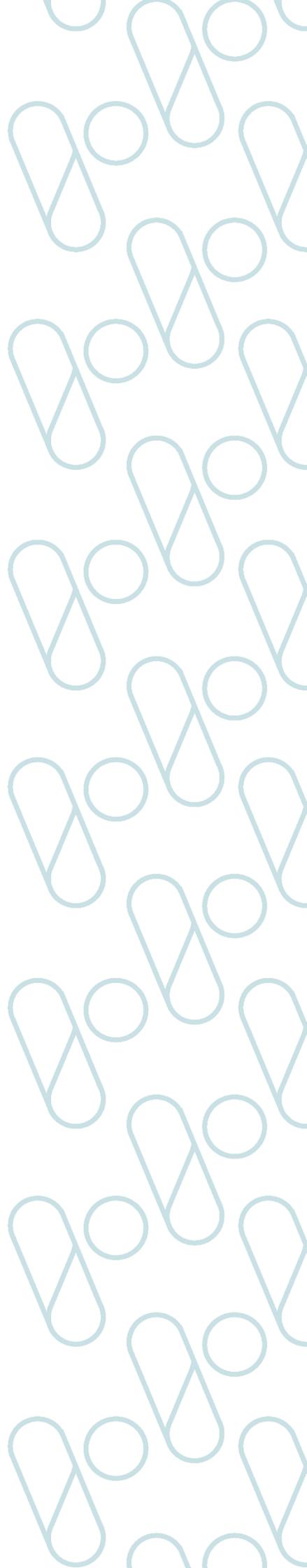


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# Adult extracorporeal membrane oxygenation (ECMO) in Victoria

Centralisation and retrieval model  
evidence review



## Abbreviations

ACHI Australian Classification of Health Interventions

ANZICS Australia New Zealand Intensive Care Society

ARV Adult Retrieval Victoria

BDM Births, Deaths and Marriages

CABG Coronary artery bypass graft

CHADx Classification of Hospital Acquired Diagnoses

DHB District health board

DRG Diagnosis-related group

ECMO Extracorporeal membrane oxygenation

ECPR Extracorporeal cardiopulmonary resuscitation

ELSO Extracorporeal Life Support Organization

ICU Intensive care unit

NHS National Health Service (UK)

NICE National Institute for Health and Care Excellence

PCI Percutaneous coronary intervention

VA Venoarterial

VAED Victorian Admitted Episodes Dataset

VSTS Victorian State Trauma System

VV Venovenous

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# About this review

Safer Care Victoria (SCV) was commissioned by the Department of Health and Human Services to review the use and outcomes of extracorporeal membrane oxygenation (ECMO) in Victoria. Together with advice from an expert reference group, this review identifies opportunities to improve access to high-quality healthcare. It details evidence and recommends possible methods for delivering adult ECMO services across the state.

**ECMO** gives temporary life support for critically ill patients with reversible acute respiratory and cardiac failure and/or patients requiring a 'bridge' to transplantation. It is a high-risk procedure but can be lifesaving. It is not a common procedure.

## How to read this report

This report is structured around the components of the volume-outcomes review:

1. **ECMO in Victoria** We assessed the statistical significance of volume effects using administrative Victorian data. This has been supported through the use of a CHADx analysis, exploring variance of complications associated with patients treated under the ECMO diagnosis-related group (DRG).
2. **ECMO outside of Victoria** We identified relevant policies and service guidelines published by peak bodies or professional groups. Domestic policies were generally prioritised over international examples.
3. **Evidence base for centralisation** We conducted a literature search and rapid review for each procedure to assess evidence of volume-outcome relationships.
4. **The ECMO procedure** We considered the barriers and difficulties that are associated with delivering the different forms of ECMO.
5. **SCV reference group** We summarised the recommendations from the sector-led reference group.

## Inclusion and exclusions

The recommendations in this report are only intended for patients aged 18 years and older, treated in an acute health service environment.

Interventions undertaken before and after the delivery of ECMO have not been considered.

Recommendations in this report are appropriate for public and private acute health services.

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## About ECMO

Three types of ECMO are used in Victoria:

- **Venovenous (VV) ECMO** Typically undertaken in patients with acute respiratory failure.
- **Venoarterial (VA) ECMO** Typically undertaken in patients with heart failure (with and without respiratory failure).
- **Extra-corporeal cardiopulmonary resuscitation (ECPR)** The least common procedure, a time-critical subset of VA ECMO undertaken in patients in cardiac arrest.

Each type of ECMO intervention requires specific timing and treatment pathways. Patients who have VV-ECMO are typically treated for longer. VA-ECMO and ECPR patients require more expeditious intervention, are on ECMO for less time, and survival rates are often lower.

All forms of ECMO considered in this report are performed within a hospital. 'Out of hospital ECPR' has not yet been performed in Victoria and is outside the remit of this report.

The initiation phase of VA-ECMO and ECPR is directly correlated with the highest risk of an adverse event occurring. Whereas patients requiring VV-ECMO are commonly managed through ventilation and may sometimes be transferrable prior to initiation of ECMO.

# Key findings

## Key question

We sought to explore whether there is a relationship between hospital ECMO volume and patient quality and safety outcomes.

### ECMO use is increasing, but service volume is generally low

Similar to the rest of the world, the use of ECMO has increased in Victoria, doubling over the past five years. International trends suggest that ECMO use will continue to rise, particularly the use of VA-ECMO and ECPR.

Over half of the ECMO procedures in Victoria are managed at The Alfred Hospital. The remaining patients are cared for at numerous health services, the vast majority of which are located in metropolitan Melbourne. In 2016–17, 16 hospitals reported at least one ECMO procedure. However, only six initiated more than 10 patients with many of these patients later transferred to the single large-volume service.

The number of Victorian services providing a small number of procedures contrasts the models successfully implemented in other countries. For example, there are five sites servicing the entire population of England for VV-ECMO, and one health service in New Zealand.

### Victorian services are not structured into formalised networks or pathways

A consistent feature of international ECMO service delivery models is the use of formalised networks and retrieval pathways. It is commonly expected that ECMO providers operate a tertiary intensive care unit (ICU), manage and wean patients on ECMO (as well as initiate) and are able to retrieve eligible patients. Furthermore, where international models centralise services there is often accreditation and performance metrics that allow a 'whole of system' overview of the quality and safety of the system.

ECMO service delivery in Victoria is not structured in this way. Although some services have informal communication and retrieval channels, many provide a low-volume ECMO service in isolation.

Furthermore, the Victorian data that currently reports ECMO activity is limited. It is not possible to determine the type of ECMO offered, the risk profile of the patient and the sequence of care that led to the use of ECMO. It is important that system managers are able to utilise data with more clarity when ECMO services are monitored in future.

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## **Survival rates are higher at high-volume sites**

While there are relatively few studies that have explored the volume-outcome effect, those that have been done show higher volume sites have higher survival rates. Most international regulators have acknowledged the volume effect and have opted to centralise the delivery of ECMO to specialist hospitals. This arrangement is not uncommon, the volume-outcome effect has led to many regulators (including our own) centralising high-risk, low-volume procedures (e.g. high acuity newborn intensive care, transplantation and trauma services).

Despite the relatively low number of procedures in Victoria and the limitations of our data, we observed a statistically significant difference in survival rates between the highest volume site and the pooled outcomes in the rest of the state. This relationship was sustained when we considered a number of patient casemix variables and sensitivity analyses, with the exception of the exclusion of transplant patients. However, as noted, the interpretation of these data is restricted given our inability to suitably risk adjust our findings and the small sample size.

## **Hospital acquired complications are lower at high-volume sites**

Our analysis used the Classification of Hospital Acquired Complications (CHADx) methodology to explore variation of secondary hospital acquired complications.

This analysis found that multiple CHADx complications were significantly lower than the statewide mean at higher volume sites (notably, the rates of haemorrhage/haematoma and post-procedural respiratory disorders).

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# Case for change

The recommendations in this report have been proposed to create a tiered, networked and accredited statewide service that provides all Victorian patients with timely care of the highest quality possible.

## Improving access

The majority of health services providing ECMO interventions are based in Melbourne with just one regional service. Our analysis demonstrated that some Victorian services presently offering ECMO work in isolation and many are unable to sustain or wean patients on ECMO, leading to inflated transfer rates and potentially sub-optimal care for those treated in sites without an experienced ECMO program. The delivery of ECMO could be grouped into three groups, the first is The Alfred Hospital which managed over half of the state's ECMO. The second group has all the major cardiac surgery centres and third group consists of sites doing very small volumes. The vast majority of ECMO undertaken in the third group is delivered by an Alfred retrieval team attending the hospital.

The volume and direction of included studies and our data-analysis demonstrates that more favourable outcomes are achieved when ECMO is centralised to high-volume centres. This review proposes a model of care that restricts the sustained management of ECMO to a limited number of accredited sites. Following the tiered model recommended in recent ELSO guidelines and that suggested by the SCV sector reference group, ECMO would be managed in a single comprehensive centre and in a finite number of intermediate sites. All ECMO centres are able to undertake all forms of ECMO, monitor patients for extended periods and wean patients that have completed their therapy. Given the current high volumes, outcomes and the capability to provide heart replacement therapy, The Alfred Hospital

should be designated as the state's single comprehensive centre.

In order to replicate ECMO outcomes at the comprehensive centre, all intermediate sites must also be capable of attaining a reasonable annual procedural volume. The threshold volumes proposed by ELSO are recognised in our recommendation, however we also note the findings in the literature showing that continued higher volumes perpetuate better outcomes. It is expected that significant resource allocation will also be required to implement and maintain the requisite accreditation standards. As such, sustaining a reasonable annual volume will support health service training and credentialing requirements.

The decision about the appropriate number of Victorian sites is ultimately under the remit of the Department of Health and Human Services. This process will also consider current risk-adjusted mortality (as required by the National Health Service (NHS) service specifications), the location of the hospital and the inter-dependencies of other statewide programs (notably the statewide cardiac plan). However, when we considered the amount of ECMO undertaken outside of The Alfred Hospital, over the past five years, we suggest that it would be pragmatic to limit the number of intermediate sites to two. This would allow these sites to attain a suitable annual volume and provide sufficient capacity for future growth.

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In the proposed model, having more than one ECMO site (if located appropriately) would provide better coverage for urgent initiation and retrieval of patients and expand the area in which ECPR can be offered. Additional sites would also be able to accommodate the expected growth in procedural volume if current expected trends continue. Finally, only having one service limits the state's surge capacity, which is important given the high levels of usage tied to seasonal influenza pandemics and the risk of centralising all highly infectious ECMO patients to a single site that manages large numbers of immunosuppressed patients.

Although the total number of sites providing a program of ECMO care (initiation, maintenance and weaning) would be reduced, the changes in accreditation and governance at the remaining sites would allow greater coverage across the state for a wider range of medical indications and potentially greater access to sites who can initiate ECMO in a timely and safe manner prior to transfer. Furthermore, the literature suggests that inter-site collaboration, consistent delivery criteria and formal retrieval pathways would likely result in better population survival rates.

The greatest risk of patients receiving ECMO is during initiation. Our analysis found that patients that are started on ECMO at high volume, accredited sites, are expected to have a lower likelihood of death and peri-operative complications (notably haemorrhage and haematoma). We therefore recommend that, where a patient is expected to need ECMO and can be transferred safely, they should be treated at an Intermediate or Comprehensive ECMO Centre, prior to initiation.

However, we recognise that a limited number of additional sites will need to be accredited to initiate ECMO prior to transfer to an Intermediate or Comprehensive ECMO Centre. ECMO is rarely elective and, as such, services undertaking high acuity cardiac procedures will need to be prepared to safely initiate ECMO in patients who need time-critical intervention.

The Victorian ECMO Service will provide the structure for statewide ECMO oversight. It will also provide a single communication channel to provide advice and retrieve patients from any Victorian health service.

### **Providing central expertise for complex cases and transfers**

It is important that a single site is able to manage ECMO for patients who require long-term heart replacement therapy, lung transplant or prolonged complex ECMO. This is consistent with accredited international models where such a site (called a Comprehensive ECMO Centre) is able to work with Intermediate ECMO Centres to manage complex patients.

A well-developed accreditation program with a clear ECMO service delivery model has been shown internationally to improve patient outcomes and safely increase the scope of practice for individual services. It is likely that the implementation of Intermediate ECMO Centres will require some health services to review their ECMO service and make changes to the governance model that they currently operate under, notably the capability to sustain and wean patients and, eventually, offer ECPR.

While in the short term this may require some investment, the benefits are likely to justify the effort with accredited sites being able to deliver ECMO to a wider patient cohort and benefit from the collaborative model to minimise patient risk.

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## **Assuring quality**

An important aspect of the ECMO delivery in Victoria is for those time-critical cases requiring ECPR and VA-ECMO. There is limited oversight in the mode of ECMO delivery and, therefore, the potential for variation in access and outcomes for these higher risk cases.

A planned linked data review will provide the detailed analysis with regards to this patient cohort and offer some clarity on more refined referral centre placement and retrieval models.

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# Recommendations

These recommendations outline a statewide adult ECMO service which aims to increase access through a clear retrieval and referral pathway. They require further review from the Department of Health and Human Services, as there are other considerations before any system implementation – notably if they complement capability and service planning and the impact on redistribution.

