A cost benefit analysis of the use of routine serology in reducing the burden of re-immunisation post chemotherapy

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Why re-immunise after chemotherapy?

- Disease and therapy may lead to a loss of previously acquired immunity to vaccine preventable infections\textsuperscript{1}
- The severity and pattern of loss of immunity varies with intensity of therapy but is not consistently predictable\textsuperscript{2}

Revaccination schedules

Either:

• Complete – all immunisations on schedule are given regardless of current immune status
  • Safety of vaccine administration to people who already have immunity has been proven\(^3\),\(^4\)

• Targeted – perform serological testing for vaccine preventable diseases and revaccinations are given only to those required.
  • Multivalent vaccine preparations may reduce the number of vaccinations avoided

CHOC (Christchurch) Re-Vaccination Policy - Complete

Before 2014:

- End of Treatment
- ~6 months
- Begin re-vaccination

Re-vaccination (~6 months)
0-10y: 12 injections
10-18y: 17 injections
Revaccination schedules

Either:

• Complete – all immunisations on schedule are given regardless of current immune status
  • Safety of vaccine administration to people who already have immunity has been proven\(^3,4\)

• Targeted – perform serological testing for vaccine preventable diseases and revaccinations are given only to those required.
  • Multivalent vaccine preparations may reduce the number of vaccinations avoided

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3. Rey Lancet 2015
4. Rodriquez JGIM 1995
Starship (Auckland) Re-Vaccination Policy - Targeted

End of Treatment

Chemotherapy

~4-6 months

Serology

Begin re-vaccination with adjusted schedule

Re-vaccination (~6 months)
• Vaccines avoided if serology positive
  0-10y: Up to 12 injections
  10-18y: Up to 17 injections

Adopted as national re-immunisation policy in 2014:
Project timeline

Mar 2013  Decision to convene a national immunisation working group to harmonise the post-chemotherapy immunisation

Apr 2013  National immunisation schedule updated and decision to implement routine serology nationwide and collected results prospectively

Sep 2013  Research project proposal completed

Jun 2014  Ethics completed and data collection commenced

Jul 2016  Data collection completed

Jan 2017  Data analysis
Study Aims

1. To determine if routine serological testing at 4-6 months post chemotherapy treatment reduces the number of vaccinations required by children

2. If serological testing reduces the number of vaccinations required, determine if this results in an overall cost saving taking into account the upfront costs of serological testing.

3. Audit the compliance with the national immunisation policy

4. Document the relationship between serology at diagnosis and 4-6 months post treatment.
Inclusions and Exclusions

**Inclusion Criteria:**
- Received chemotherapy for a diagnosis of cancer
- Alive and in remission at 6 months from end of therapy
- ≤16 years at diagnosis
- <19 years at time of revaccination

**Exclusion Criteria:**
- Therapy included allogeneic stem cell transplant
- Therapy included anti B or T cell immunotherapy
### Routine Serology Post-Chemotherapy

<table>
<thead>
<tr>
<th>Disease</th>
<th>Test</th>
<th>Result</th>
<th>Reference Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Varicella Zoster</td>
<td>IgG</td>
<td>+/-</td>
<td>(neg &lt; 10 IU/ml)</td>
</tr>
<tr>
<td>Rubella</td>
<td>IgG</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mumps</td>
<td>IgG EIA</td>
<td>+/-</td>
<td></td>
</tr>
<tr>
<td>Measles</td>
<td>IgG EIA</td>
<td>+/-</td>
<td></td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>anti-HBs</td>
<td></td>
<td>(neg &lt; 10 IU/ml)</td>
</tr>
<tr>
<td>Diphtheria</td>
<td>Abs</td>
<td></td>
<td>(neg &lt; 0.163 IU/mL)</td>
</tr>
<tr>
<td>Tetanus</td>
<td>Abs</td>
<td></td>
<td>(neg &lt; 0.2 IU/mL)</td>
</tr>
</tbody>
</table>
Study Methods

1. Patients assessed as ready for pre-immunisation serology

2. Serology was obtained 4-6 months post-treatment

3. Results collected and individualised re-immunisation schedule sent to GP.
### Recommended Immunisation Schedule

*GP must sign the sheet as all vaccines must be prescribed by a medical practitioner.*

