for the take a breath cohort study

Frank Muscara[1,2*], Kylie Burke[2], Maria C McCarthy[1], Vicki A Anderson[1], Stephen JC Hearps[1], Simone J Hearps[1], Anica Dimovski[1] and Jan M Nicholson[3]

Abstract

Background: Diagnosis of life threatening childhood illness or injury can lead to significant distress reactions in parents, with many experiencing clinically significant levels of post-traumatic stress symptoms. These symptoms can have long-term adverse impacts on parent mental health, family functioning, and the adjustment of the ill child. Independent studies have found such reactions in several different illness groups. However, very little research has systematically compared the prevalence, impact and trajectories over time of post-traumatic stress symptoms in parents across different childhood illness groups with an acute life threat. The current study seeks to map the course of post-traumatic stress reactions in parents of children with various life threatening illnesses over an 18 month period, and identify factors that predict successful adaptation in families.

Method/Design: The current study described is of a prospective, longitudinal design. The sample included parents of children admitted to four major hospital departments at the Royal Children's Hospital, Melbourne, Australia, for a life threatening illness or injury. Eligible parents were those who were caregivers of children aged 0 to 18-years admitted to the Oncology, Cardiology, Neurology and Pediatric Intensive Care Unit. Parents were recruited acutely, and completed self-report questionnaires at four time-points: within the first 4 weeks (T1); then at 4 months (T2), 7 months (T3), and 19 months (T4) after admission. Questionnaires assessed parent and child mental health and wellbeing, and a number of risk and reliance factors such child illness factors, parent demographic factors, and psychosocial factors.

Discussion: This study is one of the first to document the trajectory of post-traumatic stress responses in parents of very ill children, across illness groups. Given that it will also identify risk and resilience factors, and map the course of parent outcomes over an 18 monthperiod, it has the potential to inform novel strategies for intervention.

Keywords: Parents, Pediatric illness, Post-traumatic stress

Background

The experience of having a child diagnosed with an illness or injury that is potentially life-threatening or debilitating is highly distressing for parents. Parents of a child with a serious childhood illness or injury (SCII) must contend with the possibilities of their child's death or lasting impairment, in the context of negotiating a path through complex diagnostic and treatment processes–an experience that can overwhelm even the most resilient parents [1]. Despite initial or recurrent periods of extreme distress, most parents of a child with a SCII are able to cope and adjust well over time [2–4]. However, some experience persistently elevated or escalating distress impacting on their functioning within the family unit [4–7], with adverse effects on themselves, their sick child and other family members. Little is known about the factors that determine which parents show spontaneous recovery in their psychological wellbeing and whether there are differences in recovery trajectories according to the type of illness or age of the child. This paper describes the research design and presents some initial

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