Research as a General Paediatrician

"If I can do it anyone can"

Adrian Trenholme
MA MB BChir FRACP
Kidz First Children's Hospital Auckland
Auckland University Dept Paediatrics
RACP Congress
Auckland
7th May 2019

Overview

- Conflicts-many!/none relevant to this
- Background
- Research history (with Mentors/Local Heroes)
- Research with industry
- Reflections
- Summary

I know my place

Background

- English- North Yorkshire Farm-Wensleydale/Ure
- Ripon Grammar School 64-71
- Cambridge University 71-74
- Kings College Hospital London 74-79
- NZ Auckland Princess Mary Hospital 79-85
- Middlemore Hospital 85-current –(probation over?2022)

- 8000 deliveries
- 60% lowest socioeconomic Quintile 5
- Majority Maori/Pacific
- 1985 to current all consuming-from 2 to 40 +Paediatricians

Dr Nigel Stewart 85-93

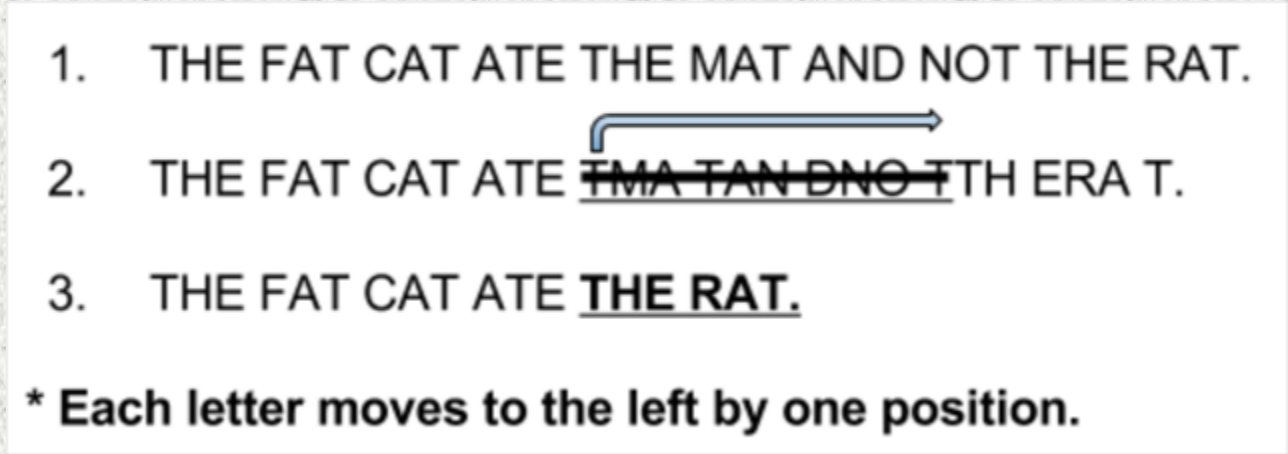
BBBB but no Equity

- Respiratory
  - Bronchiolitis
  - Pneumonia
  - Bronchiectasis
  - Asthma
- Group A Strep
  - Rheumatic Fever/RHD
  - PSGN
  - Cellulitis
- Staph Aureus
  - Cellulitis
  - Bone/Joint infections
- SUDI
- And the rest

Innes, I blame you

Professor Innes Asher

Dystrophin Analogy-are you the researcher “type”



- ANY FAT DOCTOR HAS EVERY ATTRIBUTE NEEDED FOR RESEARCH
- ANY FAT DOCTOR ~~HAS EVERY ATTRIBUTE NEEDED~~ F OR RESEARCH
- ANY FAT DOCTOR FOR RESEARCH

Research areas

- Rheumatic Fever team/research support
- Respiratory
  - LRI
  - Bronchiectasis non CF
  - Surveillance Influenza/RSV SHIVERS
  - RSV Vaccine/Immunoprophylaxis
- Emergency –PREDICT
- SUDI-Pepi Pod
- Education
- Commercial/research fund
- Palliative care

Principles

- Equity
- Belong to the problem belong to the solution
- If it works for Maori it works
- Community involvement-is it the right thing?
- Don’t just count-do something
- Helicopters are noisy then fly away

PART 2

2a. Research publications and dissemination

Peer-reviewed journal articles

1. Interactive effects of age and respiratory virus on severe lower respiratory infection. Prasad N, **Trenholme AA**, Huang QS, Thompson MG, Pierse N, Widdowson MA, Wood T, Seeds R, Taylor S, Grant CC, Newbern EC; SHIVERS team. Epidemiol Infect. 2018 Jul 26:1-9. doi: 10.1017/S0950268818002017
2. Risk factors and attack rates of seasonal influenza infection: results of the SHIVERS seroepidemiologic cohort study. Huang QS, Bandaranayake D, Wood T, Newbern EC, Seeds R, Ralston J, Waite B, Bissielo A, Prasad N, Todd A, Jelley L, Gunn W, McNicholas A, Metz T, Lawrence S, Collis E, Retter A, Wong SS, Webby R, Bocacao J, Haubrock J, Mackereth G, Turner N, McArdle B, Cameron J, Reynolds G, Baker MG, Grant CC, McArthur C, Roberts S, **Trenholme A**, Wong C, Taylor S, Thomas P, Duque J, Gross D, Thompson MG, Widdowson MA; SHIVERS investigation team. J Infect Dis. 2018 Jul 17. doi: 10.1093/infdis/jiy443.
3. McIntosh C, **Trenholme A.** Evaluation of a sudden unexpected death in infancy intervention programme aimed at improving parental awareness of risk factors and protective infant care practices 2017 Nov Journal of Paediatrics and Child Health DOI: 10.1111/jpc.13772 Internal Article ID: 14677692
4. **Trenholme AA,** Best EJ, Vogel AM, Stewart JM, Miller CJ, Lennon DR. Respiratory virus detection during hospitalisation for lower respiratory tract infection in children under 2 years in South Auckland, New Zealand. J Paediatr Child Health. 2017 Jun;53(6):551-555. doi: 10.1111/jpc.13529. Epub 2017 Apr 21.PMID:28430397
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Article:

Peer reviewed books, book chapters, books edited

Professor Diana Lennon
Henare Mason

ARF/RHD Group A Strep
Meningococcal
LRI Infants
RSV vaccine

RHD Dr Rachel Webb Dr Nigel Wilson

LRI in infants
What a waste!

High rates of severe lower respiratory tract infection among indigenous Maaori, Pacific and disadvantaged young children in South Auckland, New Zealand.

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Reprints not available

Commercial Support-nil

Key words Lower respiratory tract infection, bronchiolitis, pneumonia, infant, indigenous, Māori, Pacific.

Abstract

Background: Lower respiratory tract infections (LRI) are a leading cause of hospitalisation for young children worldwide. The objective of this study was to describe the epidemiology of severe LRI among children under two years of age in South Auckland, New Zealand.

Methods: A population based retrospective analysis was undertaken of hospital admissions with LRI (defined as being at least 3 hours) among South Auckland residents younger than two years from 2002 to 2006 (n=8703).

Results: The rate of LRI hospital admissions for children under one year of age was 154/1000 for all children, 280/1000 for Pacific, 215/1000 for Maaori and 43/1000 for other ethnicities, and also varied by deprivation level of area of residence from 73/1000 in decile 1-8 areas, 144/1000 in decile 9 areas and 244/1000 in decile 10 (most deprived) areas. Similar gradients related to ethnicity and deprivation were found for LRI hospital admissions in children 12-23 months of age and in children 0-23 months with at least one admission, but the rates were lower. Intensive care was given in 4.1 % of inpatient admissions and 9 children died during LRI admission. 9.1% of LRI admissions had a history of prematurity and 2.6% a history of an underlying medical condition.