The recommendations below are supported by the care pathway in **Appendix 1**.

1. A single Victorian ECMO Service should be formed, which is responsible for:
  - (i) 24-hour consultation
  - (ii) retrieval and transfer
  - (iii) ECMO bed management.
2. The Victorian ECMO Service must be consulted on decisions regarding: initiation, ongoing management and weaning of all patients considered for or already on ECMO.
3. All hospitals providing any ECMO service should be accredited and participate in the Victorian ECMO Service.
4. Systems and processes should be developed to monitor performance and standards of ECMO services, with oversight of: workforce and health service training; accreditation; performance management; and, future planning of ECMO services.
5. A single patient eligibility criteria protocol will be developed with clear, evidence-based indications for the initiation of ECMO.
6. The Alfred Hospital should be a designated Comprehensive ECMO Centre. This hospital should initiate and maintain at least 30 ECMO procedures each year, participate in the retrieval and support service as part of the Victorian ECMO Service, offer all forms of ECMO support, and offer heart and lung transplantation and mechanical ventricular assist devices. Additionally, they will be responsible for training and supporting other health services to become accredited ECMO sites.
7. In the first instance, a maximum of two sites should be designated as Intermediate ECMO Centres. These services should maintain a minimum of 20 ECMO procedures each year, participate in the retrieval and support service as part of the Victorian ECMO Service and offer all forms of ECMO support.
8. Where pre-operative consultation is feasible, patients who are likely to require peri-procedural ECMO (e.g. complex cardiac surgery) should be transferred, prior to the commencement of the procedure, to a Comprehensive ECMO Centre or Intermediate ECMO Centre that has the appropriate capability level.

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9. All services providing cardiac surgery which are not a Comprehensive or Intermediate ECMO Centre must be able to initiate ECMO, with the following conditions:
    - (i) The service is accredited to provide ECMO.
    - (ii) ECMO is only initiated with the intention of stabilisation and transfer to a Comprehensive or Intermediate ECMO Centre.
  10. Services that have vascular surgery and a high-volume interventional cardiology service, who do not also offer cardiac surgery, should be able to initiate ECMO, with the following conditions:
    - (i) The service is accredited to provide ECMO.
    - (ii) ECMO is only initiated with the intention of stabilisation and transfer to a Comprehensive or Intermediate ECMO Centre.
  11. The Victorian ECMO Service will support all services not included in recommendations 6-10 by providing advice for patients who may be eligible for ECMO and, where appropriate, facilitate retrieval.
  12. Patients with out-of-hospital cardiac arrest who are eligible for ECPR should be transferred directly to a site which provides a dedicated, trained and resourced ECPR service, if accessible within 60 minutes of the arrest.
  13. All sites performing ECMO must submit data on all patients and ECMO procedures to the Australia New Zealand Intensive Care Society (ANZICS) ECMO registry for public reporting. All Comprehensive and Intermediate ECMO Centres will be encouraged to report to ELSO.

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## NEXT ACTIONS

In order to successfully implement these recommendations, we suggest that the following areas are addressed over the next 12 months:

1. The establishment of the Victorian ECMO Service will be centrally coordinated.
2. A sector-led group is convened to agree appropriate eligibility criteria for initiating ECMO, hospital accreditation requirements and clinical peer review process.
3. An impact assessment is undertaken to determine system capacity, health service infrastructure and resources required to implement the proposed centralised ECMO service.
4. The future supply and demand for ECMO services in Victoria is to be assessed, with particular attention to access and demand for ECMO services in outer metropolitan Melbourne, regional and rural Victoria.

## FUNDING AND SITE DESIGNATION

5. This document was purposefully developed agnostic to resource implications. This is because we wanted to develop a vision of 'what would be best practice' for the department to consider and factor in pragmatic angles.
6. The decision-making process for the designation and funding of ECMO centres and the Victorian EMCO Service is within the remit of the department. This process will be informed by the impact assessment work to be undertaken by SCV and the implementation of the cardiac services capability framework.

# 1. ECMO in Victoria

## Key questions

The recommendations in this document have been informed through the following analysis. We sought to identify whether the variance in volume and outcomes across the state's ECMO services indicated a quality and safety risk for Victorian patients:

- What was the pattern of ECMO use in Victoria and associated outcomes?
- Was institutional volume associated with patient outcomes, and what factors influenced this?
- What was the potential benefit if outcomes were aligned to 'optimal' delivery?

## Data analysis methodology

We explored the Victorian Admitted Episode Database (VAED) inpatient data to support statewide and peer-to-peer comparison. With fewer than 200 procedures reported annually, ECMO remains an uncommon procedure in Victoria. It is therefore likely that a statistical investigation into, and the comparison of annual adverse event rates at different health services will be underpowered.

To reduce variance and improve statistical reliability, we extracted a five-year sample from the VAED, between the 2012–13 and 2016–17 financial years. Increasing the sample size to five years allows for more robust analysis, but it remains a small population with many sites reporting fewer than five procedures over this total period. Patient selection, confidence in the technology and new delivery methods are all factors that should caveat outcome comparisons.

All patients were included if they were admitted to a Victorian hospital with an ECMO Australian Classification of Health Interventions (ACHI) procedure code. Patients were excluded if they were aged less than 18 years at admission or if the patient was admitted for posthumous organ donation.

In addition to the inclusion of ECMO admissions, all other admissions of the same patient during the same financial year were also included. Data linkage with Births, Deaths and Marriages Registry (BDM) data was used to determine intermediate (>30 days post discharge) survival. The linked dataset was provided by the Centre for Victorian Data Linkage.

Death was the primary outcome, given the high frequency of this adverse event, the complexity of ECMO subjects, and absence of functional or long-term outcome data. We also explored a secondary outcome analysis using CHADx methodology to explore the frequency of clinically significant complications.

In Victoria, The Alfred Hospital acts as a retrieval and referral centre, supported by Adult Retrieval Victoria (ARV). This service supports and transfers patients receiving ECMO. This is pertinent for low-volume services where patients who are initiated on ECMO can be safely and rapidly transferred for sustained treatment at a higher volume site. This system is well developed and has been operating for several years. These transfers are an important source of statistical bias when comparing mortality rates between sites.

For example, if Hospital A initiates ECMO five times and all die but four are transferred for further ECMO treatment before death, then the inpatient mortality rate of Hospital A appears to be 20 per cent not 100 per cent. Volume-outcome relationships were analysed by displaying outcomes at each site against procedure number on a funnel plot. These plots allowed us to identify bias in our analysis and observe variation in trends across all health services included.

Pooled outcomes at lower volume sites were compared to higher volume sites. Each analysis was repeated three times in a stratified manner to account for patient transfers in the following ways:

- All cause inpatient mortality by hospital episode (i.e. if a patient had ECMO at Hospital A and continued with ECMO at Hospital B where they subsequently died, the patient was represented as a survivor at Hospital A and as a death at Hospital B).
- All cause inpatient mortality by patient admission, where patient outcomes are attributed to all sites providing ECMO (i.e. if a patient had ECMO at Hospital A and continued with ECMO at Hospital B where they subsequently died, the death was attributed both hospitals).
- All cause 30-day mortality, where deaths are attributed to the patient receiving ECMO during their admission or 30 days after separation. That is, if a patient had ECMO at Hospital A and continued with ECMO at Hospital B from where he/she was discharged alive, a death was attributed to both hospitals if it occurred within 30 days of discharge from both. If the death occurred more than 30 days from Hospital A discharge but within 30 days of discharge from Hospital B, it was attributed to Hospital B only.

Sensitivity analyses were undertaken to identify patient sub-groups or variants of the procedure were associated with markedly different outcomes, and to determine if these influenced or explained any volume-outcome relationships. Nevertheless, it was not possible to completely risk adjust outcomes and, as such, it is important to note that reported outcomes may still have been affected by unknown confounders (notably severity of condition and selection bias).

### What is the pattern of ECMO use in Victoria and associated outcomes?

During the five-year study period, we identified 563 adult admissions coded with an ECMO ACHI procedure in the VAED (**Table 1**). We observed significantly increasing numbers of procedures over the five years, rising from 76 procedures in 2012–13 to 145 in 2016–17 (odds ratio 1.07 per year, 95 per cent CI 1.01-1.16, p=0.01).

**Table 1 Adult ECMO separations**

Year	Number of adult ECMO separations
2012–13	76
2013–14	113
2014–15	114
2015–16	115
2016–17	145

VAED 1 July 2012 to 31 June 2017

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The main provider of adult ECMO in Victoria is The Alfred Hospital, accounting for 55 per cent of the state's ECMO admissions. In the remaining health services, the highest annual volumes were found at the University of Geelong Hospital, Monash Medical Centre (Clayton), Austin Hospital, St Vincent's Hospital and Royal Melbourne Hospital, who each reported between 30 and 50 procedures over the five years. In total, 22 health services reported at least one ECMO procedure, with 12 undertaking fewer than five procedures.

In 2016–17, 16 health services reported at least one ECMO procedure (**Appendix 2**). The highest volume site was The Alfred Hospital, with four further sites reporting 10 or more procedures in the financial year. As ECMO can be initiated at one site and continued at a second site, it is worth noting that at least 12 patients started ECMO at a Victorian health service and continued on ECMO at The Alfred Hospital. In addition, there are likely to be more cases where a retrieval team went to a different hospital, with the intention of providing ECMO support, that have not been captured in the VAED dataset.

Over the five years, 255 patients died in hospital (45%; 95%CI = 41%–50%) during their ECMO admission with an additional 19 dying within 30 days of their discharge. The 30-day fatality rate was 49 per cent (95%CI = 44%–53%).

In Victoria, The Alfred Hospital acts as a retrieval and referral centre, supported by Adult Retrieval Victoria. No specific guidelines or standards of practice exist for referral or retrieval. During the study period, we identified 45 patients that had ECMO and were subsequently transferred (or retrieved) to a second site to continue ECMO. Forty-three (96%) of these patients were moved to The Alfred Hospital.

The patient characteristics of admissions with an ECMO procedure are summarised in **Table 2**. The principal diagnoses of patients were predominately diseases of the circulatory system and respiratory system, accounting for 60 per cent and 20 per cent of cases respectively. When the mortality rates were compared for these two diagnoses we found that patients were less likely to die when admitted with a respiratory system disease (Odds Ratio 0.55 95% CI 0.35 to 0.85). There was no age group where ECMO procedures were overwhelmingly common. However, the use of ECMO was noticeably lower in patients younger than 30 and older than 70. Finally, two thirds of ECMO procedures reported were undertaken in men, but gender was not a significant variable for risk of death.

**Table 2 ECMO patient characteristics**

Disease category	Proportion of admissions	Inpatient mortality rate	95% confidence interval
<b>Principle diagnosis at admission*</b>			
Diseases of the circulatory system	60% (n=324)	50%	43% – 54%
Diseases of the respiratory system	20% (n=106)	35%	26% – 45%
Injury poisoning and certain other consequences of external causes	6% (n=32)	66%	50% – 84%
Certain infectious and parasitic diseases	4% (n=21)	43%	21% – 66%
Other principle diagnosis	10% (n=58)	34%	22% – 48%
<b>Age at admission (years)</b>			
<20	4% (n=22)	22%	8% – 45%
20–29	9% (n=51)	31%	19% – 46%
30–39	17% (n=94)	41%	31% – 52%
40–49	16% (n=88)	45%	35% – 56%
50–59	22% (n=124)	44%	35% – 54%
60–69	23% (n=128)	52%	43% – 61%
70–79	9% (n=52)	62%	38% – 66%
>79	1% (n=4)	25%	0 – 81%
<b>Gender*</b>			
<b>Male</b>	67% (n=361)	44%	39% – 49%
<b>Female</b>	33% (n=180)	47%	40% – 55%

\*Patient cohort does not include those aged <20-year, total sample size is 541 admissions

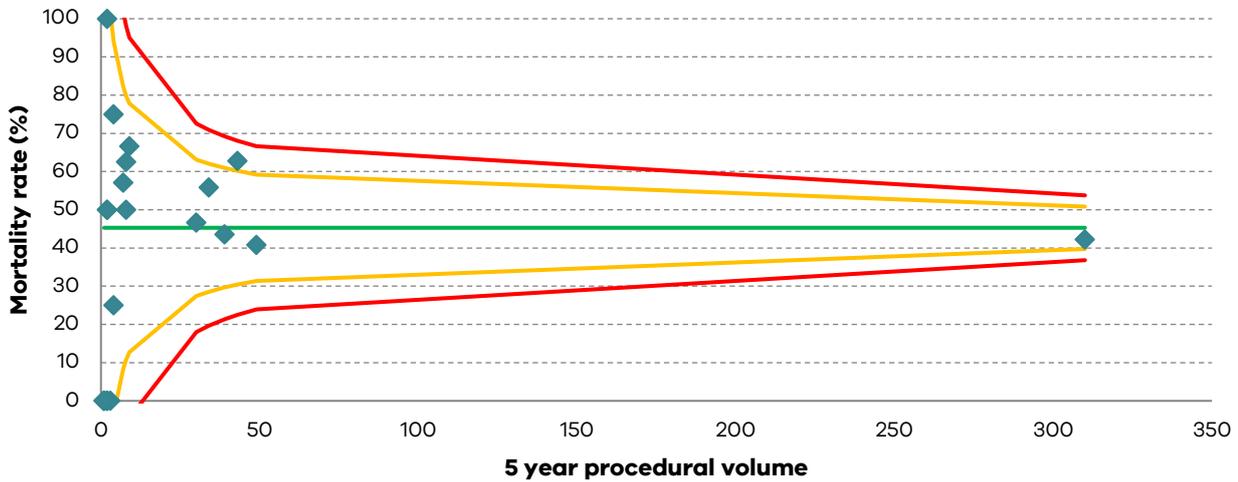
## Is institutional volume associated with patient outcomes?

