Post-surgical pain and recovery in children

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Objectives

• Choose a research topic
• Choose a mentor
• Negotiate funding
• Start a research career
Disclosures

• None
Outcomes in children after surgery

Pain Outcomes

• Over 4.5 million children have surgery in U.S. annually\(^1\)
• Half of children admitted after surgery have moderate-severe pain\(^2\)
• This is unchanged over past 2 decades\(^3\)
• Chronic postsurgical pain rates range from 13 to 52\(\%\)\(^4\)

\(^1\)Rabbitts, et al., 2010
\(^2\)Groenewald, Rabbitts, et al., 2012
\(^3\)Cummings, et al., 1996; Taylor, et al., 2008
\(^4\)Wong, Yuen, et al., 2007; Kristensen, Pedersen, et al., 2010; Fortier, Chou, et al., 2011; Page, Stinson, et al., 2013
Outcomes in children after surgery

Pain Outcomes

• Multidimensional experience
• Biopsychosocial impact
• Assessment domains¹
  – Pain intensity
  – Physical function
  – Emotional response

¹PedIMMPACT; McGrath, Walco, et al., 2008 (Pediatric Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials)
Outcomes in children after surgery

Functional Outcomes

• Impact of postsurgical pain on health outcomes is unknown

• Health-related quality of life decreased in children undergoing specific surgeries

• Functional outcomes in broader pediatric postsurgical population are unknown

¹Bekkering, Vliet Vlieland, et al., 2010; Landolt, Buechel, et al., 2008; Devine, Reed-Knight, et al., 2010
Predictors of Health Outcomes

Which children are at risk for poorer pain and health outcomes after surgery?

Hypothesized factors

- Biological factors: age
- Psychological factors: anxiety, sleep patterns
- Social factors: parental anxiety

1. Kotzer, 2000*
3. Page, Stinson, et al., 2012*
4. Kain, Mayes, et al., 2002*
5. Khan, Ahmed, et al., 2011+
6. Bringuier, Dadure, et al., 2009*

*pediatric acute pain studies, +adult studies
Predictors of Health Outcomes

Which children are at risk for poorer pain and health outcomes after surgery?

Hypothesized factors

- Biological factors: age\(^1\), gender\(^2\), pain history\(^2\)
- Psychological factors: anxiety\(^3\), sleep patterns\(^4\), pain catastrophizing\(^5\)
- Social factors: parental anxiety\(^6\)

\(^1\)Kotzer, 2000*  
\(^2\)Kalkman, Visser, et al., 2003*  
\(^3\)Page, Stinson, et al., 2012*  
\(^4\)Kain, Mayes, et al., 2002*  
\(^5\)Khan, Ahmed, et al., 2011*  
\(^6\)Bringuier, Dadure, et al., 2009*  

*p pediatric acute pain studies, *adult studies
Getting started

• Research idea
• Research training
• Mentor
• Funding
  – etc…
Getting started

• Research idea
• **Research training**
  – Research fellowship
  – Faculty fellowship
  – T32 NIH institutional research training grants
Getting started

- Research idea
- Research training
- **Mentor**
  - *key to each step
  - Project
  - Resources
  - Collaborations
  - Grant writing
  - Departmental commitment
Getting started

- Research idea
- Research training
- Mentor
- **Funding**
  - Startup support
  - Institutional grants
Getting started

• Research idea
• Research training
• Mentor
• Funding
• Planning study
  – Research team
  – Resources
Study Aims


2. Identify clinical, psychological, and behavioral factors that predict postsurgical pain, physical function and quality of life in children after major surgery.
Procedures

• Longitudinal prospective study
  – 60 youth age 10-18 years
  – Undergoing spinal fusion, pectus repair
  – Otherwise healthy

• Assessments: baseline, 2 weeks, 4 months, 1 year
  – Questionnaires: anxiety, catastrophizing, pain, QOL
  – Daily monitoring: Pain diary, actigraphy

• Assessments: In-hospital:
  – Clinical data
Daily monitoring

• Daily electronic diary\(^1\)
  – pain and medication use
  – 7 days

• Actigraphy
  – physical activity levels\(^2\)
  – sleep patterns\(^3\)
  – 7 days

\(^1\) Palermo, Valenzuela, et al., 2004
\(^2\) Rabbitts, Lewandowski Holley, Palermo, et al., 2012
\(^3\) Lewandowski, Palermo, et al., 2010
Low to medium physical activity

Sleep
High physical activity

Sleep
Recruitment

108 eligible children
9 unable to reach in time
39 declined
60 enrolled
2 dropouts

Assessments
1. Baseline
2. Hospital
3. Short-term
4. Long-term

Events
Surgery
Discharge
2 weeks
4 months
1 year

Peds-CRC
Surgery team

Seattle Children's
Hospital • Research • Foundation

UW Medicine
School of Medicine
## Preliminary data

<table>
<thead>
<tr>
<th>Variable</th>
<th>M (range) or N(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age – years</td>
<td>14.8 (10-18)</td>
</tr>
<tr>
<td>Sex – female</td>
<td>42 (70%)</td>
</tr>
<tr>
<td>Ethnicity – Caucasian</td>
<td>53 (87%)</td>
</tr>
<tr>
<td>Surgery</td>
<td>49 (82%) 11 (18%)</td>
</tr>
<tr>
<td>Spinal fusion</td>
<td></td>
</tr>
<tr>
<td>Pectus</td>
<td></td>
</tr>
<tr>
<td>Duration of surgery – hours</td>
<td>5.0 (1.8 - 8.8)</td>
</tr>
<tr>
<td>Length of stay – days</td>
<td>4.5 (2.0 – 9.0)</td>
</tr>
</tbody>
</table>
Pain prevalence