Conclusion: The risk of hospital admission for LRI among Pacific, indigenous Māori and socioeconomically disadvantaged young children in South Auckland New Zealand is high compared to all New Zealand children, and international data. The reasons for these differences need exploration to reduce this potentially preventable burden of disease.

LRI in infants 2009-11
Over ambitious

Journal of Paediatrics and Child Health

Original Article

Respiratory virus detection during hospitalisation for lower respiratory tract infection in children under 2 years in South Auckland, New Zealand

Adrian A Trenholme, Emma J Best, Alison M Vogel, Joanna M Stewart, Charissa J Miller, Diana R Lennon

First published: 21 April 2017 | https://doi.org/10.1111/jpc.13529 | Cited by: 4

SHIVERS

Dr Sue Huang ESR

Implementing hospital-based surveillance for severe acute respiratory infections caused by influenza and other respiratory pathogens in New Zealand

Q Sue Huang,[a] Michael Baker,[b] Colin McArthur,[c] Sally Roberts,[c] Deborah Williamson,[a,d] Cameron Grant,[d] Adrian Trenholme,[e] Conroy Wong,[e] Susan Taylor,[e] Lyndsay LeComte,[e] Graham Mackereth,[e] Don Bandaranayake,[e] Tim Wood,[e] Ange Bissielo,[e] Ruth Seeds,[e] Nikki Turner,[d] Nevil Pierse,[b] Paul Thomas,[f] Richard Webby,[f] Diane Gross,[g] Jazmin Duque,[g] Mark Thompson[g] and Marc-Alain Widdowson[g]

Correspondence to Q Sue Huang (e-mail:Sue.Huang@esr.cri.nz).

Background: Recent experience with pandemic influenza A(H1N1)pdm09 highlighted the importance of global surveillance for severe respiratory disease to support pandemic preparedness and seasonal influenza control. Improved surveillance in the southern hemisphere is needed to provide critical data on influenza epidemiology, disease burden, circulating strains and effectiveness of influenza prevention and control measures. Hospital-based surveillance for severe acute respiratory infection (SARI) cases was established in New Zealand on 30 April 2012. The aims were to measure incidence, prevalence, risk factors, clinical spectrum and outcomes for SARI and associated influenza and other respiratory pathogen cases as well as to understand influenza contribution to patients not meeting SARI case definition.

Methods/Design: All inpatients with suspected respiratory infections who were admitted overnight to the study hospitals were screened daily. If a patient met the World Health Organization's SARI case definition, a respiratory specimen was tested for influenza and other respiratory pathogens. A case report form captured demographics, history of presenting illness, co-morbidities, disease course and outcome and risk factors. These data were supplemented from electronic clinical records and other linked data sources.

Discussion: Hospital-based SARI surveillance has been implemented and is fully functioning in New Zealand. Active, prospective, continuous, hospital-based SARI surveillance is useful in supporting pandemic preparedness for emerging influenza A(H7N9) virus infections and seasonal influenza prevention and control.

The 2009 influenza A(H1N1)pdm09 pandemic highlighted the need for disease surveillance to monitor severe respiratory disease to support pandemic preparedness as well as seasonal influenza prevention and control.[1,2] Information generated from this type of surveillance enhances our understanding of how epidemiology and etiology differ between countries and regions of the world. The accumulated data collected in a standard and consistent way will allow rapid assessment for each influenza season and future pandemics within and among countries.[2]

The 2009 pandemic and seasonal influenza epidemics demonstrated the importance of having an established real-time respiratory disease surveillance system in the southern hemisphere to inform the northern hemisphere countries about newly emerging pandemic or seasonal influenza.[3,4] A surveillance system can provide critical data on the epidemiology, burden, impact, circulating influenza, other respiratory pathogens and effectiveness of influenza prevention and control measures at a time when similar data in the northern hemisphere are not available.

New Zealand is an excellent location for population-based research with its predominantly public funded health-care system. All New Zealanders are assigned a unique identifier allowing tracking of health-care utilization over time and linkage to multiple databases. Primary-care providers have highly computerized information systems

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[e] Counties Manakau District Health Board, Auckland, New Zealand.
[f] WHO Collaborating Centre, St Jude Children's Research Hospital, Memphis, United States of America.
[g] Centers for Disease Control and Prevention (CDC), Atlanta, United States of America.
Submitted: 27 January 2014; Published: 20 May 2014
doi: 10.5365/wpsar.2014.5.1.004

SHIVERS RSV/Influenza Burden

- Auckland /CMH
- Under 5 years-submitted
- Over 50 years-prize RSV conference Asheville
- Severity of RSV-published
- Under 1 year-Emergency Care AT project
- Namrata Prasad PHD RSV
- RSV symposium IMAC Sep 19
  - ? National screening

Cass-more blame!!

A/Prof Cass Byrnes
CF
Non CF Bronchiectasis

CSLD/Non CF Bronchiectasis

- Respiratory health outcomes 1 year after admission with severe lower respiratory tract infection.
- Trenholme AA, Byrnes CA, McBride C, Lennon DR, Chan-Mow F, Vogel AM, Stewart JM, Percival T.
- Pediatr Pulmonol. 2013 Aug;48(8):772-9. doi: 10.1002/ppul.22661. Epub 2012 Sep 19.

HRC The Healthy Lungs Study 2010-2015

- **Randomized trial of community intervention to prevent ongoing respiratory morbidity in children following hospitalisation with severe bronchiolitis or pneumonia.**
- *Associate Professor Catherine Byrnes MD, Paediatric Department, The University of Auckland, Auckland New Zealand; Starship Children's Health, Auckland, New Zealand.
- *Adrian Trenholme MD, Paediatric Department, The University of Auckland, Auckland, New Zealand; KidzFirst Hospital, Middlemore, Counties Manukau District Health Board, Auckland, New Zealand.

PREDICT NETWORK-CMH

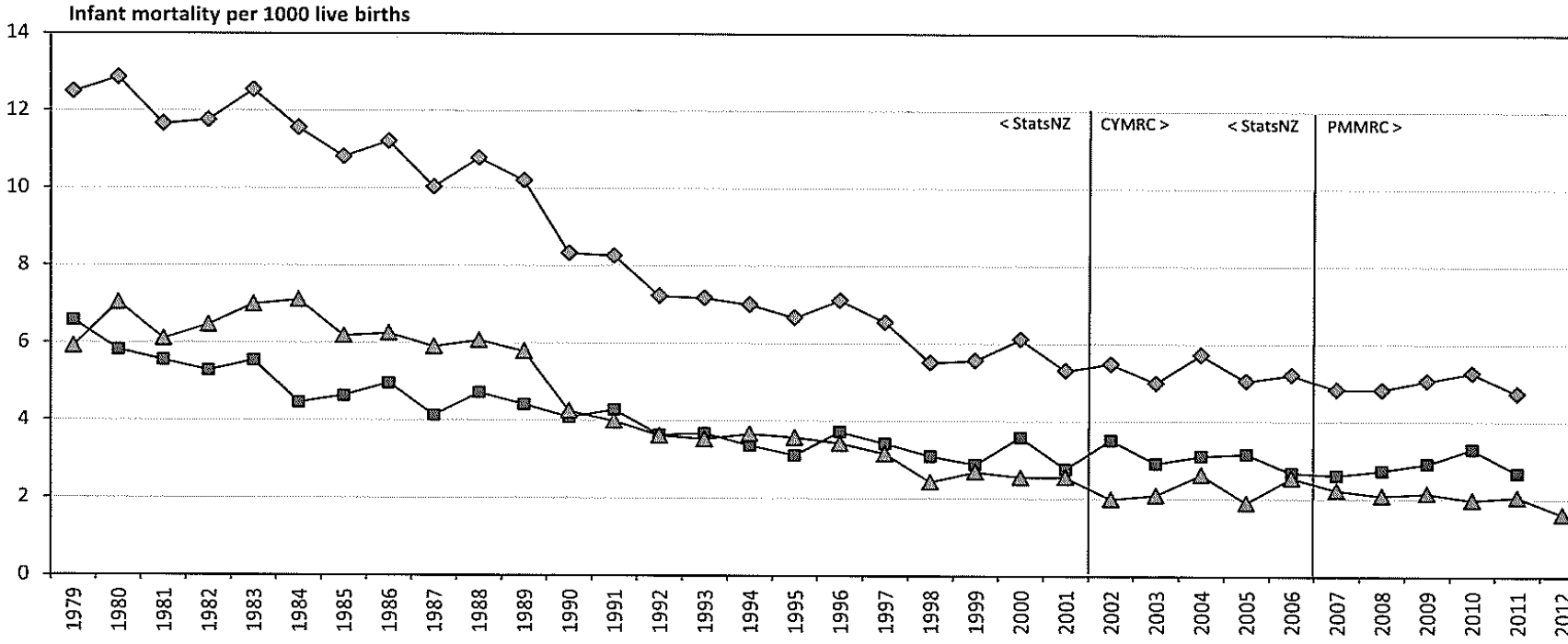
- PARIS*
- CRIB*
- Concept
- WASP
- Asthma

- *top recruiting site

Dr Jocelyn Neutze
Shirley Lawrence RN

SUDI

Figure 1.5 Neonatal, post-neonatal and infant mortality (rates per 1000 live births) in infants 0 days to less than 1 year of age, New Zealand 1979–2012

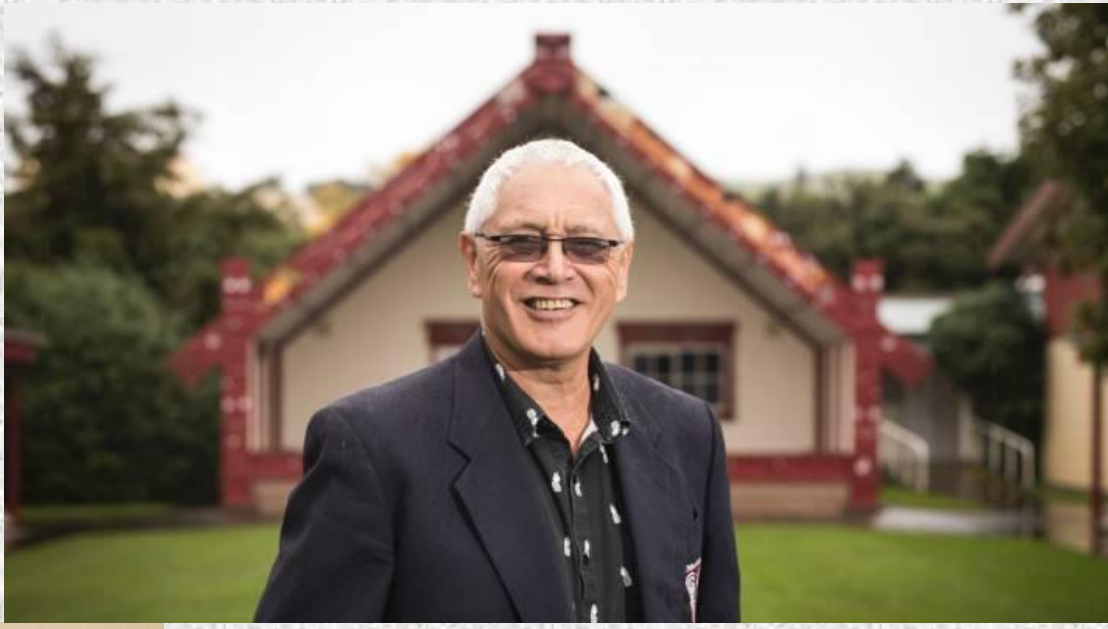


	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	201
Neonatal rate	6.6	5.8	5.6	5.3	5.5	4.5	4.6	5.0	4.1	4.7	4.4	4.1	4.3	3.6	3.7	3.3	3.1	3.7	3.4	3.1	2.9	3.6	2.8	3.5	2.9	3.1	3.2	2.7	2.6	2.7	2.9	3.3	2.7	
Post-Neonatal rate	5.9	7.0	6.1	6.5	7.0	7.1	6.2	6.2	5.9	6.1	5.8	4.2	4.0	3.6	3.5	3.6	3.6	3.4	3.1	2.4	2.7	2.5	2.5	2.0	2.1	2.6	1.9	2.5	2.2	2.1	2.1	2.0	2.1	1.6
Infant rate	12.5	12.9	11.7	11.8	12.5	11.6	10.8	11.2	10.0	10.8	10.2	8.3	8.2	7.2	7.2	7.0	6.7	7.1	6.5	5.5	5.6	6.1	5.3	5.5	5.0	5.7	5.0	5.2	4.8	4.8	5.1	5.3	4.7	

Year

Source: *Numerator* Neonatal deaths (0-27 days): 1979-2006: Statistics New Zealand. 2007-2011: Mortality Review Database (PMMRC data); Note: 2012 data for neonatal deaths not yet available.
Post-neonatal deaths (28 days to less than one year): 1979-2001: Statistics New Zealand. 2002-2012: Mortality Review Database (CYMRC data).
Infant deaths (0 days to less than one year): sum of neonatal and post-neonatal deaths, as described above.
Denominator Statistics New Zealand live births 1979-2012.

SUDI Wahakura Safe Sleep
By Maori for everyone



Professor Ed Mitchell
Professor David Tipene Leach

Safe Sleep devices
SUDI risk calculator

Journal of Paediatrics and Child Health

Original Article

Evaluation of a sudden unexpected death in infancy intervention programme aimed at improving parental awareness of risk factors and protective infant care practices

Christine McIntosh
Adrian Trenholme
Joanna Stewart
Alison Vogel

