Are Research Trials in Palliative Care safe?

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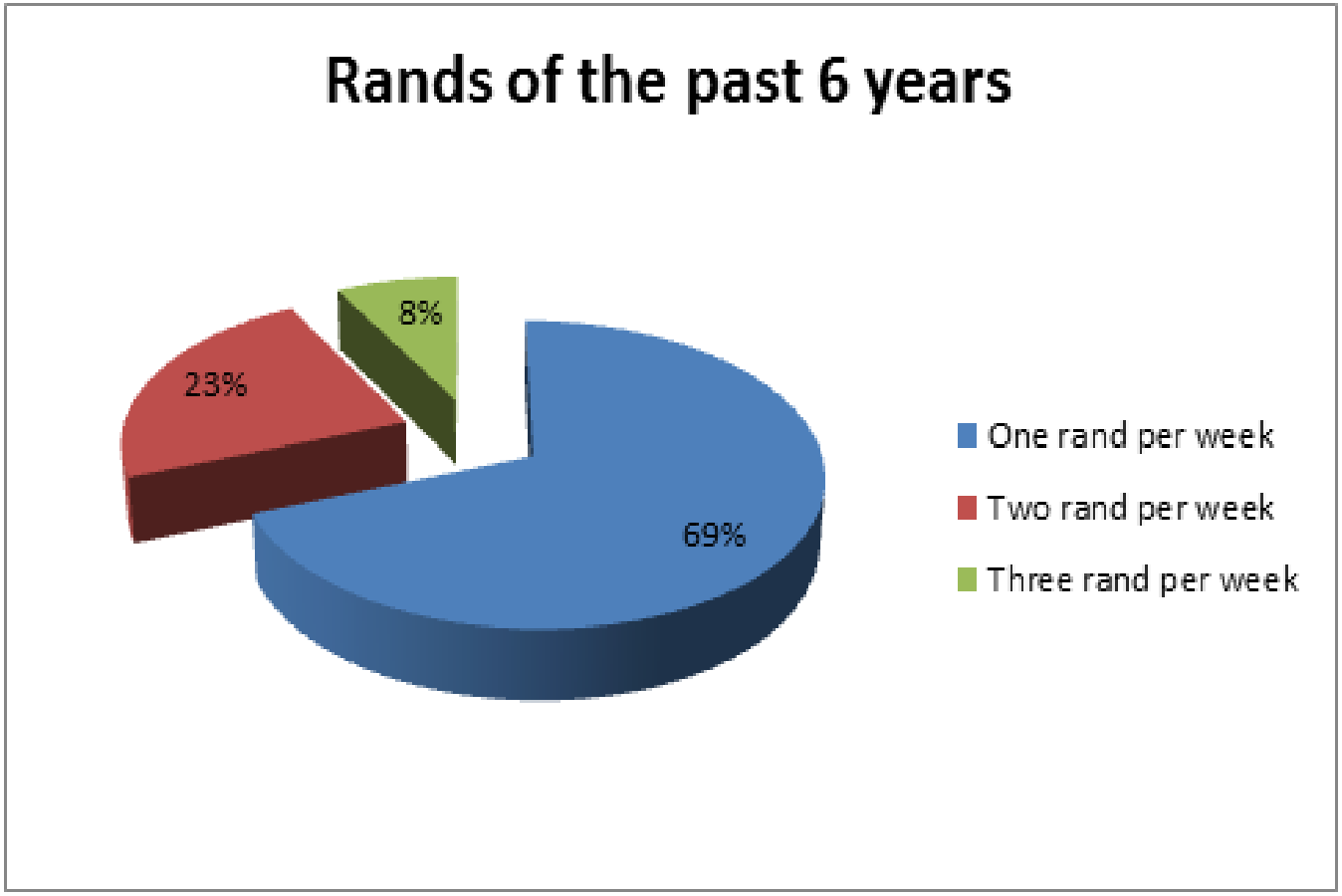
Is research safe in Palliative Care?

