

# PaCCSC

Palliative Care Clinical Studies Collaborative

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National Manager



Flinders University receives funding for PaCCSC from the Australian Government Department of Health and Ageing under the National Palliative Care Program.



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## Investigators

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Simon Eckermann  
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## Funding

- Funded by the Australian Government Department of Health and Ageing under the National Palliative Care Strategy
- Funding period April 2007 – June 2010



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## Background



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## National Medicines Policy

4 central objectives

- Appropriate standards of quality, safety, efficacy (TGA)
- Timely access to, and affordable cost of medicines (PBAC)
- Quality use of medicines (clinical community)
- Maintaining a responsible and viable medicines industry (key partnerships)



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## Challenge to providing medicines for palliative care

- The medicine is not registered for supply in Australia
- The medicine is registered but not PBS listed
- The specific dosage, indication and formulation needs for administration to palliative care patients are not covered by the TGA or PBAC data
- The discontinuation of older or low usage medicines by manufacturers



## Identifying priority palliative care medicines

- National priority setting which attempts to combine:
  - An assessment of need
  - An estimation of the likelihood of success
  - Resource requirements
  - The underlying values of those making the decisions
- National survey (2000)
  - For 25 most frequent symptoms
    - Key medicines used
    - Level of evidence
    - Current availability



## Criteria to prioritise medicines for possible PBS listing

- Availability of data
  - Indication
  - Route of administration
- Wide consensus about use
- Magnitude of the problem
- Medicines that were likely to avoid hospitalisation
- No equivalent medicines already listed
- A number of palliative indications for the one medicine



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## Progress to date

- Palliative care section with the PBS
- Some medicines not previously PBS listed now available

### **BUT**

- Medicines that remain on the PCMWG list do not have sufficient evidence to obtain PBS listing

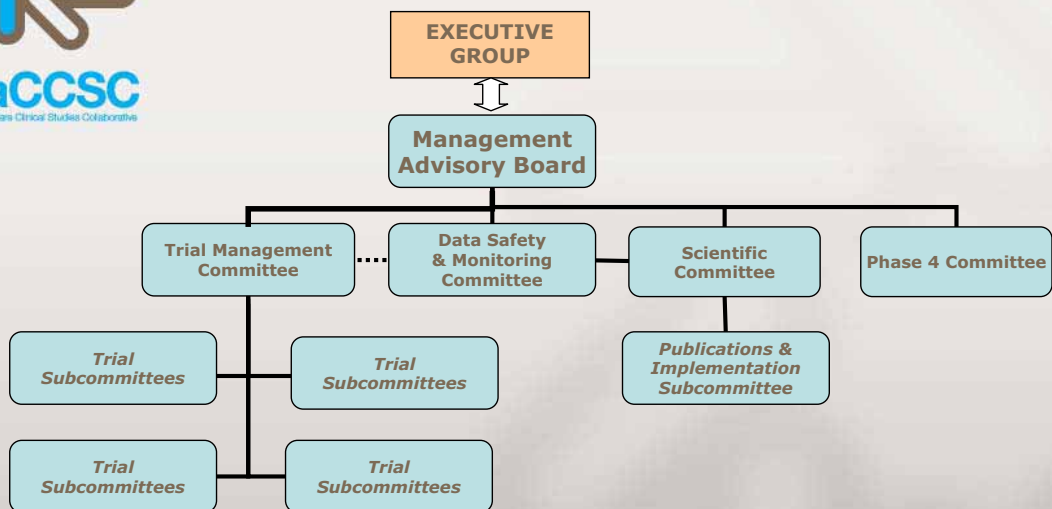
### **NEED**

- Rigorously designed prospective clinical trials at a level of quality that would allow the results to be used in registration and subsidy applications if positive



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## Structure

- Management Advisory Board
  - Chair: Prof Felix Bochner
- Scientific Committee
  - Chair: A/Prof Andrea Mant
- Trials Management Committee
  - Chair: Prof Janet Hardy
- Phase 4 Committee
  - Chair: Debra Rowett
- Data Safety Monitoring Board