### Comparison of individual site outcomes

We used stratified analyses outlined above in the methodology to determine whether hospital volume was associated with mortality. Health service outcomes are displayed below on funnel plots. A volume-outcome trend appeared to be visible with higher mortality rates at lower volume sites (**Figures 1-3**), however we note that these analyses were performed without risk adjustment.

When examining basic in-hospital mortality (without accounting for transfers) (**Figure 1**) one health service had an observed mortality rate between the 95 and 99 per cent confidence intervals.

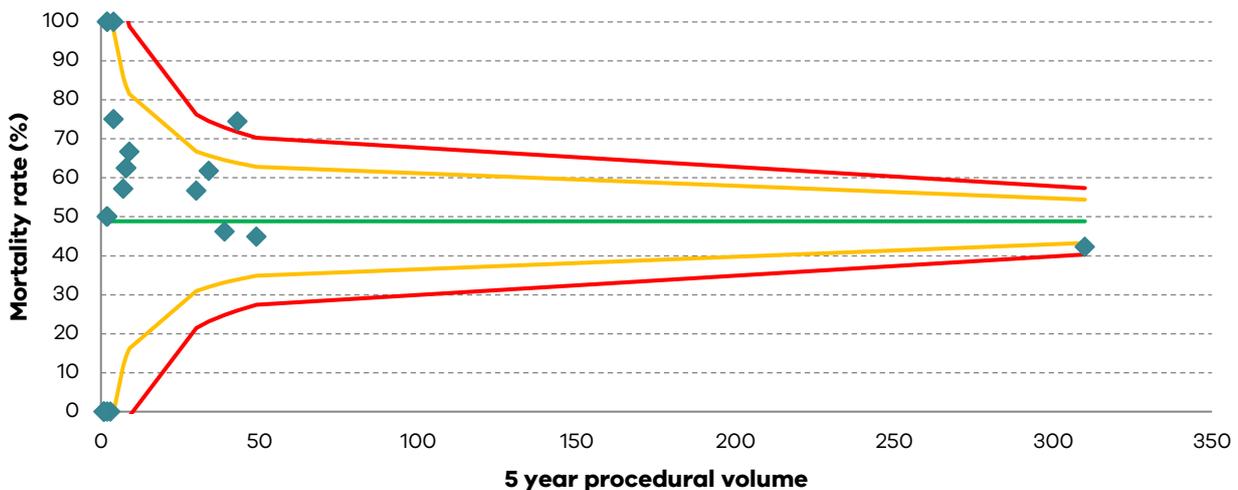
**Figure 1 Five-year all cause unadjusted inpatient mortality by hospital episode**



After assigning post-transfer outcomes to the sending and receiving sites (**Figure 2**) the mean mortality rate was 49 per cent (95% CI = 45% - 53%; p=0.20). One site had a mortality rate above the 99 per cent confidence interval (red line), with an observed rate of 74 per cent (95% CI = 59% - 86%; 32 deaths and 43 ECMO procedures). Another site had a mortality rate above the 95 per cent confidence interval (yellow line) with four deaths from four ECMO procedures (95% CI = 40% - 100%). More importantly, the largest volume site had an observed mortality rate below the lower 95 per cent confidence interval, with a rate of 42 per cent (95% CI = 37% - 48%; 131 deaths and 310 ECMO procedures).

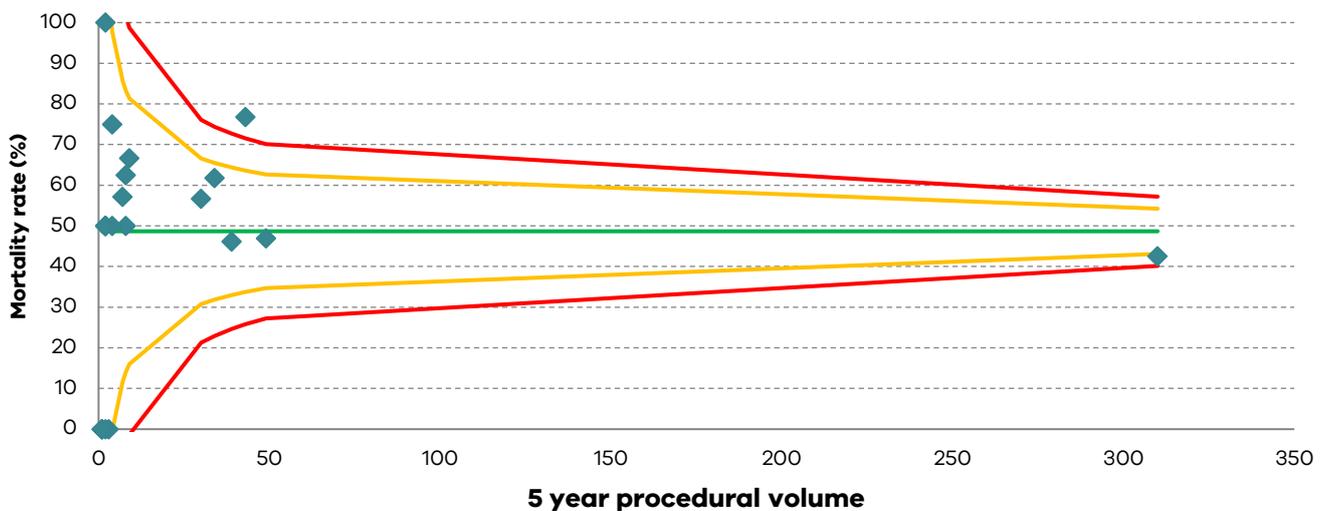
While these results are not adjusted for other important patient variables (such as severity of illness, timing of ECMO, and exclusion of eligible patients who did not receive ECMO) they do support the hypothesis that higher volume may be associated with improved outcome.

**Figure 2 Five-year all cause unadjusted inpatient mortality including for post-transfer outcomes**



The final analysis (**Figure 3**), which reports 30-day mortality, produced similar results. The population mean (statewide rate) was 48 per cent and the majority of sites fell within the state benchmark. One site had an observed mortality rate above the 99.8 per cent confidence interval, with a rate of 76.7 per cent (33 deaths and 43 ECMO procedures).

**Figure 3 Five-year all cause unadjusted 30-day mortality**



### Pooled comparisons of outcome

As one health service accounts for more than half of the ECMO cases reported, we opted to compare pooled volume outcomes through the following three analyses:

- The Alfred Hospital versus pooled outcomes across the rest of the state – **Table 3**.
- Pooled outcomes for services >10 procedures over 5 years versus pooled outcomes for low-volume services (<10 procedures over 5 years) – **Table 4**.
- Pooled outcomes for medium-volume sites (>10 procedures over 5 years) (Alfred excluded) versus pooled outcomes for low-volume services (<10 procedures over 5 years) – **Table 5**.

Each analysis was again repeated in a stratified manner to account for patient transfers.

We identified a statistically significant higher unadjusted mortality rate when the rest of the state was compared to The Alfred Hospital's outcomes, after accounting for post-transfer outcomes and when examining 30-day mortality (**Table 3**). These findings were not affected by the removal of the outlying site(s) from the analysis (**Appendix 2**).

**Table 3 Statewide pooled outcomes versus The Alfred Hospital**

Mortality measure	Pooled outcomes for the rest of the state	The Alfred Hospital	Odds ratio (95% confidence interval)
<b>Inpatient</b>	49% (n=124/253)	42% (n=131/310)	1.31 (0.94 to 1.83) [P=0.11]
<b>Inpatient adjusted for post-transfer outcomes</b>	57% (n=144/253)	42% (n=131/310)	1.81 (1.29 to 2.52) [P<0.001]
<b>30-day mortality</b>	56% (n=142/253)	42% (n=132/310)	1.73 (1.23 to 2.41) [P=0.001]

We were unable to show significant differences in the two other volume-outcome analysis (**Tables 4 and 5**). These findings were not affected by the exclusion of the outlying service(s) from the analysis (**Appendix 2**).

**Table 4 Pooled outcomes low-volume services (<10 procedures over 5 years) versus services >10 procedures over 5 years**

Mortality measure	Low-volume services (<10 procedures over 5 years)	Services >10 procedures over 5 years	Odds ratio (95% confidence interval)
<b>Inpatient</b>	47% (n=27/58)	45% (n=228/505)	1.06 (0.61 to 1.82 [P=0.84])
<b>Inpatient adjusted for post-transfer outcomes</b>	59% (n=34/58)	48% (n=241/505)	1.55 (0.89 to 2.69 [P=0.12])
<b>30-day mortality</b>	52% (n=30/58)	48% (n=244/505)	1.14 (0.66 to 1.97 [P=0.62])

**Table 5 Pooled outcomes for services >10 procedures over 5 years versus pooled outcomes for low-volume services (<10 procedures over 5 years)**

Mortality measure	Services >10 procedures over 5 years (Alfred excluded)	Low-volume services (<10 procedures over 5 years)	Odds ratio (95% confidence interval)
<b>Inpatient</b>	50% (n=97/195)	47% (n=27/58)	0.88 (0.49 to 1.58 [P=0.67])
<b>Inpatient adjusted for post-transfer outcomes</b>	56% (n=110/195)	59% (n=34/58)	0.84 (0.46 to 1.53 [P=0.57])
<b>30-day mortality</b>	58% (n=112/195)	52% (n=30/58)	0.79 (0.44 to 1.43 [P=0.44])

## Do patient factors explain the observed apparent volume outcome relationships?

Many factors influence mortality. We reviewed the following variables to determine whether they influenced the probability of death in our five-year sample and whether this might account for any volume outcome relationships:

- Elective versus emergency admission
- Length of time spent in ICU prior to transfer
- ECMO following coronary artery bypass grafts (CABG)
- Principle diagnosis of the patient (cardiac versus respiratory disease).

We found that none of these variables had a significant effect on mortality in our sample. Therefore, we suggest they are unlikely to have a substantial influence on any potential volume effect observed. The volume-outcome relationship appeared to persist for both cardiac and respiratory diagnoses. These analyses can be found in full in **Appendix 2**.

In addition to the patient factors described above, it is recognised that the unique nature of The Alfred Hospital's casemix may affect interpretation of a potential volume-outcome relationship. For instance, transplant ECMO procedures have a lower mortality and ECPR cases have a higher mortality. Further information (where available) about these types of patients requiring ECMO can be found in **Appendix 2**.

Over the past five years, 67 of the 310 (2%) episodes with ECMO at

Hospital also involved a transplant procedure. There is a significant difference in observed mortality rates for these transplant recipient patients when compared to the remaining cohort of patients (**Table 6**).

**Table 6 Mortality rates for ECMO transfer patients**

Admission type	Number of separations	Inpatient mortality rate	30-day mortality rate
ECMO to The Alfred Hospital without a transplant procedure	243	50% (n=121)	50% (n=122)
ECMO to The Alfred Hospital with a transplant procedure	67	15% (n=10)	15% (n=10)

Unlike the other sub-group analyses, the difference between the two cohorts was statistically significant for inpatient and 30-day mortality; OR 0.18 (95% CI 0.09 to 0.36 [P<0.001]) and OR 0.17 (95% CI 0.08 to 0.36 [P<0.001]), respectively.

It is reasonable to ask if this cohort explains the lower overall observed mortality seen at The Alfred Hospital. Therefore, analyses were re-run with patients undergoing a transplant during the same episode excluded. The outcomes show that, when transplant patients are removed, mortality rates are

generally still lower at The Alfred Hospital. However, this difference was no longer statistically significant (**Table 7**).

**Table 7 Pooled outcomes across the rest of the state versus The Alfred Hospital (transplant patients removed)**

Mortality measure	Pooled outcomes for the rest of the state	The Alfred Hospital	Odds ratio (95% confidence interval)
<b>Inpatient</b>	49% (n=124/253)	50% (n=121/243)	0.97 (0.68 to 1.38 [P=0.86])
<b>Inpatient adjusted for post-transfer outcomes</b>	57% (n=144/253)	50% (n=121/243)	1.33 (0.94 to 1.90 [P=0.11])
<b>30-day mortality</b>	56% (n=142/253)	50% (n=122/243)	1.27 (0.89 to 1.80 [P=0.19])

Another group that is likely to be over-represented in The Alfred Hospital's casemix are patients undergoing ECPR. Historically, this cohort of patients were almost always treated at The Alfred Hospital. More recently other hospitals have begun undertaking these procedures.

It was not possible to accurately ascertain the size and outcomes of this cohort in the data available for this review. However, it should be noted these patients are deemed high risk and commonly thought to have lower expected survival rates than patients receiving VA or VV-ECMO. It is therefore important to consider what effect these patients have on overall mortality rates when comparing statewide outcomes. The inclusion of large numbers of ECPR patients in the cohort at The Alfred Hospital would be expected to be associated with a higher mortality rate, whereas the opposite was the case, again supporting the presence of a true volume-outcome relationship being present in Victoria.

