Do Oscar Winners Live Longer than Less Successful Peers? A Reanalysis of the Evidence

Marie-Pierre Sylvestre, MSc; Ella Huszti, MSc; and James A. Hanley, PhD

In an article published in *Annals of Internal Medicine* in 2001, Redelmeier and Singh reported that Academy Award–winning actors and actresses lived almost 4 years longer than their less successful peers. However, the statistical method used to derive this statistically significant difference gave winners an unfair advantage because it credited an Oscar winner's years of life before winning toward survival subsequent to winning. When the authors of the current article reanalyzed the data using methods that avoided this "immortal time" bias, the survival advantage was closer to 1 year and was not statistically significant. The type of bias in Redelmeier and Singh's study is not limited to longevity comparisons of persons who reach different ranks within their profession; it can, and often does, occur in nonexperimental studies of life- or time-extending benefits of medical interventions. The current authors suggest ways in which researchers and readers may avoid and recognize this bias.

Ann Intern Med. 2006;145:361-363. www.annals.org
For author affiliations, see end of text.

The large survival advantage—almost 4 years—for Academy Award–winning actors and actresses over their less successful peers (1) continues to receive attention. We point out that the statistical method used to derive the statistically significant survival difference gave the Oscar winners an unfair advantage. We suggest how readers might recognize and avoid similar biases in other research reports.

Redelmeier and Singh's report (1) was based on 235 Oscar winners, 527 nominees (nonwinners), and 887 performers who were never nominated (controls). Controls were selected from performers who were the same sex and approximately the same age in years as the nominees and who performed in the movies for which the nominees were nominated. In the primary analysis, survival was measured from performers' day of birth, but other definitions of "time zero" were also used. In all but 1 of the Kaplan–Meier, log-rank, and Cox proportional hazards analyses reported, each performer was classified as a winner or nonwinner from the outset. One reported analysis used winner as a time-dependent covariate to reflect the fact that all started out as nonwinners but that some changed status over time.

In Redelmeier and Singh's more emphasized comparison, Kaplan–Meier curves showed that life expectancy was 3.9 years longer for winners. The Cox model, with winner as a fixed-in-time covariate, yielded mortality rate reductions ranging from 28% (no adjustment) to 23% (adjustment for 7 other covariates), all with 95% confidence limits more than 0%. The 1 reported set of analyses that treated each performer's status as dynamic (time-dependent) yielded a mortality rate reduction of 20%; the lower limit of the CI was 0%, that is, the reduction was just significant at the conventional level ($P = 0.05$). Redelmeier and Singh's abstract and their Figure focused on the 3.9-year life-expectancy advantage and the 28% mortality rate reduction for winners, which were obtained without adjustment and without taking into account that a performer's status changed with time.

The analyses that classified those who ultimately won as winners from the outset gave them an inbuilt survival advantage by crediting the winner's life-years before winning toward survival subsequent to winning. These "immortal" years (2, 3) were a requirement for membership in the winners' group: Winners had to survive long enough to win—more than 79 years in the 2 most extreme cases (**Figure**). Performers who did not win had no minimum survival requirement, and some died before some winners had won, that is, before some "longevity contests" could begin. For example, 145 nonwinners had already died by age 65 years, that is, before 15 of the winners had won. These unfair pairings (for example, Richard Burton vs. George Burns) were implicitly included in the overall longevity contest between the 2 groups and contributed to the apparent survival advantage of the winners, even if winning brought no survival benefit.

To estimate the longevity benefits of winning an Oscar, the comparison should begin at the time that each performer first wins, and the "remaining longevity" contest should only include those alive at the same age as the winner was when he or she won. A winner may legitimately be included in comparisons (risk sets) before winning, but only as a nonwinner.

An analysis in which the status of a performer who won is treated as a winner throughout, even in risk sets before winning, produces an "immortal time" bias. As we illustrate in the **Figure**, a longevity that is measured from a time zero that precedes the performer's Oscar win (for example, an individualized one, such as the day each per-

See also:

Print
Related letters. 392

Web-Only
Appendix
Appendix Figure
Conversion of figures and table into slides

former's first film was released, or a common one, such as each performer's initial or 50th birthday, as used in Redelmeier and Singh's analysis [1]) will necessarily contain some immortal time. No immortality guarantee exists for those who do not win. In a similar manner, the matching process, involving a performer who played opposite a nominee, ensured that a control was alive when a person who ultimately won was nominated but not necessarily when that winner won (the comparison of 235 winners vs. 527 other nominees did not involve a matching process).

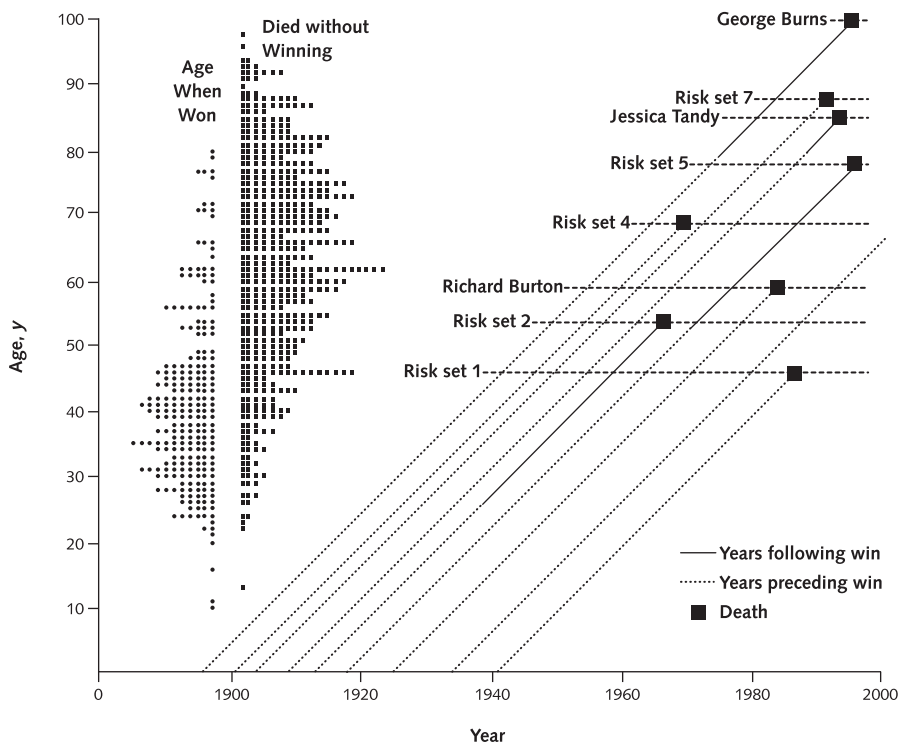
The authors reported 1 analysis in which each performer's status was updated in each risk set. In the **Table**, we compare the results from the types of analyses they used (original) with our reanalyses (new). Our methods are described more fully in the Appendix, available at www.annals.org. All of our analyses treat each performer's status as dynamic. The database on which our analyses are based is available at www.annals.org. In our reanalyses, which take the immortal time as well as the covariates sex and year of birth into account, the point estimate of the actuarial advantage is approximately 1 year and is not statistically significantly different from 0 (the 95% CI is compatible with 0). The estimated percentage mortality rate reduction is also correspondingly smaller.

We directly estimated the magnitude of the immortal time bias (Appendix, available at www.annals.org). In our comparison of winners versus nominees, we estimated that not accounting for immortal time produced an artifactual longevity advantage of 0.8 year and a mortality rate ratio of 0.94. In the comparison of winners versus controls, not accounting for the immortal time—now more substantial—between the year of a winning performer's first film and the year he or she first won produced an artificial longevity advantage of 1.7 years and a mortality rate ratio of 0.87.

In 1843, William Farr (5) described the statistical artifact created by classifying persons by their status at the end of follow-up and analyzing them as if they had been in these categories from the outset. He used as examples the greater longevity of persons who reached higher ranks within their professions (bishops vs. curates, judges vs. barristers, and generals vs. lieutenants). Despite textbook warnings (2, 6, 7), analyses overlooking this subtle bias are still common today.

In some longevity comparisons (1, 4, 8), the consequences of an incorrect conclusion are minor. In the evaluation of the time-extension benefits of therapy (3, 9, 10), the consequences are more serious. Therefore, how do we

Figure. **Lexis diagram showing life course for 9 selected performers (all nominated), along with their status at the time of the 8 risk sets (1 at each death).**



A Lexis diagram (4) represents each performer's time course as a diagonal line, with advancing age on the vertical axis and advancing calendar time on the horizontal axis. Winners, by virtue of their having lived long enough to win, were, in hindsight, "immortal" in the years that preceded their win. Circles and squares at the left of the figure indicate ages at which winners won and ages at death of those who died without winning.

Table. **Original Analysis and Reanalyses of the Longevity Difference among Oscar Winners and Less Successful Performers***

Type of Analysis†	Status‡	Reduction in Mortality Rates (95% CI), %		Survival Advantage (95% CI), *y*	
		Winners vs. Nominated	Winners vs. Controls	Winners vs. Nominated	Winners vs. Controls
Original data					
Original analysis, PH	1	25 (5 to 41)	28 (10 to 42)		
Original analysis, PH	2	Not reported	20 (0 to 35)		
Original analysis, KM-LR	1			3.6§	3.9‖
New data					
Original analysis, PH	1	23 (3 to 39)	26 (8 to 40)		
Original analysis, PH	2	11 (−12 to 30)	17 (−2 to 33)		
New analysis, PH	2	18 (−4 to 35)	15 (−5 to 32)		
New analysis, P-Y	2	18 (−4 to 36)	15 (−6 to 32)		
Original analysis, KM-LR	1			3.3¶	3.7**
New analysis, P-Y, actuarial	2			1.0 (−0.2 to 2.0)	0.7 (−0.3 to 1.6)

* KM-LR = Kaplan–Meier, log-rank; PH = Cox proportional hazards model; P-Y = performer-years analysis.
† The authors only had access to slightly updated data. See Appendix (available at www.annals.org) for discussion of analyses.
‡ 1 = those who ultimately won were treated as winners from the outset (static); 2 = those who ultimately won were treated as "not yet a winner" in risk sets before they won and as winners after they won (dynamic).
§ $P = 0.013$.
‖ $P = 0.003$.
¶ $P = 0.024$.
** $P = 0.006$.

detect potential immortal time bias? We suggest that when reports compare 2 "groups," such as winners versus nominees, one should carefully examine when and how persons enter a group. Does being in or moving to a group have a time-related requirement? Is the classification based on the status at time zero or later? If later, is this accounted for? Is the term *status*, which implies potential change, more appropriate than the term *group*, which implies, as in a clinical trial, that group membership is fixed from the outset? Is it sufficient to classify a person just once, or do we need to reclassify the "person-moments," that is, the person at different times? Showing timelines, as in the **Figure**, may help. Of course, readers and commentators should be doubly cautious whenever they encounter statistical results that seem too extreme to be true.

From McGill University and Montréal General Hospital, Montréal, Québec, Canada.

Potential Financial Conflicts of Interest: None disclosed.

Corresponding Author: James A. Hanley, PhD, Department of Epidemiology, Biostatistics and Occupational Health, McGill University, 1020 Pine Avenue West, Montréal, Québec H3A 1A2, Canada; e-mail, james.hanley@mcgill.ca.

Current author addresses are available at www.annals.org.

References

1. **Redelmeier DA, Singh SM.** Survival in Academy Award-winning actors and actresses. Ann Intern Med. 2001;134:955-62. [PMID: 11352696]
2. **Walker AM.** Observation and Inference: An Introduction to the Methods of Epidemiology. Chestnut Hill, MA: Epidemiology Resources; 1991.
3. **Suissa S.** Effectiveness of inhaled corticosteroids in chronic obstructive pulmonary disease: immortal time bias in observational studies. Am J Respir Crit Care Med. 2003;168:49-53. [PMID: 12663327]
4. **Hanley JA, Carrieri MP, Serraino D.** Statistical fallibility and the longevity of popes: William Farr meets Wilhelm Lexis. Int J Epidemiol. 2006;35:802-5. [PMID: 16543364]
5. **Farr W.** Vital Statistics: A Memorial Volume of Selections from the Reports and Writings of William Farr. Metuchen, NJ: Scarecrow Pr; 1975.
6. **Colton T.** Statistics in Medicine. Boston: Little, Brown; 1974:297-8.
7. **Hill AB.** A Short Textbook of Medical Statistics. London: Hodder and Stoughton; 1984:278.
8. **Rothman KJ.** Longevity of jazz musicians: flawed analysis [Letter]. Am J Public Health. 1992;82:761. [PMID: 1566968]
9. **Gail MH.** Does cardiac transplantation prolong life? A reassessment. Ann Intern Med. 1972;76:815-7. [PMID: 4554414]
10. **Glesby MJ, Hoover DR.** Survivor treatment selection bias in observational studies: examples from the AIDS literature. Ann Intern Med. 1996;124:999-1005. [PMID: 8624068]

Current Author Addresses: Ms. Sylvestre and Huszti and Dr. Hanley: Department of Epidemiology, Biostatistics and Occupational Health, McGill University, 1020 Pine Avenue West, Montréal, Québec H3A 1A2, Canada.

Appendix

Redelmeier and Singh's report (1), published in May 2001, first compared 235 winners with 887 performers who were never nominated (controls). It also compared them with 527 other nominees (nonwinners).

Except for the last few years of awards, the 1649 performers were identified as winners, nonwinners, or controls "after the fact," that is, in 2000. However, it is helpful to visualize this study as if it had been carried out in real time, with age- and year-specific risk sets built up over time. Seen from this vantage, the 3 groups continued to change membership over time. By the end (the year 2000), there were 1356 nominations, involving 762 unique performers. Of the 762, 235 won at least once, and the remaining 527 did not. Each year, the study would have identified 20 "same sex, nearest in age" performers who played opposite (opposites) the 20 nominees for that year. By the end, this process would generate a total of 1355 opposites. (In 1951, there was no female opposite for Katharine Hepburn). Some opposites had already been nominated or had possibly even won for performances in earlier films. Because performers were classified by their highest achievement, they already would have been upgraded before they were chosen as opposites. Other opposites were nominated for or won in a later film and would have been upgraded and have become part of the 762. The 887 unique opposites who, by the year 2000 or by the time they had died, had never been nominated were termed *controls*.

By the time we received the data file from Redelmeier and Singh (in November 2002), it had been updated to include another year (2001) of awards and deaths. This increased the number of performers from 1649 to 1670 and the number of deaths from 772 to 789. However, we did not have sufficient information to backdate the information in the received file to what it was at the time of the report.

In the file with 1670 performers, we identified a male performer (ID number 1075) who was born in 1953, died in 1994, and was first nominated in 1995. We also identified a female performer (ID number 1430) who was born 1934 and died in 2001; her first film was produced in 1952, her first nomination was in 1960, and her first win was in 1952. We excluded these 2 performers, leaving a total of 1668, comprising 238 winners (104 deceased), 528 nominees (223 deceased), and 902 controls (461 deceased).

When we performed the same analysis as the authors, on the slightly larger data set of 1668 performers, we obtained crude statistics that were similar to those in the original report. The new differences in outcomes among winners and nonwinners and among winners and controls were just slightly smaller than those of the original outcomes. For example (**Table**), the crude difference of life expectancy among winners and controls was 3.9 years in the original report; however, in the updated data report, it is 3.7 years. