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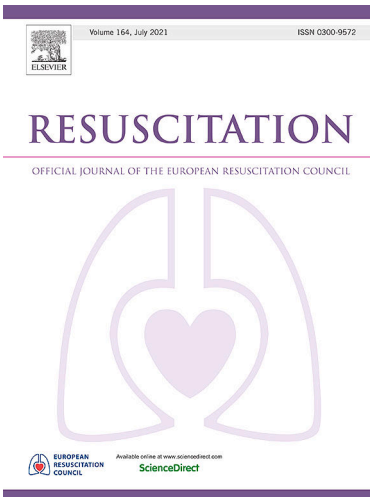

Short paper

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Aetiology of resuscitated out-of-hospital cardiac arrest treated at hospital

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Abstract

Introduction: Precipitating aetiology of out-of-hospital cardiac arrest (OHCA), as confirmed by diagnostic testing or autopsy, provides important insights into burden of OHCA and has potential implications for improving OHCA survivorship. This study aimed to describe the aetiology of non-traumatic resuscitated OHCAs treated at hospital within a local health network according to available documentation, and to investigate differences in outcome between aetiologies.

Methods: Observational retrospective cohort study of consecutive OHCA treated at hospital within a local health network between 2011-2016. Cases without sustained ROSC (≥20 minutes), unverified cardiac arrest, and retrievals to external acute care facilities were

excluded. A single aetiology was determined from the hospital medical record and available autopsy results. Survival to hospital discharge was compared between adjudicated aetiologies.

Results: In the 314 included cases, distribution of precipitating aetiology was 53% cardiac, 18% respiratory, 3% neurological, 6% toxicological, 9% other, and 11% unknown. A presumed cardiac pre-hospital diagnosis was assigned in 235 (84%) cases, 20% of which were incorrect after exclusion of unknown cases. Rates of survival to hospital discharge varied significantly across aetiologies: cardiac 64%, respiratory 21%, neurological 0%, toxicological 58%, other 32% ($p<0.001$). A two-fold difference in survival was observed between cardiac and non-cardiac aetiologies (64% versus 29%, excluding unknown, $p<0.001$).

Conclusions: Non-cardiac aetiologies represented a substantial burden of resuscitated OHCA treated at hospital within a local health network and were associated with poor outcome. The results confirmed that true aetiology was not evident on initial examination in 1 in 5 cases with a pre-hospital cardiac diagnosis.

Keywords

Out-of-hospital cardiac arrest; Aetiology; Outcome;

Introduction

In Australia there are over 26,600 out-of-hospital cardiac arrests (OHCA) each year and although survival rates are improving, in-hospital mortality remains high.[1,2] A key to improving survival in successfully resuscitated patients is rapid identification and reversal of any ongoing precipitating pathophysiology. Aetiology is typically reported in the literature as presumed cardiac and obvious non-cardiac, or medical and non-medical, based on prehospital assessment by emergency medical services (EMS).[3,4] However, in the absence of obvious causes such as trauma, homicide, suicide, or obvious drug overdose, EMS-based assessments only represent preliminary diagnoses that may not reflect true aetiology. An autopsy study of presumed cardiac OHCAs aged <40 years confirmed a non-cardiac diagnosis in 39% of cases,[5] which highlights the importance of autopsy or further in-hospital investigations for the determination of aetiology. Population-based autopsy studies suggest that 40% of sudden cardiac deaths (SCD) are caused by non-cardiac aetiologies,[6,7] but few studies have reported on aetiology as confirmed by in-hospital investigations in the minority of OHCAs achieving sustained return of spontaneous circulation (ROSC).[8–10] In addition, information on frequency and outcome after non-cardiac OHCAs is lacking because these cases are routinely excluded from many investigations due to low perceived survival and broad diagnostic heterogeneity. This study aimed to describe the characteristics and outcome of non-traumatic resuscitated OHCAs treated at hospital within a local health network according to precipitating aetiology.

Methods

Study design and setting

This is a retrospective observational cohort study of the Northern Adelaide Local Health Network (NALHN) OHCA registry, which includes all OHCAs age ≥18 years treated at either of the two public teaching hospitals within NALHN.[11] OHCA was defined as absence of signs of circulation requiring chest compressions or external defibrillation in individuals who did not occupy an emergency department (ED) or inpatient bed.[12] We identified all adult, non-traumatic OHCAs with sustained ROSC (≥20mins) treated at NALHN facilities between 2011-2016. Cases without sustained ROSC, bystander CPR with ROSC pre-EMS, retrieval to

external acute facilities, and likely syncopal episodes were excluded. The local ethics committee approved the registry and subsequent analyses as an ongoing quality improvement activity [Q20170304].

Aetiology classification

NALHN hospitals follow the Australian Resuscitation Council resuscitation guidelines,[13] which focus on rapid identification and treatment of precipitating aetiology. Investigations are guided by patient history and examination and are performed according to discretion of the treating physician. Investigations in cases without obvious cause may include emergency coronary angiography, computed tomography (CT) of brain, chest (including pulmonary angiography), abdomen and/or pelvis, pathology, echocardiography, repeat electrocardiograms, and toxicological screening. Additional cardiac tests include cardiac magnetic resonance imaging (MRI), electrophysiological tests, Holter monitor, provocative tests with flecainide and adrenaline, and genetic testing.

The single clearly documented or most likely aetiology according to the hospital medical record and available autopsy results was recorded in the NALHN OHCA registry by a single investigator and extracted for this analysis. In cases where more than one aetiology was likely the case was adjudicated by a senior expert and either a single aetiology was selected, or the aetiology was designated as 'unknown'. Six primary categories and nine sub-categories were defined:

1. Cardiac – acute myocardial infarction (AMI);[14] chronic or previous ischaemia without evidence of AMI; non-ischaemic structural heart disease; primary arrhythmia.
2. Respiratory – primary respiratory failure; hanging; other: e.g., choking, asthma, drowning.
3. Neurological – subarachnoid haemorrhage (SAH), intracranial haemorrhage (ICH), ischaemic stroke, and other e.g., seizure.
4. Toxicological – deliberate or accidental overdose of prescribed medications, recreational drugs, or ethanol.
5. Other – metabolic derangement; pulmonary embolism; other: e.g. anaphylaxis, hypovolemia, sepsis.
6. Unknown.

Data variables

Outcome measures and clinical covariates were analysed according to aetiology. The primary outcome was survival to hospital discharge. Secondary outcomes included survival with good neurological recovery (cerebral performance category 1-2) and survival at 12 months. Covariates included patient demographics, arrest characteristics, and hospital management.

Statistical analysis

Continuous data is presented as median ± interquartile range and categorical data is presented as frequency and percentage. Comparisons between groups were made using Mann-Whitney U test and Kruskal-Wallis test for continuous data, and Fisher's exact test and Fisher-Freeman-Halton exact test for categorical data. Analyses were performed using SPSS 26 (IBM SPSS Statistics, Armonk, NY, USA).

Results

From 2011-2016, 393 OHCAs were treated at a NALHN hospital. After excluding 42 without sustained ROSC, 22 with ROSC pre-EMS arrival, 11 retrieved to an external acute care facility, and 4 likely syncopal events, 314 were included in the final analysis.

Figure 1 depicts the distribution of precipitating aetiology, identified as cardiac in 53% of cases (60% of cases with known aetiology), 18% respiratory, 3% neurological, 6% toxicological, 9% other, and 11% unknown. Within sub-categories, 59% of cardiac-related OHCA were due to AMI, while 51% of non-cardiac aetiologies were respiratory (Figure 1).

Many demographic, in-hospital management, and outcome variables differed according to primary aetiology categories (Table 1). A presumed cardiac pre-hospital diagnosis was assigned in 235 (84%) cases, 20% of which were incorrect after exclusion of cases with unknown aetiology (Table 1). Survival rates according to aetiology sub-categories ranged from 0% hanging and neurological catastrophe, to 68% for AMI (Figure 2). No statistical

analyses were performed according to aetiology sub-category due to the large number of categories and low n-values.

A sub-analysis in Table 1 compared the characteristics of patients with non-cardiac and cardiac aetiologies, excluding cases with unknown aetiology. Non-cardiac aetiology was associated with younger age, lower rates of known predictors of survival, and lower rates of all survival outcomes.

Discussion

This is the first study to explore characteristics and outcome of resuscitated non-traumatic OHCA treated at hospital according to precipitating aetiology. Retrospective analysis of the medical record and autopsy results confirmed that 40% of cases with known aetiology were of non-cardiac origin, the most common being respiratory and toxicological. Survival to hospital discharge was highest for cardiac aetiologies and varied from 0-58% for non-cardiac aetiologies.

Cardiac causes of OHCA and sudden cardiac death (SCD) are well-described in the literature, but few studies have described the burden and outcomes of non-cardiac OHCA. Our results are consistent with reports of adjudicated aetiology in both population-based autopsy cohorts and hospitalised cohorts that found 40-60% of included cases were of non-cardiac origin.[6–10] After taking into consideration the differences in inclusion criteria, these studies suggest that the true burden of non-cardiac OHCA with attempted resuscitation lies up to 50-60% and may be increasing.[2] In support of this premise, we also found that a pre-hospital presumed cardiac diagnosis, commonly used as a surrogate to estimate incidence and outcome of cardiac-related OHCA and SCD, was incorrect in 20% of cases. These findings have important implications for early prevention, recognition, and treatment of non-cardiac OHCA in a setting that has primarily targeted cardiac aetiologies such as AMI and heart failure.[15–17]

Our study revealed a broad distribution of precipitating aetiologies. Consistent with previous reports,[8,9] we found that 59% of cardiac-related OHCA were due to AMI and only a

small number were due to a primary arrhythmia. Overall, respiratory causes accounted for half of all non-cardiac aetiologies, which is higher than other studies.[6,9,10,18,19] There are no standardised criteria for determining precipitating aetiology, which limits comparisons between studies especially in non-cardiac cases and cases with multiple potential causes.

Survival to hospital discharge varied significantly according to primary and sub-categories of aetiology. A cardiac aetiology was associated with high rates of survival predictors such as VF/VT and coronary angiography, and unsurprisingly, the best survival outcomes. None of the small number of cases with OHCA due to hanging or neurological aetiologies survived to hospital discharge, which is consistent with previous findings.[18,20]. Survival after other respiratory causes such as respiratory failure, choking, and asthma was also low, reflecting the impact of prolonged anoxia on neurological outcome.[21,22]

Limitations

This study provides an overview of broad categories of precipitating aetiology within a local health network but is limited in interpretation and applicability due to the retrospective design. The data is ≥5 years old and rates of non-cardiac aetiology may have increased in more recent years.[2] Aetiology categorisation was dependent on (a) diagnostic tests performed at the discretion of the treating clinician, (b) accuracy of the medical record, (c) availability of autopsy results, and (d) interpretation by a single investigator with adjudication by a senior expert for complex cases. Every effort was made to determine the single most likely precipitating aetiology, but this may have been subjective in cases where multiple aetiologies were contributory. Traumatic arrests were excluded as they are generally retrieved directly to an external acute care facility for management. Nonetheless, this in-depth analysis of aetiology provides valuable insights into factors influencing survivorship within a hospitalised OHCA population.

Conclusion

Our study highlights the diversity of precipitating aetiology in patients with non-traumatic resuscitated OHCA treated at hospital within a local health network. Adjudicated non-

cardiac aetiologies were predominately of respiratory origin, represented 40% of the cohort, and were associated with poorer outcome compared with cardiac-related OHCA. EMS-based diagnoses underestimated the burden of non-cardiac OHCA. Our results emphasise the importance of standardised criteria for determining precipitating aetiology according to autopsy or in-hospital investigations to drive optimal post-resuscitation research and care.

Declarations of interest

None.

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Legends to figures

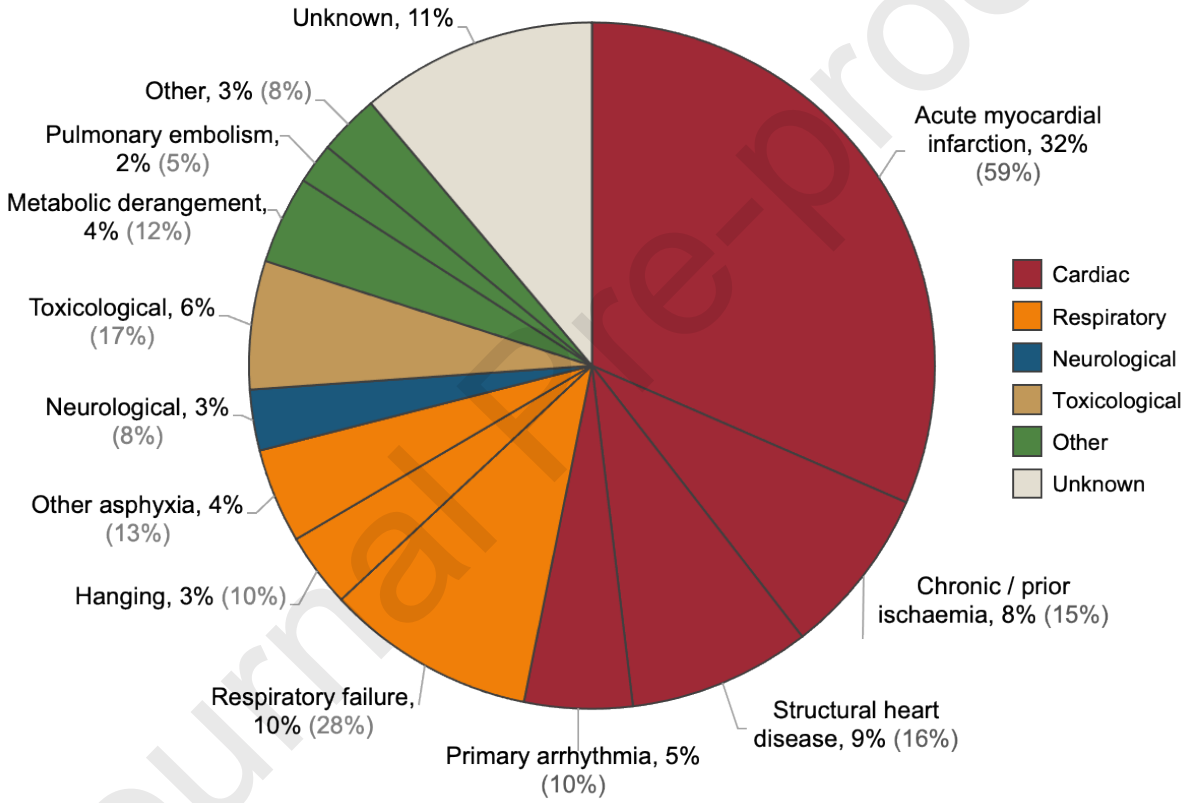

Figure 1: Adjudicated aetiology of consecutive non-traumatic resuscitated OHCA treated at hospital within a local health network, n=314. Percentage values in black reflect % of total cohort (n=314); percentage values in grey reflect % of cardiac aetiology (n=167) and % of non-cardiac aetiology (excludes unknown; n=112), respectively.

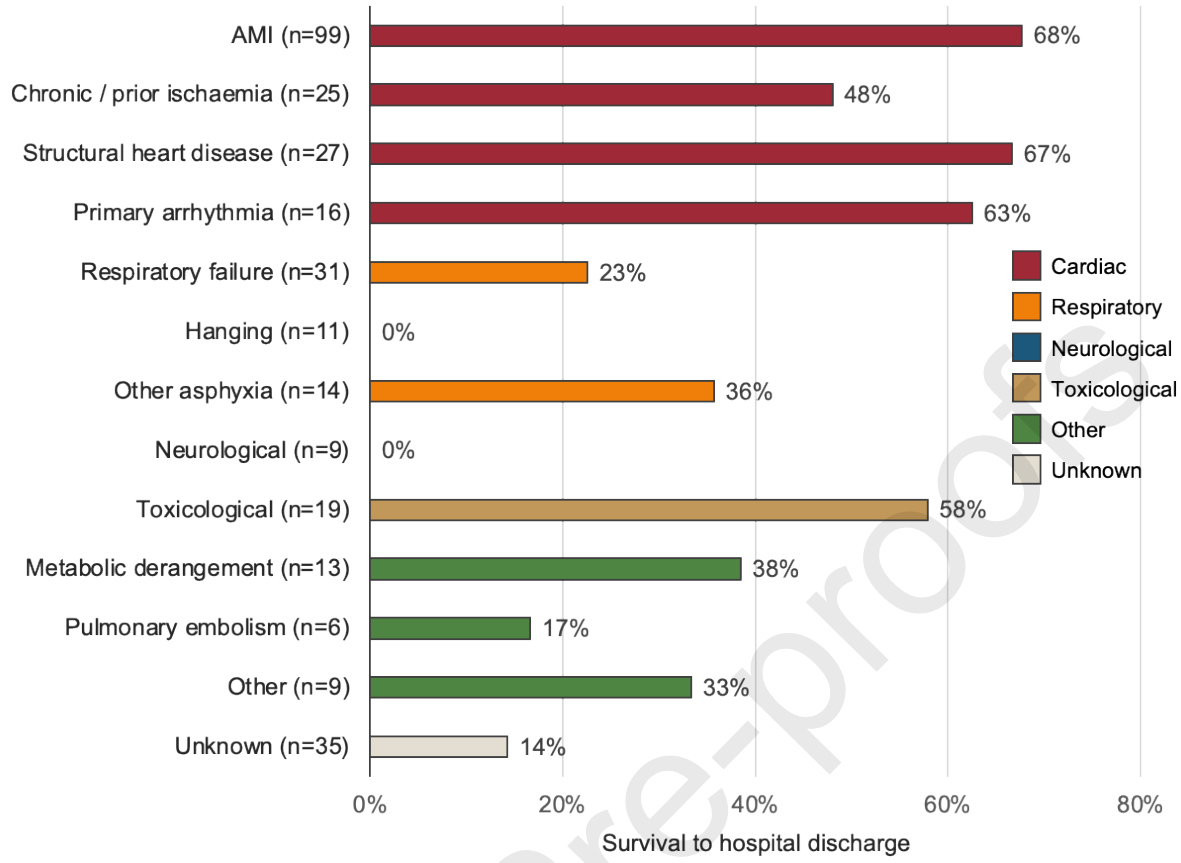

Figure 2: Rates of survival to hospital discharge after non-traumatic resuscitated OHCA treated at hospital according to precipitating aetiology.

Table 1: Characteristics of resuscitated non-traumatic out-of-hospital cardiac arrests treated at hospital according to adjudicated aetiology, n=314

	Cardiac n=167	**Respiratory n=56**	**Neurological n=9**	**Toxicological n=19**	**Other n=28**	**Unknown n=35**	**p-value***	**Non-cardiac† n=112**	**p-value‡**
Age	61 [53-74]	59 [41-73]	73 [61-74]	39 [29-43]	63 [54-72]	65 [50-81]	<0.001	59 [39-72]	<0.001
Male	120 (72%)	35 (63%)	7 (78%)	13 (68%)	16 (57%)	20 (57%)	0.347	71 (63%)	0.149

Arrest at private location	93 (56%)	45 (80%)	8 (89%)	17 (89%)	23 (82%)	23 (66%)	<0.001	93 (83%)	<0.001
Witnessed status									
Bystander witnessed	100 (60%)	22 (39%)	3 (33%)	5 (26%)	15 (54%)	15 (43%)	<0.001	45 (40%)	<0.001
EMS-witnessed	37 (22%)	11 (20%)	3 (33%)	2 (11%)	9 (32%)	4 (11%)	0.270	25 (22%)	>0.999
Unwitnessed	30 (18%)	23 (41%)	3 (33%)	12 (63%)	4 (14%)	16 (46%)	<0.001	42 (38%)	<0.001
Bystander CPR	101/130 (78%)	29/45 (64%)	3/6 (50%)	12/17 (71%)	14/19 (74%)	16/31 (52%)	0.051	58/87 (67%)	0.086
Initial rhythm									
VF/VT	140 (84%)	1 (2%)	2 (22%)	1 (5%)	7 (25%)	10 (29%)	<0.001	11 (10%)	<0.001
PEA	12 (7%)	28 (50%)	2 (22%)	10 (53%)	8 (29%)	13 (37%)	<0.001	48 (45%)	<0.001
Asystole	14 (8%)	24 (43%)	4 (44%)	8 (42%)	11 (39%)	12 (34%)	<0.001	47 (44%)	<0.001
Unknown	1 (1%)	3 (5%)	1 (11%)	0 (0%)	2 (7%)	0 (0%)	n/a	n/a	
Non-shockable initial	2/26 (8%)	6/ (12%)	0/7 (0%)	2/18 (11%)	2/20 (10%)	4/25 (16%)	0.948	10/99 (10%)	>0.999

rhythm to shockable									
Defibrillation	142 (85%)	7 (13%)	2 (22%)	3 (16%)	10 (36%)	14 (40%)	<0.001	22 (20%)	<0.001
Arrival mode: EMS vs. private vehicle	157 (94%)	54 (96%)	9 (100%)	19 (100%)	27 (96%)	32 (91%)	0.863	109 (97%)	0.254
Pre-hospital presumed cardiac diagnosis	166 (99%)	17 (30%)	4 (44%)	3 (16%)	17 (61%)	28 (80%)	<0.001	41 (37%)	<0.001
GCS 3 on arrival to emergency department	101/165 (61%)	44 (80%)	9 (100%)	15 (79%)	22 (79%)	34 (97%)	<0.001	90 (81%)	<0.001
Arrest to ROSC (minutes)	22 [13-34] (n=161)	26 [14-35]	23 [15-40]	19 [17-33]	32 [12-47]	27 [21-33]	0.442	26 [14-39]	0.240
Post-ROSC ST-elevation	67/162 (41%)	5/48 (10%)	0/7 (0%)	1/18 (6%)	1/27 (4%)	4/30 (13%)	<0.001	7 (7%)	<0.001
Elevated Troponin T	156/164 (96%)	31/39 (79%)	6/8 (75%)	9/13 (69%)	19/23 (83%)	24/26 (92%)	<0.001	65/83 (78%)	<0.001
Elevated Creatinine Kinase	111/145 (77%)	12/32 (38%)	2/4 (50%)	10/10 (100%)	12/17 (71%)	13/19 (68%)	<0.001	36/63 (57%)	<0.1

Temperature management	88/167 (53%)	22 (39%)	2 (22%)	5 (26%)	7 (25%)	13 (37%)	0.013	36 (32%)	<0.001
Coronary angiography	129 (77%)	3 (5%)	1 (11%)	2 (11%)	8 (29%)	12 (34%)	<0.001	14 (13%)	<0.001
Intensive care unit length of stay	3 [2-4] (n=125)	3 [2-4] (n=48)	2 [2-3] (n=7)	3 [2-5] (n=15)	3 [1-4] (n=24)	4 [3-5] (n=23)	0.090	3 [2-4] (n=94)	0.360
Survived to hospital discharge	107 (64%)	12 (21%)	0 (0%)	11 (58%)	9 (32%)	5 (14%)	<0.001	32 (29%)	<0.001
CPC 1-2 at hospital discharge	105 (63%	12 (21%)	0 (0%)	11 (58%)	9 (32%)	5 (14%)	<0.001	32 (29%)	<0.001
Survival at 12 months	105 (63%)	11 (20%)	0 (0%)	10 (53%)	8 (29%)	5 (14%)	<0.001	29 (26%)	<0.001

Data presented as number (percentage) and median [interquartile range]. CPC, cerebral performance category score of 1-2 indicates good neurological recovery; CPR, cardiopulmonary resuscitation; GCS, Glasgow coma scale; EMS, emergency medical services; PEA, pulseless electrical activity; ROSC, return of spontaneous circulation; VT, ventricular tachycardia; VF, ventricular fibrillation.

*p-value comparing across all categories. †Excludes cases with unknown aetiology. ‡p-value comparing cardiac with non-cardiac, excluding unknown cases.

CRediT author statement

Melanie R Wittwer: Conceptualisation, Methodology, Investigation, Formal analysis, Writing – original draft

Chris Zeitz: Supervision, Writing – review & editing

John F Beltrame: Supervision, Writing – review & editing

Margaret A Arstall: Conceptualisation, Supervision, Writing – review & editing

All authors take responsibility for the integrity of the data and the accuracy of the data analysis. All authors read, critically reviewed and approved the final manuscript

Declaration of interests

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: