MSR154

Comparison of Methods to Estimate Total Person-Time at Risk for Synthesis Studies of Incidence Rates in Observational Data

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Objective

- There is no standard recommended method to estimate total person-time at risk, which is required for the meta-analysis of incidence rates.
- Here we compare existing and novel methods to estimate total person-time for observational incidence studies.

Background

- Synthesis, such as meta-analysis, of event incidence rates from observational studies requires both the number of events and the total person-time at risk.
- Total person-time at risk is the sum of time each patient is followed-up before censoring or an event.
- While total person-time can be calculated from individual participant data (IPD), person-time is frequently unreported for published aggregate data and requires estimation from the more commonly reported mean/median follow-up duration or Kaplan–Meier curves.

Methods

Targeted Literature Search

- Brief targeted literature searches identified incidence studies investigating prostate cancer mortality that fully reported all of Kaplan–Meier curves, number at risk tables, median follow-up duration, and total person-time.

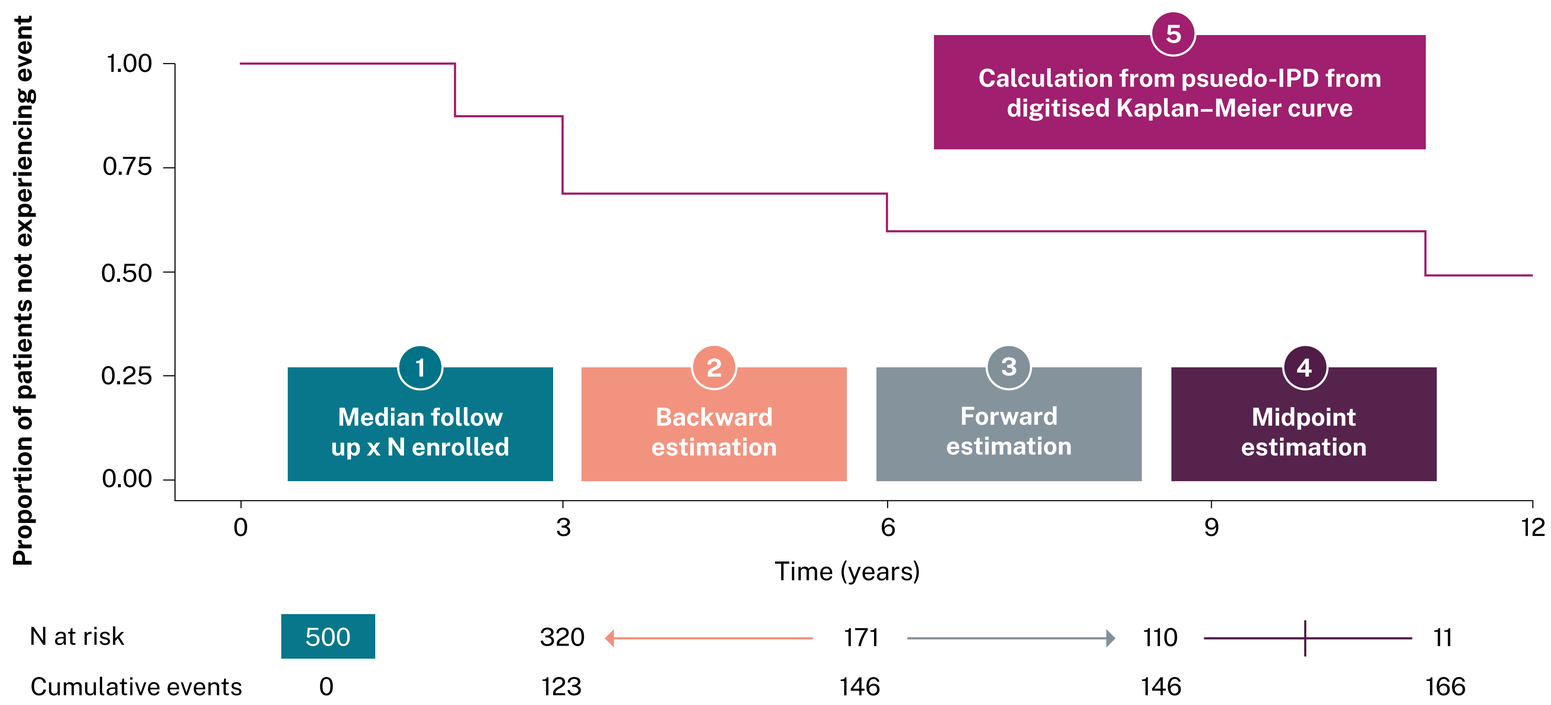
Estimations of Person-Time

- Five methods to estimate total person-time (**Figure 1**) were compared using these studies:

1. Multiplication of median follow-up by the number of patients enrolled.
2. 'Backward' estimation, whereby the reported number of patients at risk at the end of each interval is multiplied by the duration of the interval, then summed.
3. 'Forward' estimation, whereby the reported number of patients at risk at the beginning of each interval is multiplied by the duration of the interval, then summed.
4. 'Midpoint' estimation, whereby the reported number of patients at risk in each interval is multiplied by the midpoint between the previous and succeeding timepoints, then summed.
5. Calculation from pseudo-IPD reconstructed using the Guyot algorithm on digitised Kaplan–Meier curves.[1]

FIGURE 1

Diagram of methods used to estimate total person-time



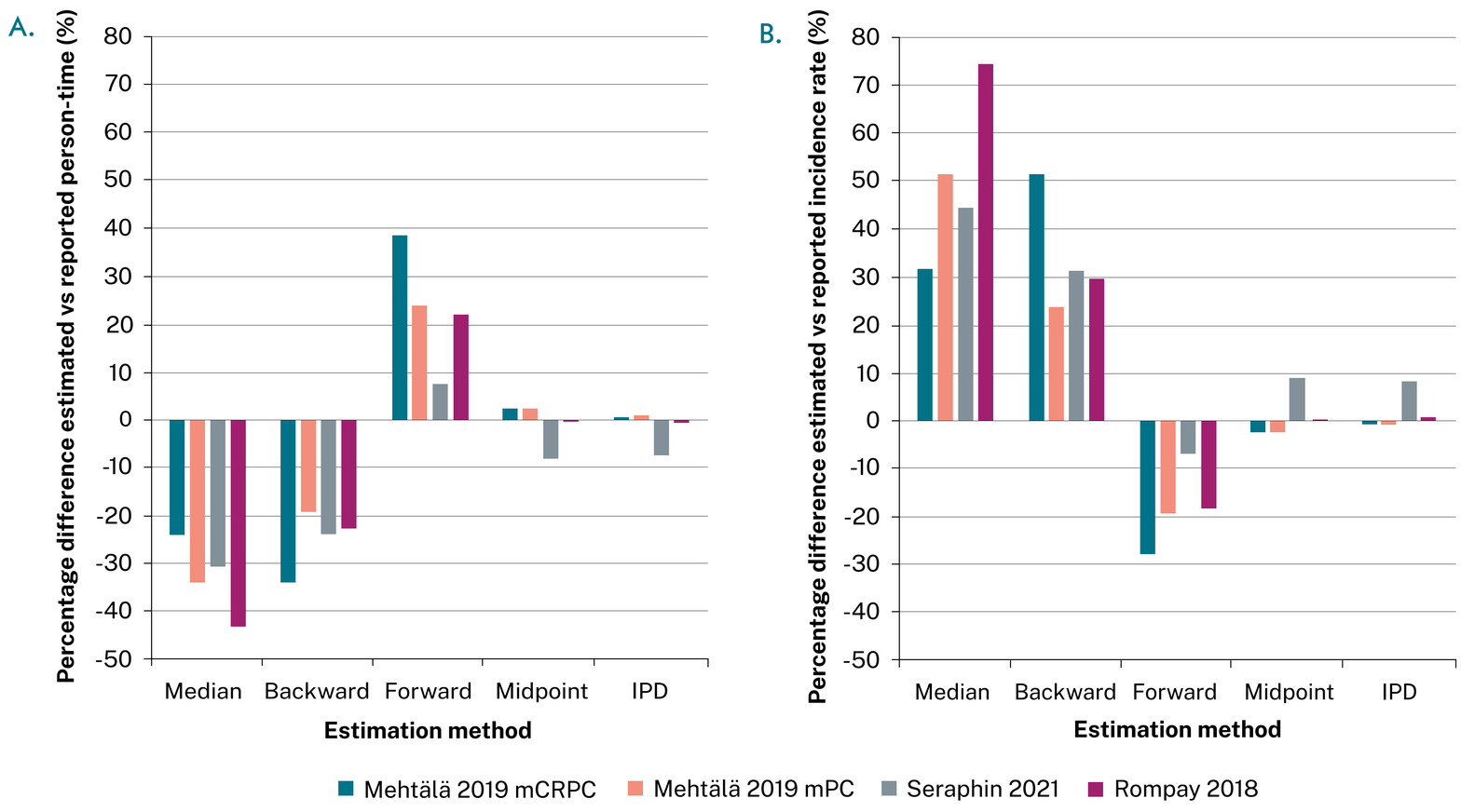
Results

Targeted Literature Search

- Few studies of prostate cancer mortality reported the required data, highlighting the expected challenges in meta-analysing incidence rates from such studies.
- Three studies reporting the required data with different follow-up durations (14, 25 and 5 years, respectively) were identified and evaluated (Mehtälä [2020], Rompay [2019] and Seraphin [2021]).[2-4]

FIGURE 2

Percentage difference of estimated versus reported (A) total person-time and (B) incidence rate



Estimation of Person-Time (Figure 2a)

- Compared to reported total person-time, median follow-up and backward estimation yielded under-estimates (percentage difference estimated vs reported person-time ranged from −43.23 to −24.07 and −34.04 to −19.17, respectively), while forward estimation yielded over-estimates (range: 7.45 to 38.99).
- Midpoint and pseudo-IPD estimation gave closer estimates to reported person-time (range: −8.19 to 2.47 and −7.70 to 0.83, respectively).

Estimation of Incidence Rates (Figure 2b)

- As expected, methods producing under-estimates of total person-time gave over-estimates of incidence rates, and vice versa.
- Compared to reported incidence rates, estimation from median follow-up and backward estimation yielded over-estimates (percentage difference estimated vs reported incidence rate ranged from 31.69 to 76.15 and 23.71 to 51.62, respectively), while forward estimation yielded under-estimates (range: −28.05 to −6.93).
- Midpoint and pseudo-IPD estimation gave closer estimates to reported incidence rates (range: −2.41 to 8.92 and −0.82 to 8.34, respectively).

Conclusion

- Midpoint and pseudo-IPD methods gave the closest estimates to the reported person-time and incidence rates, suggesting these are the most appropriate methods where data availability permits.
- Estimation from median follow-up (the most commonly used method) yielded substantial and consistent under-estimates of person-time (therefore inflating incidence rate estimates), likely as this crude method cannot account for complex patterns of loss-to-follow-up.
- This initial research suggests that when estimates of person-time and incidence rates are required (e.g. for meta-analysis), estimation from median follow-up is unsuitable or at best with limitation; however, for many studies this may be the only feasible method due to limited data reporting.
- Studies should better report data required for incidence rate meta-analysis. Where data are limited, further research is required to assess whether it would be best to use median follow-up as a unified method across studies so all are similarly biased, or to utilise the most accurate method possible per study.
- Future meta-analyses should acknowledge the potential biases of method choice for estimating person-time and explore these via sensitivity analyses.

Abbreviations: IPD: individual participant data; **mPC:** metastatic prostate cancer; **mCRPC:** metastatic castration-resistant prostate cancer.

References: [1]Guyot P. et al. BMC Med Res Methodol 2012;12:9; [2]Mehtälä J. et al. PLOS ONE 2020;15(2):e0227552; [3]Rompay M. et al. Eur J Cancer 2019;112:118–126; [4]Seraphin T. et al. Cancer Causes Control 2021;32:1001–1019. **Acknowledgements:** The authors thank Ben James, Costello Medical, for graphic design assistance.

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