A review of paediatric anaesthetic-related mortality, serious adverse events and critical incidents

L Cronjé

Introduction
The trend in perioperative outcome research is to focus on long-term, patient-centred outcomes, such as quality of life and disability-free recovery, rather than just survival. The purpose of this review was to refocus on immediate clinical safety outcomes within 24 hours of anaesthesia ending. There is a significant difference in outcome in developed and developing countries, and the contributory factors are highlighted in this regard. Challenges within the South African healthcare context are deliberated. Anaesthetic-related mortality and cardiac arrest are rare events, hence difficult to study.

Also, true anaesthetic-related mortality could be underestimated, and the effects of safety improvements that are made overestimated, because of methodological problems. Definitions in which multiple categories apply are complex, and standardised definitions do not exist with respect to the timeframe used, method of data acquisition or outcome definitions utilised. Therefore, quoted incidences vary, making comparison between studies difficult, and resulting in potentially misleading conclusions. It is the opinion of the author that simple, but inclusive definitions, are appropriate to research in the developing world. Thinking in “silos” is avoided with the use of inclusive definitions, while a wider range of cases relevant to anaesthetists is included. It has been proposed that researchers should adopt uniform, consensus definitions. It is the opinion of the author that simple, but inclusive definitions, are appropriate to research in the developing world. There is a fine balance between inclusiveness and clarity of definitions, and it is important that definitions are chosen appropriately for the study being conducted.

The importance of studying anaesthetic-related mortality, cardiac arrest and serious adverse events
The most important perioperative trigger for cardiac arrest and morbidity and mortality is the child’s disease or condition. Anaesthetic-related causes are conversely infrequent. It may not be meaningful for patients to separate anaesthetic-related mortality and serious adverse events from other causes, yet the narrow-outcome focus remains important because:

- A baseline assessment of the safety of an anaesthesia service is provided by anaesthetic-related mortality and cardiac arrest.
- High-risk patients are identified, which assists when making informed decisions on patient care.
- Informed consent is enhanced when immediate anaesthetic-related risk is accurately communicated to families and patients.

- System issues are identified which contribute to substandard anaesthetic care, especially in middle- and low-income countries.
- Research is facilitated and can be appropriately directed to improving clinical anaesthetic safety.

Definitions of “anaesthetic-related” mortality, cardiac arrest, serious adverse events and critical incidents
Event triggers or causes are divided into surgery related, patient disease or condition related, and anaesthesia related. Standardised definitions do not exist with respect to the timeframe used, method of data acquisition or outcome definitions utilised. Therefore, quoted incidences vary, making comparison between studies difficult, and resulting in potentially misleading conclusions.

Anaesthetic-related mortality or cardiac arrest
Definitions (Table 1) may be considered to be either restrictive, inclusive or multiple. The contribution of anaesthesia may be underestimated when using restrictive definitions. Thinking in “silos” is avoided with the use of inclusive definitions, while a wider range of cases relevant to anaesthetists is included. Definitions in which multiple categories apply are complex, and are more likely to be subjective. It has been proposed that researchers should adopt uniform, consensus definitions. It is the opinion of the author that simple, but inclusive definitions, are appropriate to research in the developing world.
Table 1: Definitions of anaesthetic-related mortality or cardiac arrest

<table>
<thead>
<tr>
<th>Source</th>
<th>Cardiac arrest deemed to be anaesthesia-related if</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANZCA Mortality Committee13</td>
<td>Category 1: It is reasonably certain that death was caused by the anaesthesia or other factors under the control of the anesthetist</td>
</tr>
<tr>
<td>POCA Registry10,11</td>
<td>Anesthesia personnel or the anaesthesia process played at least some role (ranging from minor to total) in the genesis of cardiac arrest</td>
</tr>
<tr>
<td>Flick et al10</td>
<td>“Inclusive”</td>
</tr>
<tr>
<td>“Restrictive”</td>
<td>It occurred after the initiation of anaesthesia, in which anesthetic management was undoubtedly a cause for cardiac arrest, regardless of severe coexisting disease</td>
</tr>
<tr>
<td>Van der Griend et al13</td>
<td>“Inclusive”</td>
</tr>
<tr>
<td></td>
<td>It is more likely than not that anaesthesia, or factors under the control of the anaesthesiologist, influenced the timing of death</td>
</tr>
</tbody>
</table>