- The evidence is limited in many areas of palliative care partly due to challenges in designing palliative interventional trials.
- It has been argued that palliative care trials may be unnecessarily:

❖ burdensome

❖ potentially harmful

❖ ethically questionable


Rands of the past 6 years
8%
23%
69%
One rand per week
Two rand per week
Three rand per week

Question?

Is Research safe in the Palliative Care population

What did we analyse

- Four Palliative Care trials conducted at the South Australian Palliative Services (SAPS) during the period Jan 1st 2013 to December 30th 2014.
- The number and severity of events, as well as relationships to study participation and intervention (or the underlying disease process), versus the number of randomized patients were evaluated.

Definition of Adverse Event (AE) & Serious Adverse Event (SAE)

- Adverse event was defined as any unusual, unfavourable, or unintended sign, response, symptom or disease where the outcome is not expected and has negative consequences for the participant.

What defines SAE

- ❖Event resulting results in death
- ❖Event that's life-threatening

- **Following events require very rapid reporting**
- ❖results in attempted suicide
- ❖requires inpatient hospitalization or prolongation of existing hospitalization
- ❖results in persistent or significant disability/incapacity,
- ❖requires ongoing medical or professional attention
- ❖are judged to represent significant hazard

Who Governs reporting

- Investigator protocol (IP)
- Data safety monitoring committee (DSMC)
- Human Research Ethics Committee (HREC)

Criteria for assessing causality

- **Unrelated** Where the adverse event is clearly not related
- **Unlikely** Where the adverse event does not have a clear relationship to the intervention
- **Possible** Where the adverse event follows a known pattern of response
- **Probable** Where the adverse event reduces or ceases with withdrawal of the intervention
- **Definite** Where the adverse event ceased with withdrawal of the intervention and recurs with re-exposure.

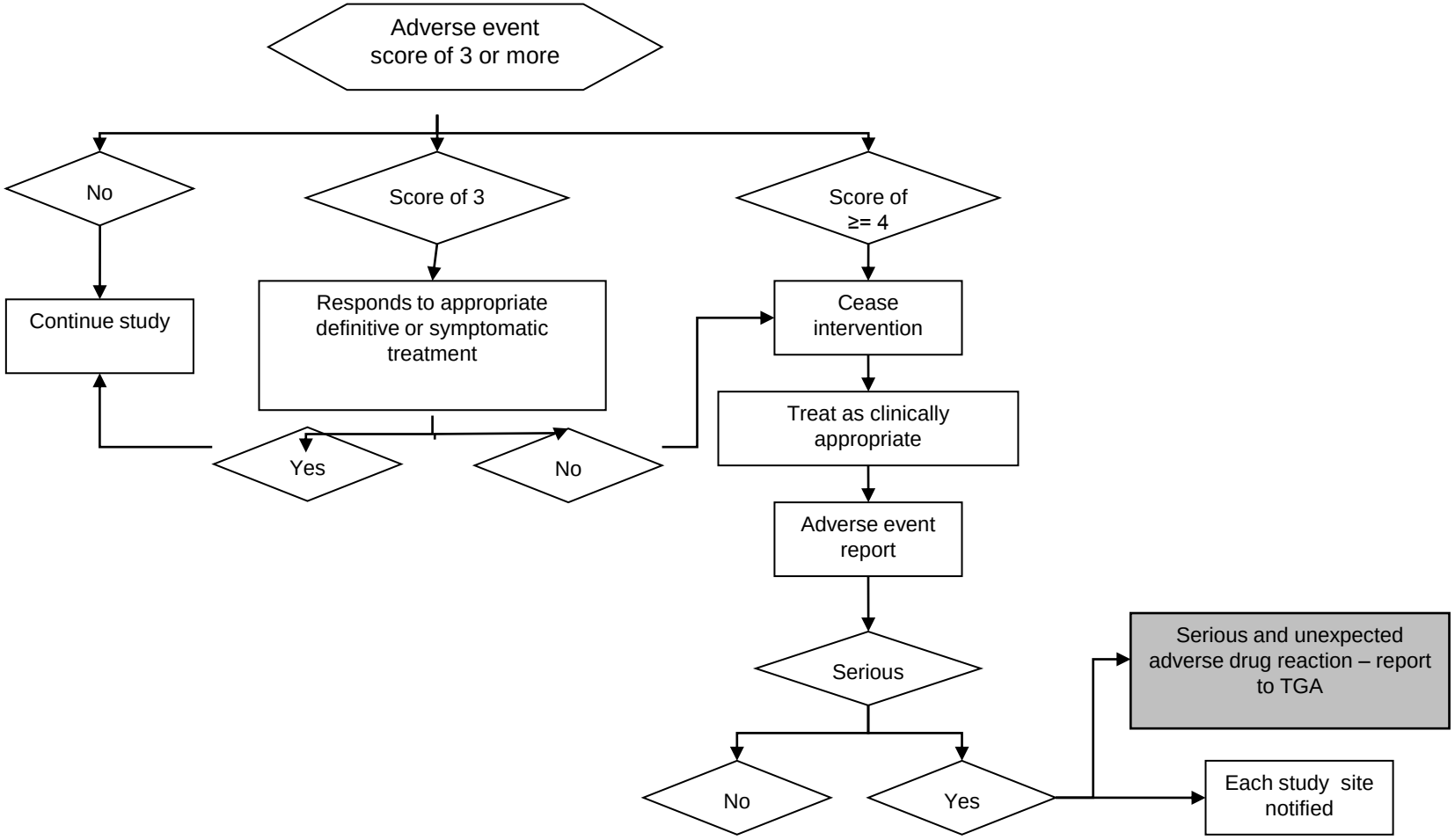
Exempt from reporting to HREC & DSMC

- Where participants are admitted as a planned admission due to respite, family or social issues, or for pre-planned treatment
- Where participants are admitted (or admission is prolonged) due to an expected and documented deterioration in their condition due to the underlying disease process
- Where participants die due to an well documented decline in their condition due to the underlying disease process

Systematic assessment of AE's and SAE's

- The time period from randomisation
- The intervention period
- 4 week extension phase safety follow up by telephone.

SAE reporting trajectory



Outcome

- 227 participants referred and pre-screened for inclusion
- 100 patients were randomized in the trials and included in this analysis.
- A total of 39 events were reported in the 100 patients randomised
  - ❖In 6 cases 2 events were reported per participant

Outcome continued

- 26 events were classified as serious
  - ❖22 Required admission to hospital due to underlying disease
  - ❖3 participants deceased due to acute disease progression
  - ❖1 reported as SAE - no hospitalization required
  - – **1 required reporting to Human Research Ethics Committee (HREC**)
- 13 events reported as non-serious

Outcome continued

- The differences between pre-screening and randomization rates demonstrate the robust nature of inclusion and exclusion criteria in these studies.
- This, coupled with systematic assessment throughout the study period, demonstrates safety of the studies.
- Research has shown potentially tenfold difference between the number of symptoms volunteered by patients and those identified using systematic assessment, explaining the high number of reported adverse events.

Primary findings

- Only 5 of 39 events (13%) were potentially related to the study intervention
  - ❖ 3 events - nausea and vomiting (2 in MOP &1 in Megestrol study)
  - ❖ 2 events - ↓ serum sodium in Sertraline/Placebo study
- The remaining 34 were related to underlying disease.
- Participants were willing to continue to be involved despite the adverse events and underlying severe illness

National Cancer Institute, Common Terminology Criteria for Adverse Events.V4.0

Conclusion

- This analysis across four studies demonstrates that the research in Palliative Care is safe.
- Without advancements in research methods, policies and procedures, the field of Palliative Care risks a future where clinical practise continues without a scientific evidence base.