**Write “omitted” if not indicated to receive vaccine.**

**Table:**

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Notes</th>
<th>Date given/omitted</th>
<th>Vaccinator</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st dose</td>
<td>DTaP-IPV-HepB/Hib (Infanrix-Hib)</td>
<td>Give as a booster even if immune to all antigens (new funded to age 10)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>PCV-13 (Prevenar 13)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 weeks later</td>
<td>DTaP-IPV-HepB/Hib (Infanrix-Hib)</td>
<td>Use even if Hep B immune</td>
<td></td>
</tr>
<tr>
<td>Date due</td>
<td>PCV-13 (Prevenar 13)</td>
<td>If less than 3 years</td>
<td></td>
</tr>
<tr>
<td>6 weeks later</td>
<td>PVV 28 (Prevenar)</td>
<td>If &gt; 9 years, reimmunise with PVV28 once more in 5 years' time only if risk persists</td>
<td></td>
</tr>
<tr>
<td>Date due</td>
<td>DTaP-IPV-HepB/Hib (Infanrix-Hib)</td>
<td>Give if Hep B immunity previously not immune. Then check anti-HBAb 3 months later. If negative, give Hep B re-immunisation with 3 doses at monthly intervals.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 weeks later</td>
<td>MMR</td>
<td>Give only if immune to all three diseases, the ages within 5 months of each other or a partner of RVG</td>
<td></td>
</tr>
<tr>
<td>Date due</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 weeks later</td>
<td>MMR</td>
<td>Give only if immune to all three diseases, do not give within 5 months of VZIG or 3 months of MMR</td>
<td></td>
</tr>
<tr>
<td>Date due</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 weeks later</td>
<td>MMR(Varicella)</td>
<td>2nd dose</td>
<td></td>
</tr>
<tr>
<td>Date due</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At age 4 years or over (Booster)</td>
<td>DTaP-IPV (Infanrix-Hib)</td>
<td>Give when at least 6 yr old and Anti-HIB &gt;22 months since last Infanrix dose</td>
<td></td>
</tr>
</tbody>
</table>
Data collection

- Patient demographics, cancer type and treatment
- Serology results used to determine number of vaccine avoided.
  - Compliance/errors in serology or schedule assessed separately.
- Re-immunisation records were crossed checked against the National Immunisation Register and/or GP records to assess compliance.
- Estimated cost of serology tests obtained from Canterbury Health Laboratories (2014) - $183 NZD per patient
- Costs of vaccines vials estimated from Ministry of Health and PHARMAC (some limited by commercial sensitivity)
Results – CHOC (Christchurch) patients only

85 patients ending treatment identified over a two year period (Jul 2014 – Jun 2016)

23 excluded:
  • 8 patients – Serology was performed too late (after 30/6/2016)
  • 3 patients didn’t have chemotherapy (radiation therapy and/or surgery only)
  • 3 patients were too young at diagnosis to have completed childhood vaccinations and therefore no need for post-treatment serology
  • 3 patients either declined immunisations or follow-up in general
  • 3 patients received rituximab
  • 2 patients moved elsewhere for completion treatment - Australia
  • 1 patient was too old at the end of treatment to fit criteria

62 included:  48% female, 52% male

Average age at serology: 9.3
Did serological testing prior to revaccination reduce the number of vaccinations required?

69% avoided at least one vaccination*

2.08 vaccines avoided per patient on average

Average vaccines per patient reduced from 14 to 12

Average needle-sticks per patient reduced from 14 to 13

* Vaccination refers to multivalent preparation where applicable
Vaccine Breakdown

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>% of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Varicella (Var)</td>
<td>60%</td>
</tr>
<tr>
<td>MMR</td>
<td>20%</td>
</tr>
<tr>
<td>Infanrix-Hexa (&lt;10y)</td>
<td>0%</td>
</tr>
<tr>
<td>Boostrix + Polio (10-18y)</td>
<td>0%</td>
</tr>
<tr>
<td>Hep B (10-18y)</td>
<td>0%</td>
</tr>
</tbody>
</table>

**MMR:** measles, mumps, rubella

**Infanrix-hexa:** tetanus, diphtheria, hepatitis B, pertussis, polio, and *Haemophilus influenzae* (type b)

**Boostrix:** tetanus, diphtheria, pertussis

*(Bold = immunity required to avoid vaccine)*
Cost-Benefit Analysis

Does the reduction in vaccinations due to serological testing result in an overall cost saving taking into account the upfront costs of the tests?