First published: 10 November 2017

Clinical Education

- An Introductory workshop in Paediatric Examination Skills Med Educ 2007 41(11) 1097-8

A/Prof Ralph Pinnock

Industry Research

- Equity issue
- Risk/benefit for population
- Community input
- What happens to any surplus

RANDOMIZED CONTROLLED TRIAL

#454

A phase 2, randomized, double-blind safety and pharmacokinetic assessment of respiratory syncytial virus (RSV) prophylaxis with motavizumab and palivizumab administered in the same season.

Pilar Fernández, Adrian Trenholme, Katia Abarca, M Pamela Griffin, Micki Hultquist, Brian Harris, Genevieve A Losonsky

BACKGROUND: Respiratory syncytial virus (RSV) is an important pathogen causing annual epidemics of bronchiolitis and pneumonia among infants worldwide. High-risk infants currently receive RSV prophylaxis with palivizumab, a humanized RSV monoclonal antibody (MAb). In preclinical in vitro and in vivo (cotton-rat model) studies, motavizumab, a new RSV MAb, was shown to have greater anti-RSV activity than palivizumab. Motavizumab is currently under review for licensing approval. Since both MAbs may be available concurrently, this study evaluated their safety and tolerability when administered sequentially during the same RSV season...

June 3, 2010: BMC Pediatrics

RSV in Pregnancy Governance Group

Middlemore Clinical Trials

Future of healthcare









RSV vaccine in pregnancy 2015-2019 CMH 155 patients

Goals and design

THE Prepare TRIAL

Primary objective

Determine the efficacy of maternal immunization with the RSV F vaccine against medically significant symptomatic RSV lower respiratory tract infection (LRTI) through 90, 120, 150 and 180 days of life in infants.

Design	Randomized, Observer-Blind, Placebo-Controlled	
	Number of Participants	• 4,636 third trimester pregnant women randomized 2:1 (vaccine:placebo)
	Length of Study Participation	• Maternal Participants: up to 9 months • Infant Participants: 1 year after delivery
	Dosing	• 1 intramuscular (IM) Injection of RSV F Vaccine or Placebo at 28-36 weeks Estimated Gestational Age (EGA)
	Safety Assessment	• Through 6 months post-partum in mothers • Through 1 year in infants

	Efficacy Assessment	• Active/passive surveillance in mothers and infants
		  • Confirmation of RSV infection by RT-PCR
		  • Medically significant tachypnea or pulse oximetry
		  • Confirmation of LRTI
		  • Data collected at clinical sites or from both site and hospitalization records

NOVAVAX

9

$

- Kidz First research fund
- With MMCTU Charitable trust
- Spending has to fit their strategy/”rules”
- Paediatric Fellows-medical, nursing, physiotherapy and midwifery

Local Heroes

- **Reducing the pain of intramuscular benzathine penicillin injections in the rheumatic fever population of Counties Manukau District Health Board**
- **Article** *in* Journal of Paediatrics and Child Health 50(2) · October 2013

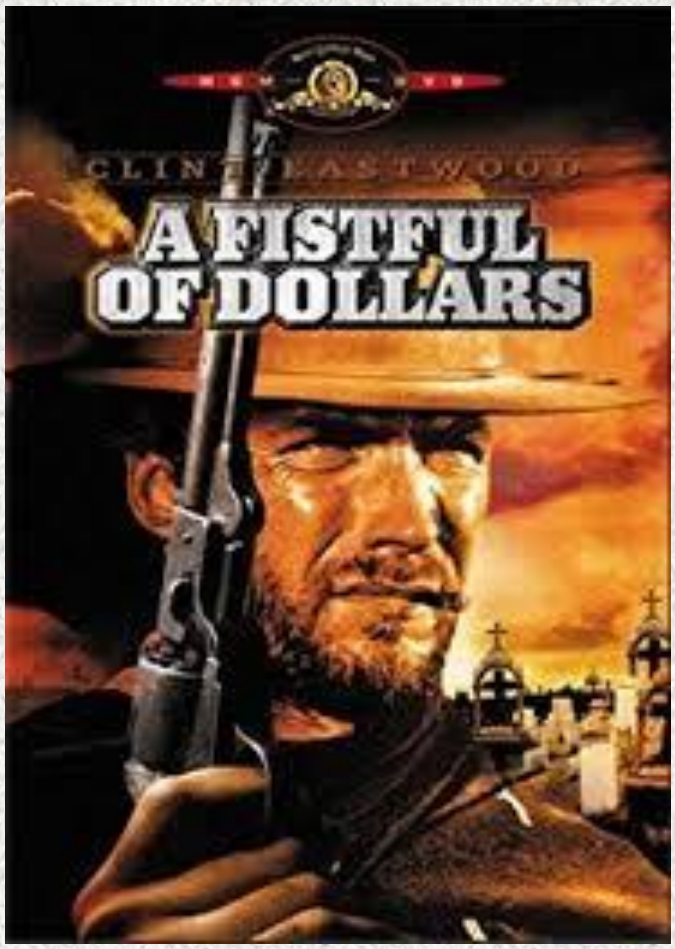
Kathryn Russell
Dr Ross Nicholson

Dr Alex Wallace Waikato Medical Students Year 6 research projects

BUT BEWARE !!

Time?

Money?



Main Message-Family

Message-life/work balance
On Any Sunday

SO

- Be mindful of your population
- Follow your passion
- Collaborate and learn
- Local team with mixed skills
- Use any research office/support you have
- Start small
- Pick a mentor
- Have fun

RSV Research Objective

APRILIA RSV MILLE