

SUPPLEMENTARY APPENDIX

Two oxygen protocols in patients presenting with a suspected acute coronary syndrome

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1. STUDY OXYGEN PROTOCOLS:

High oxygen protocol:

- In patients with probable or confirmed acute coronary syndrome give oxygen for ischaemic chest pain, ischaemic ECG changes or dyspnea related to myocardial ischaemia irrespective of the measured oxygen saturation level.
- Administer oxygen by face mask at ~8l/minute. If a face mask is not tolerated give oxygen by nasal prongs at ~4 l/minute. Increase oxygen flow rate if necessary to achieve saturation $\geq 95\%$. Continue oxygen until the patient is admitted to hospital or transferred to cardiology, or when a doctor decides it is no longer necessary.
- Caution or avoid high flow oxygen in patients at risk of hypercapnia, including those with possible obesity hypoventilation syndrome or chronic obstructive pulmonary disease.

Low oxygen protocol:

- In patients with a suspected or confirmed acute coronary syndrome do not give oxygen for ischaemic chest pain, ischaemic ECG changes or dyspnea related to myocardial ischaemia, unless the measured oxygen saturation is $< 90\%$.
- When the oxygen saturation cannot be measured only administer oxygen if there is a significant clinical concern of hypoxia.
- If oxygen is administered by face mask or nasal prongs adjust the flow rate to achieve a target oxygen saturation of 90 to 94%.
- Discontinue oxygen when no longer needed to maintain saturation $> 90\%$.
- Caution or avoid high flow oxygen in patients with possible obesity hypoventilation syndrome or chronic obstructive pulmonary disease.
- Oxygen can be administered in the ambulance to patients who need ventilation or continuous positive airways pressure (CPAP).

In individual cases the oxygen protocol can be over ruled by clinician preference or clinical indication.

2. DATA MONITORING COMMITTEE

The Health Research Council of New Zealand Data Monitoring Committee (DMC) monitored trial conduct. The DMC meets in April and October each year. Aggregate data on oxygen protocol adherence, and in-hospital and 30 day mortality from the ANZACS-QI Registry were provided to the DMC once during the study, but no interim analysis was performed. The DMC were also provided with copies of relevant research published during the trial. The DMC did not review data from the Ambulance ACS pathway.

OXYGEN Data Monitoring committee (DMC) -The Health Research Council of New Zealand

HRC DMC members: Associate Professor Katrina Sharples (Chair) - Department of Preventive and Social Medicine, University of Otago, Dunedin; Dr Mark Jeffery - Department of Oncology, Christchurch Hospital, Christchurch; Professor Ngaire Kerse - School of Population Health, University of Auckland; Professor Thomas Lumley - Department of Statistics, University of Auckland; Associate Professor Andrew Moore - Department of Philosophy, University of Otago, Dunedin; Associate Professor Conroy Wong - Department of Respiratory Medicine, Middlemore Hospital, Auckland.

3. PARTICIPATING CENTRES AND INVESTIGATORS

In addition to the study authors the following investigators and study coordinators contributed to the study.

Investigators and Co-coordinators at participating hospitals:

Northern Region

Auckland City Hospital: Ralph Stewart, Leah Howell, Catherine Patten, Peter Jones, Tracey Barley, Rebekka Costello, Karen Schimanski, Nancy Mitchell

North Shore and Waitakere Hospitals: Tony Scott, Nichola Bradford, Kim Yates, Laura Chapman

Middlemore Hospital: Andrew Kerr, Lynette Pearce, Renee Railton, Nicole Signal, Vanessa Thornton, Adrienne Adams, Andrew Brainard

Whangarei Hospital: Samraj Nandra, Sue Vallancey, Ryan Howard

Midland Region

Waikato Hospital: Gerry Devlin, Liz Low, Roselyn Pillay, John Bonning

Tauranga Hospital: Jonathan Tisch, Jennifer Goodson, Alastair Maclean

Whakatane Hospital: Terri McBride, Martin Bentley-Smith, Adele Ferguson

Rotorua Hospital: Peace Tamuno, Paula Broughton, Vijay Thumma

Taupo Hospital: Paul Malpass

Gisborne Hospital: Alyssa Thompson, Joanne Patterson, Andrew Botting, Tom Palfi

Taranaki Base Hospital: Ian Ternouth, Jonele Woodhead, Carolyn Jackson, Donald McKee, Mark Sagarin

Tokoroa / Te Kuiti Hospital: Shameem Safih

Thames Hospital: Vijaya Pera

Central Region

Wellington Hospital: Anil Ranchord, Bev Scott, Brad Peckler, Mark Hussey, Paul Quigley

Nelson Hospital: Liam Hughes, Sarah Flintoft, Liz Dalby, Lorna Johnston, Andrew Munro