Estimated* cost of serology (per 100 patients) = $18,318 NZD

Estimated† cost saving from fewer vaccines (per 100 patients) = $7,884 NZD

*Estimates based on 2014 CHL serological testing costs
†Estimates based on Ministry of Health and PHARMAC vaccination costs
Compliance with Re-Immunisation Policy

Correct serology performed: 86%
Immunisation schedule completed correctly: 78%

1. Median time from EOT to serology (aim 120-180): 172 days
   Range (49-352)

2. Median time serology to 1st injection: 69 days
   Range (16-251)

Chemotherapy → 4-6 months → End of Treatment → Serology → Vaccination begins
Compliance with Re-Immunisation Policy

Correct serology performed: 86%
Immunisation schedule completed correctly: 78%
Median time from EOT to serology *(aim 120-180)*: 172 days
Range (49-352)
Median time serology to 1st injection: 69 days
Range (16-251)
All vaccines received as per schedule: 68%
National Immunisation Register

GP records of immunisation were compared with NIR data

Percentage of vaccines given found on NIR:

- DOB: before 2005*: 4.6%
- DOB: 2005* onwards: 74.1%

*NIR was established in 2005
Aim 4: Relationship between serology at diagnosis and 4-6 months post treatment.
## Comparison with Auckland Results

<table>
<thead>
<tr>
<th></th>
<th>Christchurch</th>
<th>Auckland*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study population</td>
<td>62</td>
<td>68</td>
</tr>
<tr>
<td>Patients avoiding at least one vaccine</td>
<td>69%</td>
<td>82%</td>
</tr>
<tr>
<td>No. of vaccines avoided</td>
<td>2.08</td>
<td>2.78</td>
</tr>
<tr>
<td>Average vaccines reduced</td>
<td>14 $\rightarrow$ 12</td>
<td>13 $\rightarrow$ 11</td>
</tr>
<tr>
<td>Cost benefit analysis</td>
<td>Costs $&gt;$ Savings</td>
<td>Pending</td>
</tr>
<tr>
<td>Time from EOT to serology</td>
<td>172 days</td>
<td>141 days</td>
</tr>
<tr>
<td>Time from serology to first vaccine</td>
<td>69 days</td>
<td>74 days</td>
</tr>
</tbody>
</table>

*Analysis conducted by Joyce Chan, ADHB*
# National Data – Preliminary

<table>
<thead>
<tr>
<th></th>
<th>Christchurch</th>
<th>Auckland*</th>
<th>National†</th>
</tr>
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<tbody>
<tr>
<td>Study population</td>
<td>62</td>
<td>68</td>
<td>130</td>
</tr>
<tr>
<td>Patients avoiding at least one vaccine</td>
<td>69%</td>
<td>82%</td>
<td>76%</td>
</tr>
<tr>
<td>No. of vaccines avoided</td>
<td>2.08</td>
<td>2.78</td>
<td>2.45</td>
</tr>
<tr>
<td>Average vaccines reduced</td>
<td>14 → 12</td>
<td>13 → 11</td>
<td>13.5 → 11.5</td>
</tr>
<tr>
<td>Cost benefit analysis</td>
<td>Costs &gt; Savings</td>
<td>Pending</td>
<td>Pending</td>
</tr>
<tr>
<td>Time from EOT to serology</td>
<td>172 days</td>
<td>141 days</td>
<td>156 days</td>
</tr>
<tr>
<td>Time from serology to first vaccine</td>
<td>69 days</td>
<td>74 days</td>
<td>72 days</td>
</tr>
</tbody>
</table>

*Analysis conducted by Joyce Chan, ADHB
†Preliminary analysis – awaiting full dataset
Benefits vs Costs of Serology

Benefits:
• Slight reduction in average number of vaccines given (14 → 12)

Costs:
• Extra blood test (+1 needle)
• Serology lab costs outweigh vaccine savings
• Introduces time delay and error individualising protocol
What next?

• Publish with combined Christchurch and Auckland data
• Meeting to determine plan for immunisation schedule has happened.
  • Re-immunisation schedule will revert to **immunising with all vaccines, no serology**.
  • Revised schedule currently being drafted
  • Considering testing varicella only – probable benefit for this vaccine and will not cause delays as given later in schedule.
Acknowledgements

Project Team:

Siobhan Cross        Karen Tsui
Joyce Chan           Tony Walls
Scott MacFarlane     Elizabeth Wilson

With assistance from:

Jo Truscott – CNS surveillance and LEAP – CHOC
Hayley Morum – SCN surveillance and education – CCDHB

NCCN immunisation subgroup

• Scott MacFarlane (Starship Paediatric Oncologist)
• Elizabeth Wilson (Starship ID Specialist)
• Diane Bos (Pegasus GP Group Immunisation Coordinator)
• Siobhan Cross (CHOC Paediatric Haematologist)
• Rob Corbett (CHOC Paediatric Oncologist)
• Tony Walls (Christchurch ID Specialist)
• Melissa Wilson (NCCN Administrator)

Funding for analysis (University of Otago Summer Studentship) provided by Children’s Cancer Research Trust