### Non-mortality outcomes

We also explored whether CHADx methodology could demonstrate if volume had an effect on hospital acquired complications. During a two-year period, 59 ECMO cases were admitted electively across 11 health services and 249 ECMO cases admitted as emergencies (or statistical transfers within an organisation) across 15 health services.

We found that complication rates mirrored the findings for mortality. The highest volume site was found to have significantly lower rates of haemorrhage and haematoma, postprocedural respiratory disorders and coagulation defects when compared to the mean statewide rate. The full CHADx report can be found in **Appendix 3**.

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A lower rate of complications was also noted in patients who were cannulated by The Alfred Hospital team as part of a retrieval compared to retrievals where cannulation had already been performed by the referring site (**Appendix 2**).

### **Hypothesised benefits of a realigned ECMO system**

If the risk of mortality for all ECMO patients was the same as the lowest health service rate, approximately 35 additional patients may have survived.

Similarly, if patients were all redistributed to accredited Comprehensive and Intermediate ECMO Centres in the Victorian ECMO Service, operating with outcomes seen at the present high-volume site, approximately seven additional patients would need to be treated there to prevent one death, based on both 30-day and inpatient mortality rates.

However, given the limitations of the data, further investigation is required before more definitive figures can be established.

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## 2. ECMO outside of Victoria

### Current national guidance

The HealthPACT secretariat recently published a health technology report<sup>1</sup> on ECMO in response to a referral from the Nationally Funded Centers (NFC). It noted concerns in the jurisdictions about expanding indications to undertake ECMO and subsequent increased usage. The report highlighted limited evidence to support the use of ECMO and supported temporary use of ECMO for a limited range of conditions.

### International ECMO guidelines

ELSO produced guidelines for ECMO centres (ELSO, 2014).

The guidelines provide criteria for general structure, staffing, physical facilities and equipment, staff training and education, patient follow-up and program evaluation. These guidelines are complemented by policy statements for the management of ECMO inpatients with cardiac and respiratory indications.

In 2018, an international consensus position paper was published that outlined the organisation of ECMO programs for cardiac failure in adults (Abrams et al., 2018). A summary of the key recommendations relevant for this review are outlined below:

- The use of pre-specified inclusion and exclusion criteria for consideration of ECMO should be used to facilitate a standardised approach that can be implemented expeditiously.
- ECMO for cardiac failure should ideally be performed at experienced, high-volume centres (i.e. comprehensive care centres) capable of providing other forms of advanced cardiac support, including percutaneous coronary interventions (PCI) and long-term heart replacement therapies (e.g. ventricular assist devices and heart transplantation). Such centres should have multidisciplinary teams readily available and should ideally be equipped with mobile ECMO teams capable of cannulation and retrieval of patients from other facilities with limited ability to provide ECMO.
- Regional referral centres capable of performing ECMO, including ECMO transport, but without access to long-term heart replacement therapies, should have collaborative relationships with comprehensive care centres.
- Both local centres that may or may not have PCI capabilities and referral centres with access to PCI, but without the capabilities of ECMO management, are encouraged to have affiliations with regional referral centres or comprehensive care centres in order to have appropriate access to ECMO.
- In order to optimise outcomes, we recommend that, whenever possible, centres performing ECMO for cardiac failure achieve a minimum ECMO case volume of 30 cases per year.
- ECMO centres should have continual access to the facilities, equipment and staffing necessary for routine ECMO management and management of unanticipated emergencies of ECMO complications.

<sup>1</sup> Health Policy Advisory Committee on Technology New and Emerging Health Technology Report High-cost Assistive Technologies in Critical Care August 2016.

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There are a few recommendations that, if implemented in Victoria, would have implications on the delivery of ECMO across the state. Just one service currently meets the minimal volume threshold and performs long-term heart replacement therapies. Furthermore, under the current transfer policies there is no formalised collaborative approach for the management and transfer of patients that undergo ECMO at the low-volume site.

The same group has also previously published a position paper for the management of patients with respiratory failure (Combes et al., 2014). Similar to the position statement for cardiac failure, the statement outlines a number of recommendations that are relevant for the delivery of ECMO in Victoria. Notably:

- ECMO requires highly experienced staff and a minimum number of cases per year.
- Organisation of ECMO programs on a regional or national level is needed to provide the best, safest, and most efficient care possible to the population.
- Annual volume for any health service performing ECMO, should be at least 20 cases per year, with a minimum of 12 ECMO cases for acute respiratory failure.
- Establishing new centres in regions well served by existing high-volume ECMO centres should be discouraged.

## **New South Wales**

The New South Wales Department of Health recently revised its adult Critical Care Tertiary Referral Networks and Transfer of Care policy (New South Wales Department of Health, 2018). Within the policy, the use of ECMO in formalised partnership is recommended.

The policy notes the following with regards to the provision ECMO in the state for non-tertiary hospitals, where ECMO may be provided through a retrieval protocol:

ECMO is provided by either Royal Prince Alfred or St Vincent's Hospital via a roster system. The service involves collaboration between the active ECMO/ICU clinicians, medical retrieval services and NSW Ambulance. A combined ECMO and retrieval team is transported to the referring hospital with appropriate equipment to establish the patient on ECMO and transport the patient back to the hospitals by helicopter, fixed wing or road vehicle.

In New South Wales, the greater Sydney area is running an expansion of the Victorian CHEER trial (2CHEER). It is a multi-centre clinical trial in co-operation with St Vincent's Hospital, the Royal Prince Alfred Hospitals and NSW Ambulance Service. Its aim is to ascertain the viability of the ECPR model in the state, similar to that currently in operation in Victoria.

## **New Zealand**

The New Zealand Ministry for Health is reviewing the service delivery model for ECMO (New Zealand Ministry for Health, 2018). Currently there is one large provider of adult ECMO services in New Zealand, with a negligible number of patients treated elsewhere. In 2016–17, 31 adults had ECMO at the main provider with three others undergoing ECMO at two other sites. Mortality rates are comparable to Victoria, at around 40 per cent.

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In the current model, there are only informal referral pathways to the main provider. Similar to the Victorian model of care, referrals are initiated by the treating intensivist regional site following patient deterioration on standard ventilation. Patients may have ECMO commenced at the originating site either by the retrieval team (primary transfer) or the local clinical team and be transported while on ECMO (secondary transfer).

The objective of the service delivery plan is to develop a formalised referral pathway. The scope provides separate models for VV and VA-ECMO. In summary:

- Under the service model there will be a single provider of adult VV-ECMO services in New Zealand – Auckland District Health Board (DHB).
- For VA-ECMO, the plan notes that patients undergoing cardiac surgery should have access to ECMO if required to come off bypass. In this situation, the best outcome for patients is to remain with their local clinical team, who may seek advice from the Auckland DHB ECMO service.
- Elective high-risk cardiac surgery patients may be referred to Auckland DHB, depending on pre-operative consultation.
- Where VA-ECMO is required urgently for other acute cardiac conditions it is recommended that the treating clinicians discuss commencement of ECMO with the Auckland DHB ECMO service so that a management plan may be developed, and a retrieval timeframe agreed if required.

## United Kingdom

The National Institute for Health and Care Excellence (NICE) has published three interventional procedure guidelines for adults with severe acute respiratory failure<sup>2</sup>, acute heart failure<sup>3</sup> and in post-neonatal children<sup>4</sup>. Each of the recommendations require health services to get consent from patients, carers and their own clinical governance leads and to ensure that the procedure is only carried out by clinical teams with specific training and expertise in the procedure.

The NHS Commissioning Board (now NHS England) published the service specifications for ECMO in England in 2013 (NHS England, 2013). The specifications restrict the provision of ECMO to tertiary level ICU providers, with the expectation that all ECMO services should retrieve all patients who are accepted for treatment/consideration of ECMO.

The service specifications provide eligibility criteria and performance measures, notably a minimum volume threshold and upper limit for mortality rates (40%). The specification lists just five English hospitals for the provision VV-ECMO support for the entire nation.

<sup>2</sup> NICE. 2011. Interventional procedures guidance [IPG391]. Extracorporeal membrane oxygenation for severe acute respiratory failure in adults. National Institute for Health and Care Excellence. Manchester.

<sup>3</sup> NICE. 2014. Interventional procedures guidance [IPG482]. Extracorporeal membrane oxygenation (ECMO) for acute heart failure in adults. National Institute for Health and Care Excellence. Manchester.

<sup>4</sup> NICE. 2004. Interventional procedures guidance [IPG482]. Extracorporeal membrane oxygenation (ECMO) in postneonatal children. National Institute for Health and Care Excellence. Manchester.

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The indications for ECMO in the United Kingdom may be different from those used in Victoria. Notably, the NHS specifications are exclusively for services providing ECMO for adults with respiratory failure. Although the NICE guidelines did not find ECMO for acute heart failure to be unsafe, in 2016 NHS England did not commission this service noting that there was not enough evidence to make the treatment available at this time (NHS England 2016).

### **Italy**

In Italy, the H1N1 pandemic led to the creation of a national network to manage ECMO access and dissemination across the country. The model limits the number of sites (approximately 14 sites), provides retrieval models and organises training courses to provide theoretical and practical education to care givers unfamiliar with ECMO (Patroniti et al., 2011).

### **Germany and France**

In both countries, the number of sites offering ECMO is not restricted. Both of these countries operate a health service similar to our own.

In Germany, there is no current nationwide model for providing a uniform approach to ECMO delivery and access (Karagiannidis et al., 2016).

A similar situation is evident in France, although the recent emergence of a mobile ECMO service has received some international attention. Operating primarily in the Parisian region, the Service d'Aide Medical d'Urgence provides an ECPR response for Paris 24/7, staffed by three health professionals – operating through a call centre or on-scene protocol. In 2016, a multicentre randomised study was commenced to compare in-hospital and pre-hospital ECPR implementation. The results evaluate the model and, results pending; provide an evidence-based model that can be exported internationally (Hutin et al., 2017).

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## 3. Evidence base for centralisation

### VOLUME-OUTCOMES CORRELATIONS

#### Adult studies

The main study that provides much of the evidence base around procedural volume and outcomes (Barbaro et al., 2015) used hierarchical logistic regression modelling to compare outcomes in 56,222 patients at different volume hospitals collected in the ELSO Registry from 1989 to 2013.

The study stratified by age (adult n=10,588, children n=14,725 and neonate n=30,909) and type of ECMO (cardiac (VA), respiratory (VV) and ECPR). The authors also chose to sub-divide their findings by outcomes before and after 2008, noting the improvements in safety and quality of ECMO use during the study period.

Between 2008 and 2013, the study found significantly higher survival rates for adults at higher volume (>30 procedures per year) OR 0.61 (95% CI 0.46 to 0.80) and medium-volume (15-30 procedures per year) OR 0.72 (95% CI 0.55 to 0.96) sites when compared to sites doing fewer than six procedures per year. Their sensitivity analysis found statistically significant associations between higher age group specific hospital ECMO volume and lower mortality. However, there was no association between volume and outcome for VV-ECMO support.

A smaller, second study, (McCarthy et al., 2016) reported outcomes from 1,197 American patients (from 246 hospitals) collected in the National Inpatient Sample between 2002 and 2011. It found no significant difference in survival rate between medium-volume and high-volume hospitals ( $p = 0.81$ ). A sub-analysis of ECMO cases from 2008 to 2011 was performed and showed no significant difference in outcomes between low and high tertile (OR: 1. 95% CI: 0.74 to 1.64) and significantly worse outcomes in medium-volume tertile compared with high-volume tertile (OR: 2.4; 95% CI: 1.6 to 3.6).

Contrary to the Barbaro et al findings, the authors concluded that ECMO can be performed in properly selected patients with acceptable results in US centres that do not perform a high volume of ECMO.

#### Neonatal and paediatric studies

Two further studies explored outcomes ECMO in neonatal and paediatric settings. Although the value of these studies is limited given the adult focus of this review, they have been included due to the paucity of data in adult population.

The first study (Karamlou et al., 2013) reported the outcomes of 3,867 paediatric ECMO procedures collected in the US Healthcare Cost and Utilization Project Kids' Inpatient Database between 2000 and 2009. It found that a higher annual ECMO volume (>30 patients) was associated with reduced in-hospital mortality ( $P = .01$ ) within nearly all risk adjustments for congenital heart surgery categories.

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The second study (Freeman et al., 2015) reported outcomes of 7,322 children and neonates from 40 US hospitals, collected in the US Pediatric Health Information System (PHIS) database. The study found that patients treated at medium-volume (20 to 49 procedures) (OR 0.86, 95% CI 0.75 to 0.98) and high-volume (>50 procedures) (OR 0.75 95% CI 0.63 to 0.89) centres had significantly lower odds of death compared to those treated at low-volume centres.

### **Geographic variation**

Under the current model, there is only one ECMO program in a regional health service with the other health services predominately located in inner metropolitan Melbourne. This distribution could, in theory, adversely affect metropolitan and regional patients. Patients living in regional Victoria have no local providers and so there may be an issue around unequitable access. Whereas, patients living in metropolitan Melbourne will have little choice in their treating site and therefore may not receive optimal care at the high-volume centres. Under the auspice of the Victorian ECMO Service, it is expected that this is resolved through rapid retrieval utilising ARV to either a Comprehensive or Intermediate ECMO Centre and the accreditation of ECMO providers.