Hutt Valley Hospital: Tim O'Meeghan, Ria Kleintjes, Jo-Anne Kovacs, Criselda Sayoc, Tracy Langhorn, Ben Ross, Tanya Wilton

Hawkes Bay Hospital: Richard Luke, Diana Schmid, Julia Mackenzie, Craig Ellis

Palmerston North Hospital: Dave Tang, Lia Sinclair, Thomas Cheri

Wairarapa Hospital: Laura Davidson, Mary Quayle

Wanganui Hospital: Tom Thompson

Southern Region

Dunedin Hospital: John Edmond, Shona Willers, Bruce Lambie, Deb Scott, Caroline Collins, John Chambers

Christchurch Hospital: David Smyth, Michael Hume, Martin Than

Ashburton Hospital: John Lyons

Timaru Hospital: Matthew Hills, Robyn Carey, Bernhard Kuepper, Maria Hammond, Catherine Baker, Kathy Patrick

Wellington Free Ambulance: Andrew Swain

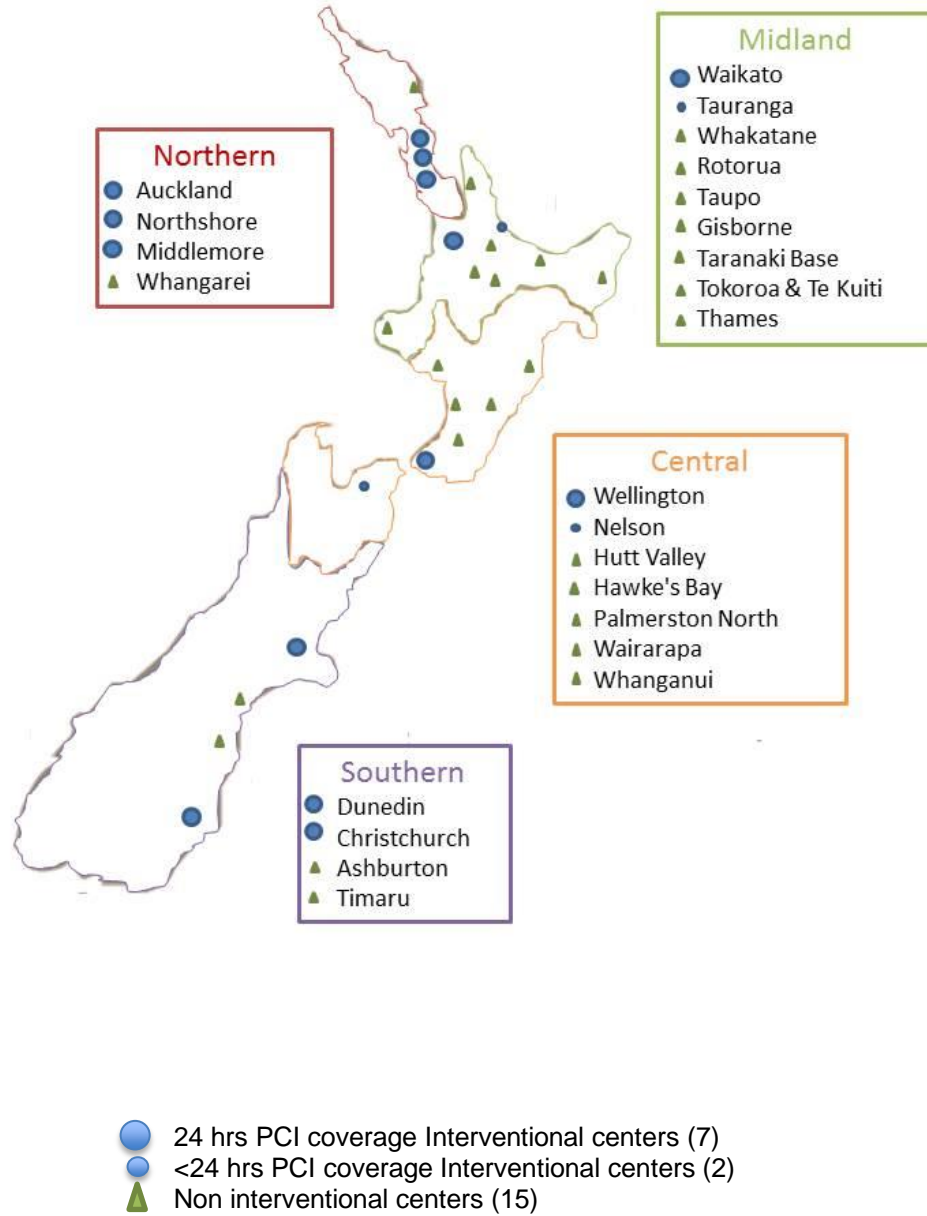
St John Ambulance: Bridget Dicker, Tony Smith, Verity Todd