Baseline (N=43)
In-Hospital (N=43)
2-Weeks (N=37)
4 Months (N=24)

Percentage of participants at timepoint

No Pain (0)
Mild Pain (1-3)
Moderate-Severe (4-10)

0-10 NRS
Longitudinal course of pain intensity over 4 months

GEE population averaged modeling adjusted for age and gender
Longitudinal course of quality of life over 4 months

GEE population averaged modeling

Quality of life (PedsQL 0-100)

Baseline 2 weeks 4 months

74.6 P < 0.001 61.1

79.3 P = 0.093
Longitudinal course of physical activity over 4 months

GEE population averaged modeling adjusted for age and gender

732 days of actigraphy data used for analysis

Mean activity level (counts/min)

- Baseline: 369.1
- 2 weeks: 224.1
- 4 months: 355.1

P = 0.198

P < 0.001
# Baseline predictors of acute postsurgical pain

*p = < 0.05, linear regressions adjusting for age, gender, and surgical procedure

Rabbitts, Groenewald, et al., 2014

<table>
<thead>
<tr>
<th>Predictors of maximum pain</th>
<th>In-hospital pain</th>
<th>Pain at 2-weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$\beta$ (SE)</td>
<td>$\beta$ (SE)</td>
</tr>
<tr>
<td>Pain catastrophizing (rumination)</td>
<td>0.21 (0.10)*</td>
<td>0.03 (0.10)</td>
</tr>
<tr>
<td>Baseline sleep (minutes)</td>
<td>-0.02 (0.13)*</td>
<td>-0.01 (0.01)</td>
</tr>
<tr>
<td>Baseline pain</td>
<td>0.08 (0.13)</td>
<td>0.53 (0.16)*</td>
</tr>
</tbody>
</table>

*p = < 0.05, linear regressions adjusting for age, gender, and surgical procedure

Rabbitts, Groenewald, et al., 2014
Planned analyses

• Trajectories of pain, activity and quality of life
  – Identify subset with persistent pain and poorer outcomes
  – Examine predictors of pain and functional trajectories

• Temporal relationships between daily pain, activity and medication usage
Memory of pain

- Model of acute pain memory development\(^1\)
- Parents and children report memories of postsurgical pain

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<tr>
<td>Events</td>
<td>Surgery</td>
<td>Discharge</td>
<td>2 weeks</td>
<td>4 months</td>
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2 Months

Memory Assessment

- Test predictors of pain memories and whether memories for pain mediate the relationship between early and late pain

\(^1\)Noel, Chambers et al., 2013
Pain and Quality of life

• Health-related quality of life: physical, psychological, and social function
• HRQOL (PedsQL) is measured in every child as part of the Outcomes Assessment Program
• Change in HRQOL predicts readmission rate of hospitalized children\(^1\)
• How does pain affect quality of life in children after surgery?

\(^1\)Mangione-Smith, et al., 2011 (Outcomes Assessment Program)
# Pain and Quality of life

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<th>Variable</th>
<th>M (range) or N(%)</th>
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<tr>
<td>Age – years</td>
<td>7.3 (1 month - 18 years)</td>
</tr>
<tr>
<td>Sex – female</td>
<td>579 (47%)</td>
</tr>
<tr>
<td>Ethnicity – Caucasian</td>
<td>686 (56%)</td>
</tr>
<tr>
<td>Medical complexity¹</td>
<td></td>
</tr>
<tr>
<td>Acute</td>
<td>535 (44%)</td>
</tr>
<tr>
<td>Chronic</td>
<td>344 (28%)</td>
</tr>
<tr>
<td>Complex chronic</td>
<td>344 (28%)</td>
</tr>
</tbody>
</table>

¹Pediatric Medical Complexity Algorithm, Simon, Cawthon, Mangione-Smith, et al., 2013
Pain and Quality of life

1 month postop
• 6.5% moderate-severe pain
• 10.2% pain 5 or more days a week
• 10.6% greater intensity pain than baseline
## Pain and Quality of life

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<th>Predictor</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain intensity (1 month)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Change in pain intensity (baseline-1 month)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*linear regressions adjusting for age, baseline pain, chronic illness and hospital LOS
Rabbitts, Mangione-Smith, Palermo, 2014
Future directions

• Neural mechanisms of postoperative pain
  – Sympathetic nervous system function
  – Descending neural inhibitory control
• Medical and behavioral interventions to improve pain and health outcomes in children after surgery
  – Sleep
  – Anxiety
  – Parental skills
  – Pain management
Extramural Funding

Tips for career development applications

- Area of expertise
- Research experience
- Record of funding
- Preliminary data
- Interdisciplinary mentorship team
- Institutional resources
- Institutional commitment