ESTIMATING PREVALENCE IN ONCOLOGY: THE DEVELOPMENT OF A MORE ACCURATE PREVALENCE FORMULA

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Background

- Prevalence is defined as the number and/or the proportion of people within a defined population living with a certain disease, at a fixed point (or period) in time.
- Estimates of disease prevalence are crucial for health services planning and resource allocation.
- With respect to cancer, incidence and mortality can often be calculated directly from data collected by cancer registries and national health statistics.
- In contrast, cancer prevalence can only be derived from survival and mortality data over a long follow-up period. Therefore, economic and epidemiologic models in oncology often use indirect approaches to calculate disease prevalence using median overall survival (OS).

Objective

In this study, we propose an alternative approach that provides more accurate estimates of prevalence.

Methods

- Derived formula from base principles to provide a reasonable estimate of prevalence for diseases of **long duration but high mortality**, such as cancer.
- Prevalence can be calculated as incidence times the area under the survival curve.
- Traditionally, prevalence is simplified to incidence times average disease duration. In oncology, median OS is routinely substituted as average disease duration
- A more accurate formula can be derived assuming:
    1. Median instead of average
    2. Only median OS known (constant hazard)
    3. Nonzero cure rate

Table 1. Published oncological budget impact models estimating the number of eligible patients

Author (Year)	Cancer type	Overall survival	Estimating the number of patients			
			Incidence	Prevalence (old method)	Prevalence (new method)*	Prevalence (New method, no cure assumption)
Bui (2016)	Metastatic prostate cancer	Enzalutamide: 35.3 months Abiraterone acetate: 34.7 months Sipuleucel-T: 25.8 months Radium Ra 223 dichloride: 14.9 Docetaxel: 24.3 months Weighted median: 28.91 months	115	277	304 (+10%)	399 (+44%)
Graham (2018)	Non-small cell lung cancer	Afatinib: 46.26 months Erlotinib: 41.89 Gefitinib: 40.13 months Pemetrexed/cisplatin: 37.06 Weighted median: 42.65 months	34	121	108 (-11%)	174 (+44%)

*Assuming survival > 5 years = cured

Figure 1. Derivation of the simplified prevalence equation

Standard prevalence equation

$$Prevalence = \iint_0^C I(y) * S(t,y)\, dt\, dy$$

$I(y) = Incidence\ as\ a\ function\ of\ time$

$S(t,y) = Survival\ as\ a\ function\ of\ time\ and\ diagnosis\ date$

$C = Survival\ time\ to\ be\ considered\ cured$

Assuming $S(t,y)$ is constant across diagnosis date (stable treatment landscape)

$$Prevalence = \iint_0^C I(y) * S(t)\, dt\, dy$$

Assuming $I(y)$ is constant (stable rate of incidence)

$$Prevalence = I \int_0^C S(t)\, dt$$

Assuming $S(t)$ is reasonably approximated with constant hazard

$$S(t) = e^{-\lambda t}$$

$$Prevalence = I \int_0^C e^{-\lambda t} dt$$

Given a single summary statistic for Overall Survival (OS) at a specified number of months (M)

$$OS = e^{-\lambda M}$$

$$\lambda = \frac{-\ln(OS)}{M}$$

Solving the integral

$$Prevalence = \frac{I}{\lambda}\left(1 - e^{-\lambda C}\right)$$

$I_m = Incidence\ per\ month$

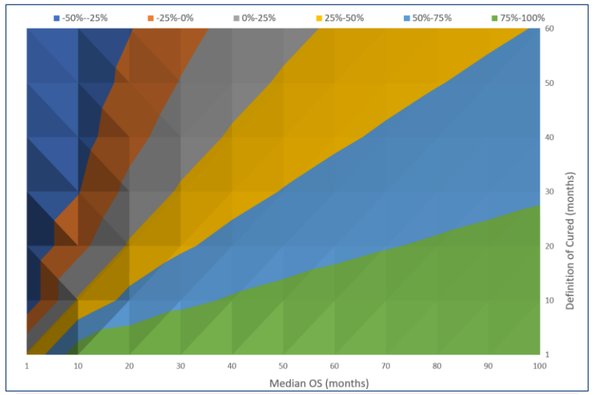
$$Prevalence = \frac{I_m * M}{-\ln(OS)}\left(1 - OS^{\frac{C}{M}}\right)$$

$C_m = Cure\ time\ in\ months$

Results

- The derived formula (displayed below) predicts that true prevalence is up to 44% higher than estimated using the simplified approach of incidence times median OS for diseases with median OS less than 12 months.
- Conversely, the formula predicts that true prevalence is at least 25% lower than current estimation methods for diseases with long median survival (e.g., more than 5 years).

Figure 2. Error between existing rule of thumb and new concept



In many cases, median OS is provided as the only summary statistic and incidence is per year, in which case the equation becomes:

$$\boldsymbol{Prevalence \approx 0.12 * I_A * Median\ OS_m \left(1 - 0.5 \frac{C_m}{Median\ OS_m}\right)}$$

$\boldsymbol{I_A = Incidence\ per\ year}$

In the case where there is no curative intent, the equation further simplifies:

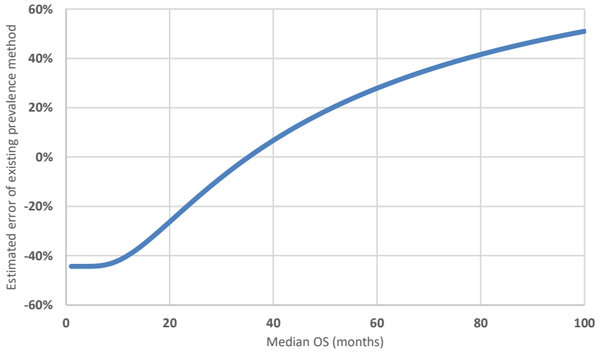
$$\boldsymbol{Prevalence \approx 0.12 * I_A * Median\ OS_m}$$

Whereas the existing rule of thumb states : $\boldsymbol{Prevalence \approx I_A * Average\ Duration}$

A common misconception is to use median OS as "Average Duration" : $\boldsymbol{Prevalence \approx I_A * \frac{Median\ OS_m}{12}}$

When compared to the derivation above, this common misconception leads to underestimating the prevalence by approximately 44%

Figure 3. Expected error between the two methods as a function of median overall survival (OS)



Existing rule of thumb method:

$$Prevalence \approx I_A * \frac{Median\ OS_m}{12}$$

Constant hazard derivation method:

$$Prevalence \approx 0.12 * I_A * Median\ OS_m \left(1 - 0.5 \frac{C_m}{Median\ OS}\right)$$

Assuming $C_m = 60\ months$ (a typical clinical definition):

$$Prevalence \approx 0.12 * I_A * Median\ OS_m \left(1 - 0.5 \frac{60}{Median\ OS}\right)$$

Limitations

This approximation is best used when the constant hazard assumption holds in order for the survival curve to be reasonably approximated by the exponential function, which is not a valid assumption in every disease area. Further research can be conducted to apply this derivation method to more complex survival curves.

Conclusions

This formula provides a simple alternative approach for more accurate estimation of disease prevalence. Given the essential role that prevalence estimates play in oncology models, this has important implications for future health care decision-making.

References

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