A recent study explored the effect regional variation and population density had on the outcomes of 27,705 patients with presumed out-of-hospital cardiac arrests across the state (Nehme et al., 2014). The study found that the risk adjusted odds ratio of survival to discharge for patients living in high density areas was 4.32 (95% CI 2.67 to 6.99) compared with 1.88 (95% CI 1.15 to 3.07). The authors noted that population density was a significant risk factor for survival, irrespective of response times.

An earlier study, again undertaken in Victoria, found that significantly higher survival rates were observed in patients with out-of-hospital cardiac arrests that were transported to a hospital with 24-hour cardiac intervention services (OR 1.40 95% CI 1.12 to 1.74) (Stub et al., 2011). However, the authors noted that hospital volume did not have a significant effect.

## **USE OF ECMO RETRIEVAL MODELS**

### **University of Geelong Hospital regional ECMO model**

As noted, there is no current formal process for accreditation or retrieval in Victoria. However, the University of Geelong Hospital has published their experiences of developing a regional ECMO model which highlighted the importance of both of these factors (McCaffery et al., 2016).

The study observed the outcomes and characteristics of 61 patients before and after the implementation of a clinical service model. Established in 2011, the service model was developed over 36 months in collaboration with The Alfred Hospital.

Before the service model was introduced the median annual volume was two cases. Following the introduction of the service model, the annual caseload increased to a median of 10 cases, with more recent data projecting that this volume will exceed 20 in the near future. Despite increased volume, there was no significant difference in patient characteristics before and after the model was introduced.

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Aside from volume, following the introduction of the clinical service model, there were some notable differences in the delivery of ECMO at the hospital:

- Significantly more patients received VA-ECMO after admission to the ICU, with a lower proportion receiving ECMO after cardiac surgery.
- A significant increase in the proportion of patients receiving ECMO for cardiogenic shock.
- Intensivists performed more cannulations, with the number of central cannulations decreased.
- Significantly longer lengths of stay (including time spent in ICU).
- Significantly lower transfer rates of patients on VV-ECMO.
- Significantly fewer mechanical complications and reduced rates of major bleeding and technical complications (although not statistically significant).
- Increase survival rates (although, again, not statistically significant).

The authors concluded the introduction of the ECMO service allowed the hospital to provide ECMO for more patients with more medical indications – while reducing the transfer rates of patients receiving VV-ECMO – with no effect on those patient’s mortality rates.

## **CHEER 1 trial**

In Victoria, the CHEER 1 trial explored the management of patients with refractory cardiac arrest (Stub et al., 2015).

Over three years, 26 patients with refractory cardiac arrest (11 out of hospital cardiac arrest and 15 in-hospital cardiac arrests) were treated with the CHEER protocol. Of these patients, 21 patients received ECPR. Survival to hospital discharge occurred in 54 per cent (14 of the 26 patients).

The CHEER protocol was for patients with refractory out-of-hospital cardiac arrests if following criteria were met:

- Aged 18 to 65 years.
- Cardiac arrest due to suspected cardiac ethology.
- Chest compressions commenced within 10 minutes by bystanders or emergency medical services.
- Initial cardiac arrest rhythm of ventricular fibrillation.
- Mechanical CPR machine available.

Patients with in-hospital cardiac arrests were eligible for ECPR at the discretion of the attending critical care physician when it was considered likely that the cardiac arrest would be reversible if VA-ECMO and definitive treatment could be provided immediately.

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## German experience

A retrospective review of ECMO use in Germany observed the temporal trends and the increasing utilisation of VA-ECMO for cardiac failure (Karagiannidis et al., 2016).

The study noted that rate of both VV and VA-ECMO had significantly increased between 2007 and 2014. The authors noted that while VV-ECMO had plateaued, the use of VA increased to the point where the population rate had exceeded that of VV indications. Further, the authors noted the in-hospital mortality rates decreased over the study period. There are no networks in Germany restricting ECMO treatment to specialised reference centres, with the authors suggesting the lack of such a network contributed to the mortality rates.

## Single site studies

As noted, in Victoria, The Alfred Hospital acts as the main referral centre. In 2017, a case-series study of 198 patients found that 6-month survival rates were not significantly different when the outcomes of retrieved patients were compared to ECMO centre patients (Burrell et al., 2018):

A single site study in the United States reported the experience of receiving 100 ECMO retrievals (Biscotti et al., 2015). The retrieval team successfully cannulated patients from interstate and international sites, the majority of which were placed on VV-ECMO (n=79).

A further single site study reported the outcomes of 221 transferred patients between 1990 and 2012 (Bryner et al., 2014). The authors were able to demonstrate that survival of transported patients was not significantly different compared with all ECMO procedures.

A French study explored the outcomes of a program that provided circulatory support distant from specialised ECMO centres, for patients with refractory cardiogenic shock in remote locations in France (Beurtheret et al., 2013). Eighty-seven patients were eligible for the program, 75 of who were successful transferred to tertiary care centre. The survival rate was 36.6 per cent, with comparable outcomes to 123 consecutive patients who received ECMO at a single tertiary care centre during the same period.

A review of the Swedish model of retrieval discussed the outcomes of more than 700 transferred patients (Broman et al., 2015). Between 2010 and 2013, the ECMO mobile team was dispatched 387 times covering a range between 6.9 and 13,447, of which the majority were primary transfers (n=282). The authors found no deaths occurred during transports between 2010 and 2013, and no differences were seen in mortality rates in any age group or category (pulmonary, cardiac or extracorporeal cardiopulmonary resuscitation) compared with in-hospital patients.

A further study explored the outcomes of 17 patients that were successfully cannulated and placed on a simplified ECMO circuit at other institutions and transported via ambulance to a single referral centres (Javidfar et al., 2011). The majority of patients had acute respiratory failure (n=14) and were placed on VV-ECMO, the remaining had VA-ECMO. The authors found no transport-related morbidity or mortality.

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## ECMO USE FOLLOWING THE H1N1 INFLUENZA PANDEMIC

An Australian paper reported the use of ECMO in response to the pandemic in 2009 (Davies et al, 2009). Sixty-eight patients with suspected H1N1 were admitted to 15 ICUs for ECMO between 1 June and 31 August 2009. The authors noted the advantageous effect that regional referral centres had on outcomes. Although some patients remained under observation at publication, there was a 21 per cent mortality rate for patients. Centralisation of patients meant 15 of the 200 ICUs managed these patients, with clear eligibility criteria.

An Italian paper reported the impact on their ICU network between 2009 and 2010 (Patroniti et al., 2011). The Italian service had 14 ICUs with ECMO capability with a national call centre. In response to the pandemic, the Italian network centralised severe patients to these ECMOnet centres – 153 patients with suspected H1N1 were admitted to one of the 14 ICUs, 60 of these patients received ECMO. There was a 68.3 per cent survival rate at discharge. Seventy-one patients were transferred, of which 28 were on ECMO. The authors concluded that the centralisation of these patients improved survival rates and provided a mechanism for safe and effective transfers.

In the United Kingdom, patients with suspected H1N1 were transferred to one of four ECMO centres (Noah et al., 2011). During the pandemic, 80 patients were deemed eligible for EMCO of which 69 received ECMO and 22 died prior to discharge. The authors used propensity score matching to compare ECMO referred and non-ECMO referred patient outcomes, finding mortality rates of 24.0 per cent versus 46.7 per cent, respectively (RR, 0.51 [95% CI, 0.31-0.81]). The authors concluded that referral to ECMO sites was associated with improved outcomes for this cohort of patients.

## 4. The ECMO procedure

Although ECMO is widely acknowledged as an option for acute heart failure and severe respiratory impairment, most international commissioners have taken steps to restrict its use citing uncertain evidence of benefit, cost and complexity. Most developed countries offer some form of ECMO but there is no consensus on the benefits or harms of the procedure.

### USE OF ECMO

While there is debate in the sector on the effectiveness of ECMO, there has been a marked increase in the use ECMO in Victoria and internationally. This trend is expected to continue in the use of the ECMO as a potentially lifesaving intervention.

Over the past five years the use of adult ECMO in Victoria has doubled, with a particularly rapid increase observed in VA-ECMO for cardiovascular indications. With increased use, the number of sites undertaking ECMO has also risen – with multiple sites initiating fewer than five procedures each year.

It is also widely anticipated that there will be rise in ECPR procedures in the near future. International and domestic observational studies show advantageous outcomes for unresponsive patients and a number of European randomised controlled trials are in development. The CHEER trail demonstrated that ECPR is an effective option in Victoria. However, it is only currently available in The Alfred Hospital's catchment. Although Barwon Health has recently commenced an ECPR program, there remains little availability for much of metropolitan Melbourne and almost all of regional Victoria.

The maintenance of patients on ECMO is resource intensive. Patients require 1:1 nursing and, often, on-site medical supervision. While ECMO can be initiated and maintained for a short period of time, services can face difficulties with patients on prolonged support where there is a limited accredited workforce able to maintain effective ECMO intervention.

### ECMO outcomes

As noted in a recent International ELSO report (at July 2018), survival rates are highest for VV-ECMO indications, with the lowest expected survival rates for ECPR procedures.

**Table 8 Indications for ECMO reported to ELSO**

ECMO procedures	Total runs of ECMO	Inpatient mortality rate
Pulmonary	16,337	41%
Cardiac	15,942	58%
ECPR	4,952	71%

ELSO international report (2018)

When assessing the use of ECMO, it may also be pragmatic to differentiate between the initiation of ECMO, the maintenance of the therapy and the weaning from ECMO to discharge. A retrospective study reviewed the duration of VA-ECMO from data reported to the ELSO registry (Smith et al., 2017). The mortality rates were highest in the early stages of ECMO, with increasing survival up to four days. However, after four days, the survival rates began to decrease again.

The authors noted that the higher mortality rates during first days of ECMO reflect the treatment failure, with the optimal four days correlating with the amount of time to 'bridge' the period of cardiogenic shock. During the first day, the authors also noted that fatal hemorrhage was disproportionately represented – suggesting that risk may be highest in the initiation phase of ECMO.

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The duration of VV-ECMO for acute respiratory failure is generally thought to be longer than VA-ECMO intervention. A review of the ELSO database found that the median duration of ECMO was 25.2 days, with favorable survival rates for prolonged support (Poslisszny et al., 2016).

### **VV-ECMO**

ECMO interventions in patients with acute respiratory failure have historically been the subject of investigational studies. A prominent example was the CESAR study in the United Kingdom which randomised patients with acute respiratory failure to receive ECMO or conventional management (Peek et al., 2009).

The study found six-month survival rates were significantly higher in those that received ECMO (relative risk 0.69; 95% CI 0.05 to 0.97). The authors noted that ECMO, while expensive, was cost-effective under the NHS willingness to pay model. This type of intervention, however, rapidly expanded following the H1N1 influenza pandemic (between 2009 and 2011). Multiple retrospective international and domestic studies showed comparative benefits when ECMO was compared to conventional therapies during the outbreak, along with marked increase in use.

More recently the use of VV-ECMO has stabilised to the point where runs of VA-ECMO are more common. The prognosis of patients on VV-ECMO is often multifaceted compared to other types, it involves more complex support and can require the resources to maintain therapy for one to two months. This is reflected in our analysis which has shown longer lengths of stay in ICU and higher proportion of patients transferred to The Alfred Hospital for sustained therapy. The ELSO recommendations acknowledged this complexity in their recommendations for sites offering VV-ECMO should achieve an annual volume of 12 procedures.

As noted, VV-ECMO support is almost never required in an emergency, unlike many patients indicated for VA-ECMO. This means that there is often enough time to facilitate referral and retrieval, often prior to the initiation of ECMO.

### **VA-ECMO**

The use of ECMO for cardiovascular care has rapidly increased in most developed countries over the past five years. This rise can partially be explained following the findings of the SHOCK-II trial which showed that intra-aortic balloon counterpulsation did not significantly reduce 30-day mortality in patients with cardiogenic shock complicating acute myocardial infarction for who an early revascularisation strategy was planned (Thiele et al., 2012).

Where the use of intra-aortic balloons has diminished, VA-ECMO has filled the gap as an emergency cardiac intervention.

Despite increased use, uncertainties around the benefits and indications for VA-ECMO for cardiovascular intervention remain. Retrospective observational studies have shown benefits for some patients with a range of cardiac complications but there is still a requirement for high quality evidence showing conclusive advantages with the use of VA-ECMO, along with consistent eligibility criteria and etiology (Combes et al., 2017).

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## ECPR

As with the increase in all cases of VA-ECMO, the use of ECPR (a subset of VA ECMO cases) has grown progressively over recent years. Although it is acknowledged that such interventions can be lifesaving for otherwise unsalvageable cardiac arrest patients, the eligibility criteria and indications are also yet to be agreed by international and domestic regulators.

Some observational studies, notably undertaken in Japan (Kagawa et al., 2012), have shown that where ECPR is used within established time sensitive protocols it can be an effective intervention for unresponsive cardiac arrest patients. However, randomised controlled trials are still required to definitively demonstrate effectiveness.

Geography of populations dictates that such emergency use of ECMO will not be able to be completely centralised, and ambulance options for transfer to hospitals undertaking this procedure are currently limited in Victoria.

The potential development of accredited sites which can initiate ECMO and stabilise patients prior to transfer may also address this issue and increase equity of access for patients in urgent need of this therapy.

In current practice, ECPR is typically only undertaken at the treating hospital. Although there are trials exploring mobile ECPR teams, these types of interventions are not feasible for a contemporary Victorian model of care.

## 5. SCV reference group

### SCV reference group

Between December 2017 and June 2018, SCV established a reference group to advise on the delivery of ECMO across the state. The reference group included representatives from all the major ECMO providers in Victoria. The report from the group can be found at **Appendix 4**.

The key message from the report was that ECMO should be provided through a tiered, networked, accredited model. The group's recommendations are in **Table 9**. This report builds on the advice of the reference group, with the following alterations to the proposed tiered model:

- Stream 1 (high-volume) services are designated as coordinated care centres with the additional requirement to provide long-term heart replacement therapies.
- Stream 2 (medium-volume) services are designated as Intermediate ECMO Centres. In order to increase local access, the recommendations in this report have emphasised the retrieval and referral responsibilities of these services (including ECPR).
- The recommendations in this report note that stream 3 (low-volume services) should only initiate ECMO, pending transfer.
- The recommendation for retrieval and transfer will actually require the current service to be expanded under the new Victorian ECMO Service
- The ECMO advice line to The Alfred Hospital ICU clinicians recommended by the reference group is administered through the Victorian ECMO Service with shared responsibility across participating members based at Comprehensive and Intermediate ECMO Centres.

**Table 9 Recommendations from SCV working group report**

Patient journey	Recommendation	Problem to solve
<b>Access and assessment</b>	Standardise advice process: clinicians call and rapidly access experts from The Alfred Hospital (Stream 1) to seek advice	Untimely referral – sentinel event
<b>Care and treatment</b>	Standardise criteria, accreditation: provide agreed criteria that provides clearer decision making for appropriate use of ECMO	Multiple services perform ECMO No agreed accreditation for service delivery
<b>Retrieval and transfer</b>	Status quo	Nil. Currently coordinated via Adult Retrieval Victoria
<b>Outcomes</b>	Measured dataset: activity, safety, quality data for benchmarking and monitoring patient outcomes	Limited to compare activity data

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## A TIERED, COLLABORATIVE MODEL FOR VICTORIA

Internationally, regulations have been introduced around ECMO use; often restricting these services to high-volume sites with the use of an integrated national/regional retrieval network.

Victoria has no such formalised regulations in place, leading to a current model that is increasingly at odds with the volume and direction of published literature.

### Centralisation of high-risk, low-volume procedures

The principle of a volume–outcome relationship came to prominence in the 1980s following the paper published by Luft and colleagues in the United States (Luft et al., 1987). In the early-2000s, Birkmeyer and colleagues published their landmark study showing hospital volume’s effect on a range of high-risk cardiac and cancer procedures (Birkmeyer et al., 2002). This paper and others led to many international system regulators opting to centralise high-risk, low-volume services in order to improve their population’s outcomes.

While there are relatively few studies that have explored volume–outcome relationships for ECMO services, there has been more research undertaken in comparable procedures.

The designation of specialist centres to manage acute emergency patients is well established for trauma services in Victoria and internationally. This is underpinned by strong evidence that centralisation to high-volume providers improves mortality and morbidity outcomes (Demetriades et al., 2005; Nathens et al., 2001).

There are also models employed in other countries that already centralise patients requiring intervention following cardiac arrest (notably primary percutaneous coronary intervention) that, again, are based on studies showing beneficial outcomes when treated a high volume specialist services (Tranberg et al., 2017; Kajino et al., 2010; Nichol et al., 2008).

### Key message

In Victoria, it is unclear what the delivery of ECMO looks like in practice given the limitations of the data available. Advice from the reference group suggests it is likely that many of the hospitals currently offering ECMO provide a limited service. It is also likely that a proportion of hospitals choose to provide ECMO procedures for selected indications, only provide ECMO for a short period following initiation and/or transfer patients who need to be weaned from ECMO following extended lengths of stay in ICU.

A well-developed Victorian accreditation service with a clear ECMO service delivery model has been shown to improve outcomes of ECMO and safely increase the scope of practice for the service. It is likely that the implementation of Intermediate ECMO Centre criteria will require some sites to review their ECMO service and make changes to the governance model they currently operate under – while in the short term this may require some investment the benefits will justify the effort with accredited sites being able to deliver ECMO to wider patient cohort and benefit from the collaborative model to minimise patient risk.

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## Safety in higher volumes

There is international evidence that demonstrated higher volume ECMO sites have better survival rates. Despite the few studies that have explored volume relationships, most regulators acknowledge that beneficial ECMO treatment is associated with higher procedural volume and centralisation – noting the expertise, infrastructure and workforce requirements to manage ECMO effectively.

A review of five-year admission data in the VAED demonstrates that, even within the limited Victorian sample size, a volume effect appears evident with better survival rates at large-volume sites. Although risk adjustment is difficult with the current dataset's limitations, when retrievals were accounted for within inpatient mortality rates and when 30-day mortality rates are observed there are statistically significant differences when the highest volume site's outcomes are compared against the rest of the state.

We also reviewed the influence of multiple variables on the expected mortality rates. Lower rates of mortality in transplant patients potentially affected the observed volume-outcome effect. However, it is noted that influence of these patients may be counterbalanced by those treated with ECPR at the same site, which are known to have higher mortality rates when compared to VV and VA-ECMO. Without risk adjustment it is impossible to ascertain the absolute impact of these two patient groups.

As noted, it is difficult to draw robust conclusions in the absence of detailed analysis of confounding factors, patient characteristics, retrieval models, procedural complexity and selection bias. Unfortunately, no registry data can support this review although the forthcoming multiagency review into cardiac arrest may provide more granularity.

In addition to the mortality analyses, the CHADx review found that peri-operative adverse events were largely less common at higher volume sites. Furthermore, the analysis highlighted that some lower volume sites are likely to have undertaken limited types of ECMO or had a different patient casemix.

## Expanding ECMO use

International regulatory bodies have recognised the expanding use of ECMO in developed countries. The International ECMO Network and ELSO have produced position papers for ECMO for acute respiratory failure and cardiac failure, with both advocating the restriction of ECMO centres and the use of a coordinated nationwide or regional retrieval and referral networks. Notable ECMO networks have also been established in the United Kingdom, Italy and New Zealand – all of which restrict the use of ECMO to high-volume accredited sites with clear retrieval models to ensure national access.

The most recent international position paper for the organisation of ECMO programs for cardiac failure in adults stressed the importance cooperation and coordination between hospitals providing ECMO. Similar sentiments are shared throughout regulatory policies and the literature; with most noting that appropriate, safe and effective ECMO requires strong regional and/or national collaboration between sites.

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In the Victorian model there is no such formalised collaboration, with many sites undertaking ECMO in isolation and little communication or support shared between low and high-volume sites.

The number of Victorian sites that initiated ECMO is also high compared to international examples, given our population. In 2016–17, 16 Victorian hospitals initiated ECMO at least once. Whereas in Italy 14 sites manage the national ECMO demand and in the United Kingdom less than 10 sites undertake ECMO. The ratio between catchment size and placement of ECMO services was raised in the ELSO guidelines for ECMO centres, which noted that hospitals should be placed within a catchment that can maintain at least six procedures a year. In 2016–17, six Victorian sites met this threshold.

The current delivery of ECMO in Victoria is largely centralised to metro hospitals. In regional Victoria, just one site has a sustained ECMO program with a minority of ECMO procedures delivered by other hospitals outside of Melbourne. Under this arrangement, it is likely that the number of sites providing ECMO for the metropolitan population exceeds the demand. Conversely, there may be legitimate concerns around the access for regional Victoria with very few sites offering an ECMO service. Although all regional services are unlikely to reach a suitable annual volume, there is evidence to suggest a viable program can exist in selected regional sites.

Finally, if outcomes of ECMO improve, there is likely to be an impact on ICU lengths of stay. Patients who do not survive typically die within a week on ECMO, whereas patients with successful interventions will remain in intensive care for a prolonged amount of time. It is therefore reasonable to hypothesise that improved outcomes across the state will require more resource for the current cohort, in addition to ECMO being provided to additional patients.

## Procedure types

The literature around ECMO often differentiates between procedure types, often advocating separate recommendations and models of care for each. Patients with respiratory indications will typically require VV-ECMO; these patients generally have higher survival rates but are typically on ECMO for a longer amount of time. Patients with deteriorating respiratory function, who are indicated for VV-ECMO, often have some time to manage their condition with other interventions prior to ECMO – thereby it is feasible that such patients can be transferred prior to ECMO initiation. Such an approach is likely to be advantageous given the amount of time most will be on ECMO.

VA-ECMO is typically used in patients with cardiovascular complications, most commonly progressive cardiogenic shock. These indications often require time-critical ECMO intervention following the rapid deterioration of the patient. The length of time on VA-ECMO is usually shorter than VV-ECMO, with most patients requiring support while recovering from an acute cardiac event. Many patients that require VA-ECMO will often be indicated while in admitted care – whether post-operatively or in intensive care – where VA-ECMO is used to bridge patients while the underlying pathology is attended to. A smaller cohort of patients may require extended VA-ECMO where long-term heart therapies are indicated – for example, those requiring a transplant or a ventricular assist device. Initiation of VA-ECMO is thought to be the highest risk part of the procedure – with survival rates increasing from initiation towards four to five days on ECMO.

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It is therefore important that the decision to undertake VA-ECMO is made quickly and undertaken (or supported) by experienced practitioners.

ECPR is indicated for unresponsive patients to restore circulation during cardiac arrest. A notable difference between VA-ECMO and ECPR is the location in which the procedure can be initiated. There may be a significant proportion of patients that will require ECPR in a pre-hospital setting. Further research is needed to explore whether an out-of-hospital ECPR program is feasible in Victoria, noting the limited evidence of benefit and the significant resource cost to implement such a model.

### **Patient transfer**

Transfer of patients while on ECMO is often compared to retrieval models for trauma patients and neonates. Similar to these models, patient outcomes are often better when patients are transferred to a capable, high-volume, site prior to intervention. While this may be practical for some patients indicated for VV-ECMO, many patients requiring VA-ECMO and ECPR require immediate intervention. Therefore, ECMO protocols require the ability to initiate ECMO at non-referral centres that manage high-risk patients (notably those services that undertake cardiac surgery and/or receive patients indicated for primary percutaneous coronary intervention. In such scenarios the collaboration with and support from the Victorian ECMO Service is important, so that transfer of patients while on ECMO is appropriate. Such models have been shown to be effective, with international studies demonstrating no worse outcomes for transferred patients when compared to those initiated at a high-volume accredited hospital.

### **Interaction with DHHS capability frameworks and policy**

The delivery model for ECMO will be a standalone policy. However, there are likely to be interactions with DHHS capability frameworks, currently in development.

The most notable crossover will likely be with the Cardiac Capability Framework and the service specifications for cardiac surgery and primary PCI sites. It is not pragmatic for all cardiac surgery services to be an accredited ECMO service, however all cardiac surgery services should be able to initiate short-term peri-operative ECMO in the event of a critical surgical complication.

The recommendations in this report support short-term ECMO in such sites, however these patients must be managed with advice from the ECMO collaborative and will almost always need to be transferred to a Comprehensive or Intermediate ECMO Centre within a short timeframe. A similar arrangement may also be pragmatic for high-volume PCI centres managing acute, time-critical patients.

In addition to the forthcoming capability frameworks, we found value in comparing our proposed model to that implemented for the Victorian State Trauma System (VSTS). The recommendations proposed mirror much of the effective standards used in VSTS. Both suggest designating specialist sites, utilise a statewide system organisation and management of trauma response and offer enhanced retrieval and transfer services

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## Review limitations

In Victoria there is no current registry that reports ECMO outcomes, although this will be provided from 2018 within the ANZICS-CORE dataset.

Therefore, our data analysis is restricted to VAED, which has a single procedure code for ECMO. Although the VAED is able to provide a comprehensive count of procedures, the type of procedure or the complexity of the patient is unclear.

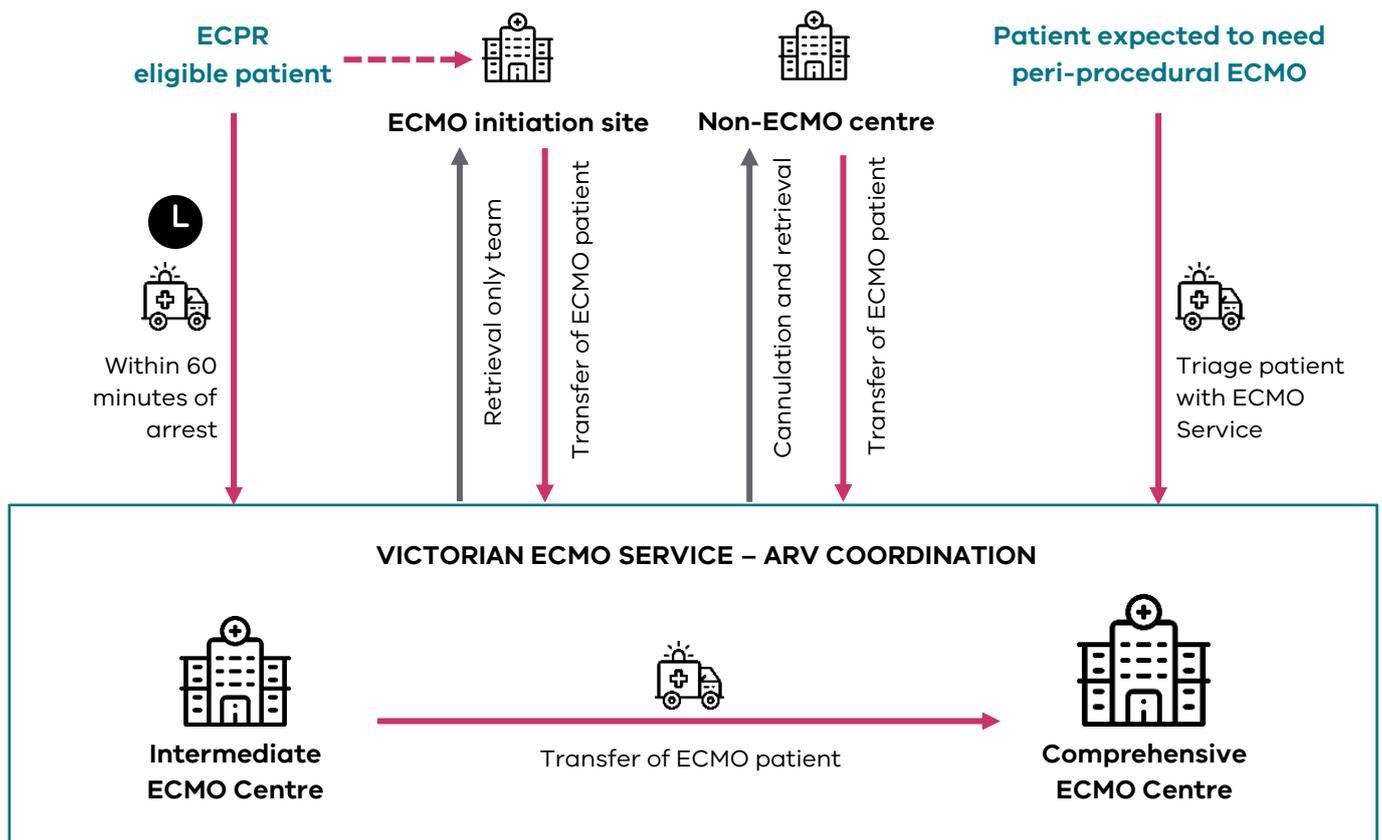
In order to describe a volume-outcome association, we used limited measures to adjust for some procedural risk factors. Nevertheless, it is not possible to totally adjust for contributing factors without multivariate regression modelling, particularly to mitigate the effect of the treated condition on survival rates.

Selection bias may also affect outcomes particularly where retrieval is required and/or health service capability is variable. For example, eligible patients may not receive ECMO at all (and therefore excluded from analysis) or ECMO may be delivered as a very last resort. Timing of procedure and indications were not available in our dataset.

The VAED is also unable to accurately differentiate between the different types of ECMO, this is important as retrospective analysis of international registry data has shown higher mortality rates for VA-ECMO and ECPR procedures. Furthermore, the movement and escalation of patients to established high-volume sites may bias our view of peer-to-peer mortality rates. It is impossible to determine the retrieval method for transfers in the VAED and often the underlying pathology of the patient that transferred is unclear.

# Appendix 1

## ECMO RETRIEVAL PATHWAY



# Appendix 2

## 2016-17 analysis of ECMO service provision

The following table outlines the delivery of ECMO over the past year captured in our analysis, the volumes at each health service are reflective of the typical service distribution. However, we note the the 95 per cent confidence interval of observed mortality rates are wide and overlap and therefore we cannot conclude there is any significant difference between sites.

Campus name	Number ECMO separations	Number ECMO patients transferred	Number deaths at 30 days	30-day mortality rate (%)	95% confidence interval
<b>The Alfred Hospital (Prahran)</b>	76	0	32	42%	31%-59%
<b>University Hospital Geelong</b>	16	2	6	38%	15% - 65%
<b>Monash Medical Centre (Clayton)</b>	14	2	11	79%	49% - 95%
<b>Austin Hospital</b>	10	1	5	50%	19% - 81%
<b>Royal Melbourne Hospital (City Campus)</b>	10	3	5	50%	19% - 81%
<b>St Vincent's Hospital</b>	6	0	4	67%	22% - 96%
<b>Epworth Hospital (Richmond)</b>	3	0	0	0%	0 - 71%
<b>Northern Hospital (Epping)</b>	2	0	1	50%	1% - 99%
<b>Knox Private Hospital (Wantirna)</b>	1	0	1	100%	3% - 100%
<b>Frankston Hospital</b>	1	1	0	0%	0 -98%
<b>Dandenong Hospital</b>	1	1	0	0%	0 -98%
<b>Jessie McPherson Private Hospital (Clayton)</b>	1	0	1	100%	3% - 100%
<b>Sunshine Hospital</b>	1	1	0	0%	0 -98%
<b>Epworth Eastern Hospital</b>	1	0	1	100%	3% - 100%
<b>Peninsula Private Hospital (Frankston)</b>	1	0	0	0%	0 -98%
<b>Box Hill Hospital</b>	1	1	0	0%	0 -98%

VAED: all separations 1 July 2016 to 30 June 2017 and Births Deaths and Marriages Registry.

## Sensitivity analysis after exclusion of outlier institutions

A series of sensitivity analyses were undertaken to further examine the observed volume-outcome relationship.

The volume-outcome relationship (lower mortality at higher volume sites) persisted after exclusion of outlier institutions.

As noted in main report we found (a) service(s) that had mortality rate(s) that were above the upper control limits. We re-ran our analyses with these service(s) excluded to remove the influence this site may have on our findings. As presented in **Tables A** and **B**, the exclusion had no influence on the significance of the outcomes or presence of the volume-outcome relationship described in the main report.

**Table A The pooled outcomes across the rest of the state versus The Alfred Hospital with the outlying site excluded**

Mortality measure	Pooled outcomes for the rest of the state	The Alfred Hospital	Odds ratio (95% confidence interval)
<b>Inpatient</b>	46% (n=97/210)	42% (n=131/310)	1.17 (0.82 to 1.67 [P=0.37])
<b>Inpatient adjusted for post-transfer outcomes</b>	53% (n=112/210)	42% (n=131/310)	1.56 (1.10 to 2.22 [P=0.013])
<b>30-day mortality</b>	52% (n=109/210)	43% (n=132/310)	1.46 (1.02 to 2.07 [P=0.036])

**Table B Pooled outcomes for low-volume services (<10 procedures over 5 years) versus medium-volume services (>10 procedures over 5 years) (outlying service excluded)**

Mortality measure	Low-volume services (<10 procedures over 5 years)	Services >10 procedures over 5 years) (Alfred and outlying service excluded)	Odds ratio (95% confidence interval)
<b>Inpatient</b>	47% (n=27/58)	46% (n=70/152)	1.02 (0.56 to 1.87 [P=0.95])
<b>Inpatient adjusted for post-transfer outcomes</b>	59% (n=34/58)	51% (n=78/152)	1.34 (0.73 to 2.48 [P=0.34])
<b>30-day mortality</b>	52% (n=30/58)	52% (n=79/152)	0.99 (0.54 to 1.81 [P=0.97])

## Patient factor sensitivity analysis

The volume-outcome relationship (lower mortality at higher volume sites) persisted after accounting for different patient types at each institution.

### Respiratory versus cardiac indications for ECMO

In the overview section above, we identified that mortality rates were significantly different when cardiac indications were compared to respiratory causes. Respiratory conditions often require VV-ECMO whereas cardiac indications are more commonly associated with VA-ECMO. However, coding within the VAED data does not specifically differentiate between the different types of ECMO.

The number/proportion, 30-day mortality and mean length of time spent in ICU for each of the cardiac and respiratory groups are shown in table C. Patients with respiratory disease diagnoses spent longer in ICU and had lower 30-day mortality. Furthermore, the transfer rates for continued ECMO provision for the two different diagnoses were both 15 per cent. Although small numbers limit statistical comparisons, there was a consistent trend to better outcomes at a higher volume centre for both diagnostic groups.

**Table C Variation in principle diagnoses and ECMO use (medium/high volume sites only)**

Health Service	No. ECMO separations	Respiratory Disease Principle diagnosis			Cardiac Disease Principle diagnosis		
		Proportion of cases (%)	30-day mortality	Mean ICU hours	Proportion of cases (%)	30-day mortality	Mean ICU hours
<b>Alfred, The [Pahran]</b>	310	23%	37%	545	54%	46%	395
<b>University Hospital Geelong</b>	49	16%	38%	474	65%	44%	346
<b>Monash Medical Centre [Clayton]</b>	43	9%	75%	286	74%	84%	160
<b>Austin Hospital</b>	39	13%	20%	510	74%	48%	343
<b>St Vincent's Hospital</b>	34	15%	20%	685	56%	74%	135
<b>Royal Melbourne Hospital [City Campus]</b>	30	10%	100%	32	53%	69%	132
<b>All ECMO procedures</b>	563	20%	37%	488	59	54%	314

## Other subgroups examined

### CABG Surgery

VA-ECMO can be used for patients following CABG surgery, often for a limited amount to support the intervention. Over the past five years, approximately 10 per cent of ECMO separations had a CABG procedure reported in prior to ECMO (table D). The mortality rate in these patients was slightly higher, although the difference was not statistically significant.

**Table D ECMO after coronary artery bypass graft (CABG) surgery**

Admission type	Number of separations	Inpatient mortality rate	30-day mortality rate
ECMO undertaken before or without concomitant CABG	499	44% (n=219)	47% (n=236)
ECMO undertaken after CABG procedures	64	56% (n=36)	59% (n=38)

### Elective versus emergency admissions

Patients that require ECMO do so because they are critically unwell. Patients admitted electively may be more likely to have ECMO as part of a planned treatment plan. In comparison, patients that are listed as emergency admissions may have received ECMO without such planning and may be a higher risk group (e.g. ECPR) This may affect measured survival rates. However, when inpatient and 30-day mortality rates were observed for each admission type, the mortality rate was similar for both elective and emergency procedures. The similarity in outcomes may be partially explained by the nature of ECMO, which is seldom considered "elective" in practice. Patients may be electively admitted (for example to undergo a cardiac bypass procedure) and require urgent ECMO during their admission.

**Table E Number of separations and mortality rates by admissions type**

Admission type	Number of separations	Inpatient mortality rate	30-day mortality rate
Emergency	412	44% (n=180)	49% (n=197)
Elective*	151	50% (n=75)	51% (n=77)

VAED: all separations 1 July 2012 to September 2017

\*includes VAED admission type: Planned admission – waiting list, other planned admission, Elective admission

### Transferred versus same site ECMO patients

Similar to the route of admission, there may have been differences in the outcomes of patients that were transferred versus those that remained at the treating hospital.

There were 43 patients listed in the VAED as retrieved on ECMO over the five-year study period, of which, all but one of these patients were transferred to The Alfred Hospital. As the table below notes, the mortality rates are slightly higher in the transferred cohort. However, there is no statistically significant difference between the two groups.

**Table F Number of separations and mortality rates by transfer type (5 year)**

Admission type	Number of separations	Inpatient mortality rate	30-day mortality rate
<b>Transferred with ECMO to The Alfred Hospital</b>	42	48% (n=20)	50% (n=21)
<b>ECMO initiated at The Alfred Hospital</b>	268	41% (n=111)	41% (n=111)

Alfred Health recently compared the outcomes of primary retrieved patients (cannulation by a high-volume ECMO centre retrieval team) against secondary retrieved patients (initiation of ECMO by a low-volume ECMO centre team followed by transport). They found both primary and secondary VA-ECMO retrieval were associated with similar initial lactate levels, ECMO duration and mortality. However, higher complication rates were found with higher rates of bleeding (22 per cent vs 64 per cent,  $p=0.001$ ), vascular complications (13% vs 46%,  $p=0.004$ ) and sepsis (26 per cent vs 67 per cent,  $p=0.001$ ) in secondary retrievals. As VAED cannot determine whether ECMO was initiated by a retrieval team, this analysis cannot be replicated.

Of the 43 patients listed in the VAED as retrieved with ECMO, there were differences in the mortality rates depending on the length of stay at the intensive care unit (ICU) prior to the retrieval. The shorter length of stay prior to transfer appears to be associated with a higher the likelihood of death. This likely reflects underlying patient illness severity.

**Table G Number of separations and mortality rates of transferred patients depending on length of stay in ICU prior to retrieval.**

Length of stay in ICU prior to retrieval	Number of separations	Inpatient mortality rate	30-day mortality rate
<b>All transfers</b>	44	48% (n=20)	50% (n=21)
<b>&gt;24 ICU hours prior to transfer</b>	28	35% (n=10)	39% (n=11)
<b>1-24 ICU hours prior to transfer</b>	14	64% (n=9)	64% (n=9)
<b>No ICU hours prior to transfer</b>	1	100% (n=1)	100% (n=1)

# Appendix 3

## Analysis of hospital acquired complications

In the cases submitted to DHHS by July 10, 2018 for 1 July 2016 to June 30 2018 there were 59 ECMO cases admitted electively across eleven organisations and 249 ECMO cases admitted as emergencies (or statistical transfers within an organisation) across 15 organisations.

We expect that the electively admitted ECMO cases will be cases where the patient is admitted for another treatment (e.g., cardiac surgery) and an event during their hospital stay results in the need for ECMO.

In **Table A**, the list of complications is outlined along with the number of low outliers for each.

**Table A CHADX where multiple low outliers exist for emergency and statistical ECMO admissions**

CHADX LBL	Number of low outliers
CHAPX_03_02 - Packed cells	6
CHAPX_03_08 - Other serum	5
CHAPX_01_01 - Invasive ventilatory support	4
CHAPX_01_02 - Non-Invasive ventilatory support	2
CHAPX_06_01 - Nutrition support	1
CHADX_16_03 - Other nervous system complications	1
CHADX_17_01 - Major symptoms	1
CHAPX_03_03 - Platelets	1
CHADX_04_06 - SIRS and other sepsis	1
CHADX_05_04 - Conduction disturbances / abnormal he	1
CHADX_13_10 - Other neonatal complications	1
CHADX_14_03 - Coagulation defects	1
CHADX_01_19 - Postprocedural disorders: Respiratory	1
CHADX_05_11 - Cardiogenic and other shock	1
CHAPX_07_01 - Fluid management	1
CHADX_13_05 - Aspiration and other respiratory disord	1
CHADX_13_06 - Circulatory disorders of newborn	1
CHADX_13_09 - Gastrointestinal (GI) and feeding dis	1
CHADX_01_04 - Haemorrhage and haematoma (see also Mat	1
CHADX_09_01 - Acute renal failure	1
CHADX_10_03 - Delirium	1

The frequencies (outcomes column) for most events in **Table B** are low that their results are of no clinical significance with the exception of haemorrhage and haematoma, coagulation defects and administration of platelets. In each of these examples the highest volume service had the lowest complication rate when compared to the statewide mean.

The campuses that are low outliers for RBC transfusion all have two or less cases in their cohort. This suggests that these organisations have a different complement of cases or provide a different style of ECMO treatment.

As a way of fast-tracking the analyses we created a listing of all low outliers for emergency and statistical admissions (Table B). As the bar for qualifying as a low outlier (95% CI) is not corrected for multiple tests, the single outliers should be treated with caution.

**Table B All low outliers by campus across the panel of 174 CHADX for emergency and statistical admissions that include ECMO.**

Campus name	CHADX name	Cases	Outcome(s)	Health service rate	Vic outcome(s)	Vic rate
Alfred The [Pahran]	CHADX_01_04 - Haemorrhage and haematoma (see also Mat	98	7	0.07	35	0.14
Alfred The [Pahran]	CHADX_01_19 - Postprocedural disorders: Respiratory	98	0	0.00	11	0.04
Alfred The [Pahran]	CHADX_13_05 - Aspiration and other respiratory disorders	98	0	0.00	20	0.08
Alfred The [Pahran]	CHADX_13_06 - Circulatory disorders of newborn	98	0	0.00	25	0.10
Alfred The [Pahran]	CHADX_13_09 - Gastrointestinal (GI) and feeding dis	98	0	0.00	12	0.05
Alfred The [Pahran]	CHADX_13_10 - Other neonatal complications	98	0	0.00	34	0.14
Alfred The [Pahran]	CHADX_14_03 - Coagulation defects	98	13	0.13	54	0.22
Sunshine Hospital		2	1	0.50	233	0.94
St Vincents Hospital		7	5	0.71	233	0.94
Peninsula Private Hospital [Frankston]	CHAPX_01_01 - Invasive ventilatory support	1	0	0.00	233	0.94
Frankston Hospital		1	0	0.00	233	0.94

Campus name	CHADX name	Cases	Outcome(s)	Health service rate	Vic outcome(s)	Vic rate
Monash Medical Centre [Clayton]	CHAPX_01_02 - Non-Invasive ventilatory support	17	1	0.06	107	0.43
St Vincents Hospital		7	0	0.00	107	0.43
Sunshine Hospital		2	0	0.00	201	0.81
Ballarat Health Services [Base Campus]		1	0	0.00	201	0.81
Dandenong Campus	CHAPX_03_02 - Packed cells	1	0	0.00	201	0.81
Peninsula Private Hospital [Frankston]		1	0	0.00	201	0.81
Box Hill Hospital		1	0	0.00	201	0.81
Frankston Hospital		1	0	0.00	201	0.81
Alfred The [Prahran]	CHAPX_03_03 - Platelets	98	46	0.47	153	0.61
Ballarat Health Services [Base Campus]	CHAPX_03_08 - Other serum	1	0	0.00	209	0.84
Dandenong Campus		1	0	0.00	209	0.84
Peninsula Private Hospital [Frankston]		1	0	0.00	209	0.84
Box Hill Hospital		1	0	0.00	209	0.84
Frankston Hospital		1	0	0.00	209	0.84
Alfred The [Prahran]	CHAPX_06_01 - Nutrition support	98	0	0.00	33	0.13
Alfred The [Prahran]	CHAPX_07_01 - Fluid management	98	0	0.00	20	0.08

# Appendix 4

## ECMO TOWARDS A VICTORIAN STATEWIDE SERVICE

Between December 2017 and June 2018, Safer Care Victoria established a reference group to advise on the delivery of ECMO across the state. The reference group included representatives from all the major ECMO providers in Victoria. The report from the group is provided below. The key message was that ECMO should be provided through a tiered, networked, accredited model. The group's recommendations are in Table 17 and have been used to inform the recommendations in this document.

Ten of these 26 health services only delivered ECMO five or fewer times over the five-year period (VAED). A statewide patient retrieval process exists for adults (Alfred Health) and paediatrics (Royal Children's Hospital). However, there is currently no statewide agreement regarding which health services can safely carry out the procedure, when a patient should be transferred, or a threshold of ECMO procedures.

The purpose of this document is to convey expert clinical opinion solicited by Safer Care Victoria, to inform recommendations for a statewide service that is safe, timely and effective. The intent is to provide this information to the Department of Health and Human Services (the department).

Based on the expert advice from clinicians contained in this report, Safer Care Victoria recommends establishing a statewide ECMO service that includes:

- an ECMO advice line for clinicians to call Alfred Health ICU clinicians
- agreed patient indicators for Venous-arterial (VA) and Venous-venous (VV) ECMO procedures
- clear guidance related to number of ECMO procedures per year:
  - **health services with low volume of ECMO procedures:** accredited to deliver the procedure, may initiate ECMO, must then ensure the patient is retrieved to Alfred Health for ongoing care
  - **health services with medium volume of ECMO procedures:** accredited, can initiate ECMO and deliver ongoing care
  - **health services with high volume of ECMO procedures:** Alfred Health, accredited to initiate, sustain and retrieve.

A small workgroup was convened to oversee the consultation. Their recommendations are outlined below. This work focuses on adult ECMO services. However, there is potential to outline the same for paediatrics services.

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## Principles and criteria

One of the key elements identified by clinicians is the need to have clear principles and criteria for the appropriate use of ECMO, including:

- equity of access (versus institutional experience)
- acknowledging important differences between VA and VV-ECMO
- the importance of rapid referral and delivery of service both between and within a hospital
- a defined, consistent referral process
- consistent models of care in order to minimise ECMO related morbidity/mortality
- coordinated, timely and safe retrieval
- clear indications/contraindications adjusted according to outcome data.

Currently there is some information regarding criteria available via The Alfred Hospital website.

However, further work is required to ensure that all providers of ECMO agree on the following criteria for patient selection:

- Dependent on anticipated mode (VA versus VV) of ECMO support.
- Reversible severe illness where survival is possible.
- Severe illness which may not be reversible, but destination therapy (e.g. ventricular assist device) is available/possible.
- Severe illness, but reversibility unclear (bridge to a decision).

## Model and processes

The clinician workgroup identified that a statewide service should be: **Tiered, Networked, and Accredited**. This means there is a clear relationship between Alfred Health and other health services delivering ECMO in a model that uses agreed rules. A **tiered** system means that Victorian health services are categorised into tiers (streams) based on their number of ECMO procedures or volume:

- **Stream 1 (high volume, Alfred Health):** Initiate, sustain and retrieve VA, VV and extracorporeal cardiopulmonary resuscitation (ECPR).
- **Stream 2 (medium volume):** Initiate and sustain selected ECMO. Accredited Stream 2 services may potentially receive patients retrieved by Stream 1/Alfred Health.
- **Stream 3 (low volume):**
  - (a) Initiate ECMO and transfer the patient to Alfred Health
  - (b) Stream 1 health service attends the stream 3 health service to initiate ECMO and retrieve the patient.

Each of the streams would be connected or **networked** to a higher stream, to reduce patient complications often seen in health services with a low volume of ECMO procedures.

Common patient complications can be avoided by seeking expert advice within agreed timeframes. The advantage of a networked system is that it can reduce unnecessary ECMO use (early transfer may result in ECMO not being required, as other procedures/therapies can be delivered instead) and decrease costs.

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A networked model would achieve:

- standard ECMO clinical practice
- early completion of patient assessment and clinical advice, and improved patient outcomes
- full consideration of the patient's incidence of disease.

An accredited model ensures that before a health service delivers ECMO, they have undergone appropriate **accreditation** to deliver the procedure safely. Accreditation requires the health service to:

- have dedicated staff/defined roles
- address the complexity
- use best available staff.

### What does this look like practically?

In practice, a Stream 1 ICU would have an agreement with a Stream 2 ICU to provide clear referral, advice, training and support for Stream 2 to achieve accreditation of an ECMO service. This would increase safe and timely patient-centred care. In this model the retrieval would remain centrally with ARV and Alfred Health (not for paediatrics, as that is outside the scope of this work).

A tiered, networked and accredited model would lead to earlier assessment, meaning the patient could be transferred before ECMO delivery, and may result in ECMO not being required.

## Dataset and training

Currently the only information on ECMO is department datasets (VAED) with little regarding the appropriateness, patient outcomes, or timeliness of the procedure. To ensure a safer system, a dataset would encompass a range of markers that support the safety of ECMO, demonstrate improved patient outcomes, and a reduction in complications. Currently this information cannot be effectively reviewed or analysed.

To establish an ECMO dataset, the following points need to be considered:

- ANZICS has commenced work to establish a minimum dataset.
- Extracorporeal Life Support Organization (ELSO) international dataset as the minimum collected by Streams 1 and 2.
- Collection of patient data beyond discharge, as mortality increases post discharge.
- Possible use of patient identifier in databases, to follow up and track outcomes across health services.
- Comparative analysis and benchmarking with other states.
- Possible mandatory submission to this database.

When a procedure carries a high risk but is delivered in low volumes, training is an integral element to ensure it is performed safely and effectively. Clinicians highlighted the below key training considerations:

- A defined training program for ECMO: cannula insertion and ongoing care.
- A minimum number of ECMO procedures per year to maintain cannulation and ongoing care.
- Centralised with provision for satellite training.
- Comprehensive, including assessment, initiating, care and weaning.
- Ensure that the best available personnel are credentialed.

## Recommendations

The four main recommendations each align to a particular phase of the patient journey (outlined in Table 1). The recommendations are designed to counter problems identified at each stage and would be measured as part of the dataset to ensure their effectiveness. Retrieval and transfer are the only component of the patient journey that does not have a recommendation, as it is considered to already be an effective and robust process.

## Problems and associated recommendations

Patient journey	Recommendation	Problem to solve
<b>Access and assessment</b>	Standardise advice process: clinicians call and rapidly access experts from Alfred Health (Stream 1) to seek advice.	Untimely referral - sentinel event
<b>Care and treatment</b>	Standardise criteria, accreditation: provide agreed criteria that provides clearer decision making for appropriate use of ECMO.	Multiple services perform ECMO No agreed accreditation for service delivery
<b>Retrieval and transfer</b>	Status quo	Nil. Currently coordinated via Adult Retrieval Victoria
<b>Outcomes</b>	Measured dataset: activity, safety, quality data for benchmarking and monitoring patient outcomes.	Limited to compare activity data

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## Advice for a cardiac capability framework

The statewide service would be delivered through Stream 1 ICUs, with Stream 2 ICUs as secondary providers (initiate, sustain selected patients, or transfer to Stream 1). Retrieval would only be performed by Alfred Health. Stream 3 services would not deliver ECMO beyond referral and initiation for transfer with retrieval support.

## Options for completing the recommendations

There are a number of mechanisms available to complete the work:

- Alfred Health has received a Better Care Victoria Innovation Grant to support the progression of Recommendation 1: standardised advice process, to reduce delays in seeking expert advice for patients who are critically unwell.
- Establish a subcommittee to complete Recommendation 2: standardise criteria, accreditation.
- Partner with ANZICS national ECMO database development project.
- Use the Department Cardiac Capability Framework to determine health service delivery of ECMO.

## Summary

ECMO is recognised as a high-risk, low-volume procedure with growing rates in Victoria. Key clinicians recommend a **Tiered, Networked, Accredited** Victorian ECMO service would ensure the most safe and effective approach to delivering ECMO in Victoria.

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