National Oxygen Study Mangers:

Darryl McGuire, Diana Gatland, Cardiovascular Research Unit, Auckland City Hospital

4. SUPPLEMENTARY FIGURE 1: NEW ZEALAND MAP SHOWING 4 REGIONS AND HOSPITALS CONTRIBUTING TO ANZACS-QI REGISTRY

All transfers between hospitals for patients with ACS occur within these four regions



Supplementary Table 1: 30-Day all-cause mortality by oxygen protocol in selected groups

	High oxygen N (%)	Low oxygen N (%)	OR (95%CI) Unadjusted	P value	OR (95%CI) adjusted	P value
All patients+	20,304	20,568
Mortality	613 (3.0%)	642 (3.1%)	0.97 (0.86, 1.08)	0.55	0.96 (0.86, 1.08)	0.50
Men	11777	11943
Mortality	364 (3.1%)	408 (3.4%)	0.90 (0.78, 1.04)	0.16	0.89 (0.77, 1.04)	0.14
Women	8527	8625
Mortality	249 (2.9%)	234 (2.7%)	1.08 (0.90, 1.29)	0.41	1.08 (0.90, 1.31)	0.42
Geographic region						
Northern	6913	7109
Mortality	175 (2.5%)	203 (2.9%)	0.88 (0.72, 1.09)	0.24	0.88 (0.71, 1.09)	0.23
Midland	4815	4916
Mortality	179 (3.7%)	163 (3.3%)	1.13 (0.91, 1.40)	0.28	1.12 (0.90, 1.40)	0.31
Central	3658	3836
Mortality	113 (3.1%)	138 (3.6%)	0.85 (0.66, 1.10)	0.22	0.87 (0.67, 1.13)	0.30
Southern	4918	4707
Mortality	146 (3.0%)	138 (2.9%)	1.01 (0.80, 1.28)	0.91	0.95 (0.75, 1.22)	0.71
ANZACS-QI registry						
	9726	9840
Mortality	286 (2.9%)	299 (3.0%)	0.97 (0.82, 1.14)	0.69	0.95 (0.80, 1.13)	0.58
Ambulance pathway+						
	10,578	10,728
Mortality	327 (3.1%)	343 (3.2%)	0.97 (0.83, 1.13)	0.66	0.93 (0.79, 1.10)	0.38

Legend:+ patients on the ambulance ACS pathway who were not included in the ANZACS-QI registry

Abbreviations:

ACS - Acute Coronary Syndromes; STEMI- ST-elevation myocardial infarction; NSTEMI – Non ST-elevation myocardial infarction

Supplementary Table 2: Baseline characteristics of patients randomly selected for audit of oxygen use, compared to other ANZACS-QI patients admitted during the study periods.

	ANZACS-QI		Audit cohort	
	Number	%	Number	%
All suspected ACS	18754	100.0	812	100.0
Age <68 years	9819	52.4	420	51.7
Age ≥68 years	8935	47.6	392	48.3
Sex, male	12403	66.1	533	65.6
Ethnic group				
Māori	2295	12.2	94	11.6
Pacific	913	4.9	40	4.9
Asian	1463	7.8	60	7.4
NZ European or Other	14083	75.1	618	76.1
Clinical characteristics				
Prior myocardial infarction	2363	12.6	101	12.4
Prior heart failure	1137	6.1	46	5.7
Charleson co-morbidity score (non-cardiac)				
0	14810	79	643	79.2
1-2	3156	16.8	139	17.1
3+	788	4.2	30	3.7
Current Smoker	3237	17.3	149	18.4
Diabetes	4398	23.5	207	25.5
Socioeconomic Status in Quintiles+				
1	3061	16.3	112	13.8
2	3175	16.9	152	18.7
3	3652	19.5	142	17.5
4	4329	23.1	195	24.0
5	4347	23.2	198	24.4
Geographic region				
Northern	6041	32.2	251	30.9
Midland	5457	29.1	238	29.3
Central	3641	19.4	166	20.4
Southern	3615	19.3	157	19.3
Final Diagnosis				
STEMI	3744	20.0	159	19.6
NSTEMI	8991	47.9	381	46.9
Unstable angina	2612	13.9	118	14.5
Non-ACS condition	3407	18.2	154	19.0

Legend:

+ Socioeconomic status determined from NZDEP2013 census data in quintiles of the New Zealand general population.

Abbreviations:

ACS - Acute Coronary Syndromes; STEMI- ST-elevation myocardial infarction; NSTEMI – Non ST-elevation myocardial infarction