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## Structure

- Trial Subcommittees for each medicine being studied
  - Ketamine (Janet Hardy)
  - Risperidone (Meera Agar)
  - Ondansetron (James Stevenson)
  - Megestrol Acetate (Paul Glare)
  - Octreotide (David Currow)
  - Ketorolac (Odette Spruyt)
- Central management
- Site staff
  - Coordinator, consultant, study nurses – Phase 3
  - Coordinator – Phase 4



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## Coordinating Centre

- Flinders University
- Based at the Repatriation General Hospital
- Staff
  - National Manager
  - Project Officer
  - Administration Officer



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## Coordinating Site

- Overall study management
- Statistical management
- Financial management
- Administrative management
- Training of site staff on relevant legislation



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## Scope of work to be done

- 6 initial sites/ investigators working in 5 states
- Prospective phase 3 clinical studies
- Prospective phase 4 pharmaco-vigilance studies on phase 3 medicines being studied
- Development of consumer impact statements on medicines being studied
- All studies to be completed by June 2010



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## Current Phase 3 sites

Selected by national consensus process

- NSW Cancer Centre, NSW
- Braeside Hospital, NSW
- Peter MacCallum Cancer Centre, Vic
- Mater Adult Hospital, QLD
- Southern Adelaide Palliative Services, SA
- Western Australia Centre for Cancer and Palliative Care, WA



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## Medicines being studied

- Ketamine for complex pain
  - Ketamine vs placebo
  - 5 day study
  - In-patients with chronic cancer pain
  - Haloperidol and/or Midazolam rescue
  - Primary outcome: average pain score at start of day 6
  - Sample size 150 patients



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## Medicines being studied

- Risperidone for delirium
  - Risperidone vs Haloperidol vs placebo
  - 3 day study
  - In-patients with delirium
  - Midazolam rescue
  - Primary outcome: sum of scores on Nu-Desc scale items 2,3 and 4 at 72 hours
  - Sample size 165 patients



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## Medicines being studied

- Octreotide for bowel obstruction
  - Dexamethasone, renitidine & octreotide vs Dexamethasone, renitidine & placebo
  - 72 hour study
  - Advanced cancer patients with bowel obstruction and vomiting that precipitates hospital admission or change in clinical care
  - Primary outcome: number of days without an episode of vomit
  - Sample size 92 patients



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## Medicines being studied

- Megestrol acetate for anorexia
  - Dexamethasone vs megestrol acetate vs placebo
  - 1 week primary outcome with up to 4 weeks treatment if beneficial
  - Cancer patients with self-reported loss of appetite and weight loss
  - Primary outcome: appetite score at day 7
  - Sample size 210 patients



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## Medicines being studied

- Ondansetron for cholestatic itch
  - Protocol still under development
  - Ondansetron vs placebo
  - Standardised skin care in both arms
  - 5 day study
  - People with intractable cholestatic itch
  - Promethazine rescue
  - Primary outcome: self-reported itch at day 5



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## Design of phase 3 studies

- Randomised
- Double-blind
- Controlled
  - Current practice comparator
  - Placebo
- Health economic evaluation built into each study
- Efficacy end-point with effectiveness continuation



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## Challenges for Phase 3 studies

- Will need to have multi-site recruitment
- Multiple Research Ethics Committees
- Not all sites may have the same level of research expertise
- Study designs must be sensitive to the needs of people with a life-limiting illness
- Maintaining enthusiasm over the length of the studies
- Recruitment, particularly in the complex studies



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## Phase 4 studies

- Pharmacovigilance of specific symptoms studied in phase 3
  - Pain
  - Delirium
  - Anorexia
  - Cholestatic itch
  - Bowel obstruction
- Prospective
- Look at net benefit (benefit and burden)
- Reflect real world use of medicines



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## Other work

- Effect of Dual listing of medicines in the PBS schedule
  - Palliative care specific pages and general pages
- Benzodiazepine use in palliative care
  - Audits to be conducted by phase 4 sites
- Patient impact statements to accompany any subsidy applications



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## Achievements to date

- Established a working governance structure
- PaCCSC infrastructure in place –SOPs
- Contracts signed
- Literature reviews of key medicines
- Feasibility audit
- Scientific committee approval for 4 studies
- 1 trial currently recruiting
- Phase 4 pilot audit underway



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## Acknowledgements

- Palliative Care Medicines Working Group, chaired by Professor Peter Ravenscroft
- Communications working group chaired by A/Professor Geoff Mitchell
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