Table 2: Categories of serious adverse events and their definitions14,16

<table>
<thead>
<tr>
<th>Serious adverse events</th>
<th>Category</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>Death</td>
<td>Death during anaesthesia, or within 24 hours of anaesthesia</td>
</tr>
<tr>
<td>Life threatening</td>
<td>Airway event</td>
<td>Severe hypoaxemia or hypercapnia while receiving emergency intubation and medication during anaesthesia, or within 24 hours of anaesthesia</td>
</tr>
<tr>
<td>Life threatening</td>
<td>Cardiac arrest</td>
<td>Bradycardia or hypotension while receiving cardiac compressions during anaesthesia or within 24 hours of anaesthesia</td>
</tr>
<tr>
<td>Disability or incapacity</td>
<td>Awareness anaesthesia</td>
<td>Patient memory of events during general anaesthesia</td>
</tr>
<tr>
<td>Disability or incapacity</td>
<td>Musculoskeletal, joint and cutaneous injury</td>
<td>Injury to muscle, bone, joints, the skin or soft tissue from an anaesthesia care-limiting function, and requiring medical or surgical treatment (includes intravenous infiltration)</td>
</tr>
<tr>
<td>Disability or incapacity</td>
<td>Nervous system injury</td>
<td>Injury to the brain, spinal cord or peripheral nerves unrelated to a surgery - limiting function</td>
</tr>
<tr>
<td>Disability or incapacity</td>
<td>Visual system injury</td>
<td>Injury to the eye or visual pathway unrelated to surgery lasting beyond 24 hours of the anaesthesia</td>
</tr>
<tr>
<td>Disability or incapacity</td>
<td>Wrong surgery</td>
<td>The start of surgery or anaesthesia care on a body part for which consent for the procedure had not been given by the patient</td>
</tr>
<tr>
<td>Hospitisation</td>
<td>Acute lung injury</td>
<td>New-onset impaired gas exchange with parenchyma signs which escalated the care</td>
</tr>
<tr>
<td>Hospitisation or life threatening</td>
<td>Cardiovascular event</td>
<td>Unanticipated cardiovascular support during anaesthesia, or within 24 hours of the anaesthesia, which escalated the care</td>
</tr>
<tr>
<td>Hospitisation</td>
<td>Care escalation</td>
<td>Fire, malignant hyperthermia, medication or an equipment error during anaesthesia care, which escalated the care</td>
</tr>
</tbody>
</table>

The page number in the footer is not for bibliographic referencing

The line between serious adverse events, which measure death, permanent disability and care escalation, and critical incidents. Critical incidents measure a wider variety of events, including “near misses” and have been defined as “any event that affected, or could have affected, the safety of the patient while under the care of an anesthetist from the induction of anaesthesia until discharge from the post-anaesthesia care unit.”25 Discrimination is lacking with the use of adult reporting tools in paediatric events.29 Paediatric-specific monitoring tools have been devised in the Wake Up Safe programme for serious adverse events (Table 2),14,16 and by de Graff et al., for critical incidents.29

Data sources and their limitations

Information is gathered from three main sources, i.e. liability claims, incident-reporting systems (registries) and anaesthetic information systems (databases). Liability claims are subject to outcome bias, and are not always generalisable, but may reflect what families perceive to be unacceptable outcomes.35,36 Incidence cannot be estimated using voluntary registries, which feature selective or inaccurate reporting bias, but can be the source of a large number of cases.28,37-39 Valuable insight into trends and associations has been gained from these sources, and patient safety improved by routine respiratory monitoring and the reduction of preventable cardiac arrest from medication errors.13,35,40

Selection and reporting bias can be overcome with the use of databases and anaesthetic information systems featuring non-voluntary reporting. Large datasets with numerators and denominators for accurate incidence calculation are provided through such systems. Retrospective analysis may lead to inaccuracies, unless the database was designed for the outcome measures sought.15 Comparative analysis is hampered with the use of a case mix and institutional audit with a small sample size.2,27,28,41 Collaborative, prospective collection through paediatric-specific databases facilitates the accurate calculation of incidence, the elucidation of causality and the development of neonatal and paediatric perioperative risk models.16,41-44

Incidence and morbidity risks in paediatric operations

Because of changes in clinical practice and advances in anaesthetic care, data from a systematic review in 2011,12 and from original studies not included in the review or published afterwards, are summarised in three eras (Table 3). A significant correlation exists between the Human Development Index (HDI)
Incidence of morbidity

Despite the methodological limitations presented, large volumes of paediatric data are available from high-income countries.²,¹²,⁴⁵ Since the first era, anaesthetic-related mortality has declined to approximately 1 in 10 000 anaesthetics.¹²,¹³,⁴⁶ Twenty-four hour perioperative mortality from any cause varies widely, and may relate to case mix.¹²,¹³ This is evident in a study from Australia in which a higher-than-expected 24-hour perioperative mortality of 13.4 per 10 000 anaesthetics was reported, and which included cardiac and neurosurgery cases.¹³ The mortality rate for complex cardiac operations may be up to 100-fold higher that of noncardiac surgery.²⁰

There are relatively little paediatric data from developing countries, compared to those from high-income countries. Anaesthetic-related mortality in middle-income countries is 2–3 times higher than that in developed countries.¹¹,¹²,⁴⁶,⁴⁷–⁴⁹ Perioperative mortality trends may initially increase in middle-income countries with increasing access to surgical care, the increased provision of surgery for unwell patients undergoing complex procedures, and more reliable data.²⁰,²ⁱ,²²,²³ A 2014 study from Brazil demonstrated this, as 24-hour perioperative mortality increased when compared against the incidence of mortality reported in previous studies.¹¹,⁴⁷,⁵⁰

Anaesthetic-related mortality increases by a factor of 50–100 in low-income countries, but may be 1 000-fold higher in certain poor countries.¹¹,¹⁶,¹⁹,²¹,⁴⁷,⁵⁵ Bainbridge reported a similar trend in adult patients.¹⁹ Unlike the case in high HDI countries, anaesthetic-related mortality in low HDI countries has not declined. A reverse trend has been demonstrated, perhaps relating in part to improved data collection.¹⁹

Cardiac arrest from all causes during anaesthesia is approximately 20–30 per 10 000 anaesthetics, while anaesthetic-related cardiac arrest ranges from 1–5 per 10 000 anaesthetics.¹¹,⁴²,⁴⁷,⁵⁶ Mortality following anaesthetic-related cardiac arrest is 30% in high-income countries, but far higher in low-income countries.¹¹,⁴²,⁴⁷,⁵⁶–⁵⁸

Table 3: Twenty-four hour anaesthetic-related and 24-hour perioperative mortality per 10 000 anaesthetics

<table>
<thead>
<tr>
<th>Era</th>
<th>24-hour anaesthetic related mortality</th>
<th>24-hour perioperative mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt; 18 years</td>
<td>&lt; 1 year</td>
</tr>
<tr>
<td>1947–1983</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High-income* (n = 47111)</td>
<td>1.57–2.9</td>
<td>NR</td>
</tr>
<tr>
<td>1980–1999</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High-income* (n = 1374750)</td>
<td>0–0.42</td>
<td>NR</td>
</tr>
<tr>
<td>Middle-income* (n = 37420)</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Low-income*</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>2000–2015</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High-income* (n = 1190486)</td>
<td>0–1.19</td>
<td>0–3.51**</td>
</tr>
<tr>
<td>Middle-income* (n = 62519)</td>
<td>2.4–3.3***</td>
<td>3.7–4.7</td>
</tr>
<tr>
<td>Low-income* (n = 26057)</td>
<td>37–60</td>
<td>NR</td>
</tr>
</tbody>
</table>

n: number of cases recorded, ND: no data found, NR: data not recorded
**Includes studies with data until post-anaesthesia recovery only
***:Includes studies with data from high-risk surgical cases
****:Data from an externally funded hospital

Mortality and morbidity risks

Three high-risk categories for mortality and morbidity have emerged, and are consistent across developed and developing countries. These are age, i.e. neonates and infants aged ≤ 1 year, American Society of Anesthesiologists (ASA) status III-V, and emergency surgery.¹²,¹³,¹⁴,¹⁵,¹⁶,¹⁷,¹⁸ Limited data in low-income countries expose a critical incident rate double that of high- and middle-income countries.⁶⁰ More events are associated with infants and inexperienced practitioners,⁵⁹,⁶⁰ and respiratory events involving ear, nose and throat surgery.³⁷

Emergency surgery

The increased risk of emergency surgery is calculated at an odds ratio of 2.8 (95% confidence interval: 1.3–5.9), (p 0.007).²³ Emergency surgeries are more common in developing countries.¹²,⁴⁵

Age

On average, in comparison to older children, 24-hour perioperative mortality is 50-fold⁴⁵ greater in neonates, and approximately 20-fold⁴⁵ greater in infants, and may be higher depending on ASA status and surgical complexity.¹¹,³⁰,⁴⁵ Anaesthetic-related mortality is conversely low in high-risk age groups, indicating causes of cardiac arrest that predominantly relate to the patient’s condition.¹¹,⁴⁵ Low anaesthetic-related mortality may also be due to management by experienced anesthetists at appropriate levels of care,¹³,³⁰,⁴³,⁵⁷ and the influence of a restrictive or inclusive definition.¹³

American Society of Anesthesiologists status

Anaesthetic-related mortality in ASA I and II children is not recorded in most studies from high- and middle-income
countries. Although death from anaesthesia is not nonexistent, this confirms the inherent safety of anaesthesia in these patients. However, the vulnerability of even healthy children anaesthetised with cardiac depressants and arrhythmogenic volatile agents was demonstrated in the first Pediatric Perioperative Cardiac Arrest (POCA) Registry. A decrease in such arrests with the use of sevoflurane, in combination with the routine use of pulse oximetry to detect hypoxia, capnography to detect hypoventilation and hypercapnia, and advances in airway management, e.g. laryngeal masks, was established in subsequent studies and analysis. An essential safety message for clinicians and health authorities is the use of safe agents, appropriate monitoring and the availability of airway equipment. ASA III–V patients account for the only mortalities in most studies, and such patients are consistently at increased risk of cardiac arrest and 24-hour mortality.

The relationship between heart disease and mortality is complex. Despite under-representation in studies, children with heart disease account for 80–100% of cardiac arrests and deaths, most during cardiac surgery or interventions. A different pattern was found in the POCA Registry. Of 372 cases of cardiac arrest, heart disease was present in only 34%, and 54% cases of cardiac arrest occurred in the general operating room. This may reflect selection and outcome bias. It was demonstrated through multivariate analysis, in a comparison of children without heart disease and those with heart disease, that although mortality was higher in children with heart disease, it did not differ when adjusted for ASA status. It was shown in another study that approximately 7% of children presenting for noncardiac surgery had heart disease and increased mortality, and significantly so in the younger age groups and with increasing ASA status. These findings suggest that heart disease is not an independent risk factor during noncardiac surgery. High-risk factors are patients with aortic stenosis lesions, cardiomyopathy, pulmonary hypertension and single ventricle physiology. However, the patient numbers are small.

Factors contributing to ongoing poor outcomes in low-income countries
Valuable insight into the problems experienced in delivering safe care can be gleaned from a small institutional audit or report by volunteer organisations. Such reports also highlight successful interventions.

Access and patient factors
Access to elective surgery is limited. Thus, patients present predominately for emergency or very basic surgery. Important differences in patient demographics and disease patterns exist. Poor baseline health status, sepsis and trauma are greater contributors to perioperative mortality in the developing world. Patients often present late or in extremis as lack of priority to health facilities, transport problems and cultural mistrust of hospitals result in delays in seeking health care.

Staff skills and resource factors
Hypoxaemia from hypoventilation and laryngospasm and bronchospasm are frequent anaesthetic-related events with poor outcomes in high- and middle-income countries. Data from parts of Africa show that respiratory monitoring by pulse oximetry or capnography, even when available, is not routinely used, delaying the detection of hypoxaemia, hypoventilation or hypercapnia. Pulse oximeter monitoring during an arrest in the operating room was performed in only 28% of patients in a university teaching hospital. Outcomes from such arrests are poor. The majority die or have permanent disability. Contributing factors are:

- Lack of medication, or the use of inappropriate medication, such as ketamine-only anaesthesia, cardiac depressants, arrhythmogenic volatile agents and long-acting, outdated neuromuscular blockers.
- Manual ventilation only, as ventilator equipment and oxygen is lacking in certain hospitals.
- Limited airway devices and airway skills training.
- Poor cardiopulmonary resuscitation (CPR) technique.
- Inexperienced or untrained practitioners.

Cardiac arrest and mortality, as a result of failing to recognise hypovolaemia, is common in developing and developed countries. Hypovolaemia, from blood loss and sepsis in Africa, is poorly managed owing to a lack of blood or inappropriate fluid choices. There is an established blood transfusion service in less than 30% of countries.

Infrastructure, human resources and external support
Very few hospitals in low-income countries, even those that perform major operations, meet the World Health Organization (WHO) safety standards for essential surgery. Problems with electricity, water, oxygen supply and lack of anaesthesia machines or pulse oximetry have been identified. Staff shortages and surgical and anaesthesia services offered by non-specialist or non-physician practitioners are often the norm. An in-theatre mortality rate of 7.7 per 10 000 anaesthetics was found in a study from Uganda with respect to paediatric surgery performed in mission and nongovernmental hospitals, despite the majority of the anaesthetics being delivered by non-physician anaesthetists. This rate is comparable with that in middle-income countries. Although only basic surgery was offered, anaesthetic staff training, the availability of safe equipment and essential drugs, as well as externally funded surgeons, contributed to the good outcome. Similar improvements have been demonstrated by volunteer organisations, especially when protocol-driven care is introduced, and even in conflict zones.

Governance and data availability
Large datasets are lacking from low-income countries, partly because of poor governance, but also because of an inadequate information technology infrastructure and problems with patient follow-up, which make data collection difficult. The creation of simple data tools, pragmatic reporting, the innovative use of cellular phone technology and support from volunteer organisations and externally funded data platforms, have been shown to assist in the collection and reporting of data in low-income countries.

South African health care
South Africa is classified as an upper- to middle-income country, and has a complex and fragmented healthcare system. There is a marked maldistribution of funding and quality of, and accessibility to, care, between the private and public health sectors. Funding is almost equally divided between the sectors, yet private health care serves only 16% of the population, and is funded on par with Western Europe.

By contrast, the public health sector serves 84% of the population, who have a greater need of health care, have poor health indicators and are at increased risk of adverse outcomes.
The late presentation of paediatric surgical patients increases the complexity of surgery, and may result in poor outcomes.81,82 While public academic and urban regional hospitals are generally well resourced and utilise skilled anaesthesia providers, problems such as staff shortages and equipment challenges have been identified.83 Non-urban regional and district hospitals face similar challenges to those of low-income countries, including staff with minimal or no anaesthesia training.83-85 Equipment challenges, transport and referral problems and an inadequate supply of medication.85,86 Blood shortages are reported in 54% of district transport and referral problems and an inadequate supply of morbidity is preventable in 75% of cases. The recognition of high-risk patients and identification of common precipitators of anaesthetic-related events may improve outcomes in both low- and high-income countries. Risk factors for mortality across developed and developing countries age, i.e. neonates and infants aged ≤ 1 year, ASA III–V status and those undergoing emergency surgery. Skilled anaesthesia providers and appropriate resources are required to anaesthetise such children, both of which are lacking in low-income countries.

The significant ongoing disparity in outcome between developed and developing countries is of concern. The majority of anaesthetic-related causes of death are highly preventable through basic interventions and investment in surgical and anaesthetic services in the developing world.8 WHO initiatives have been introduced to address these issues,89 but will fail if health system issues, governance and funding are not urgently addressed.18,20,54,66

Recommendations
Access to and the safety of surgery is key in addressing the unmet global burden of surgically treatable disease.71,85 Simple metrics, such as 24-hour perioperative and anaesthetic-related mortality rates, are essential indicators of access and safety achieved, and must be reported on and monitored.8 It is the author’s opinion that the lack of large, prospective datasets from the developing world contribute to ongoing anaesthetic-related and perioperative mortality. It is essential that South Africa join such efforts to provide reliable data and establish the baseline safety of paediatric anaesthesia services and direct interventions accordingly. A pragmatic research agenda is required in these regions through the adoption of inclusive definitions and simple data collection tools.9

Once this has been carried out, information must be disseminated to clinicians to improve clinical safety practices, to families and patients for the purposes of obtaining informed consent, and most importantly, to healthcare funders to direct appropriate resources and strengthen systems for surgery and anaesthesia. Until this has been achieved, patients will continue to die from treatable surgical diseases and preventable events during anaesthesia.

References
35. Pediatric Perioperative Cardiac Arrest (POCA) Registry. Secondary


24. The Safe Anesthesia for Every Tot (SAFETOTS) Initiative. Secondary


- Decreased exposure to anesthesia during surgery may reduce the risk of anaphylaxis.

- A decreased risk of anaphylaxis during surgery may be achieved by minimizing exposure to anesthetics.

- Minimizing exposure to anesthetics during surgery may reduce the risk of anaphylaxis.

- The risk of anaphylaxis during surgery may be reduced by minimizing exposure to anesthetics.

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83. Green-Thompson LP. A critical evaluation of the anaesthetic services in the province of Gauteng outside of the greater Johannesburg area [Masters Dissertation]. Johannesburg: Faculty of Health Sciences, University of the Witwatersrand; 2011.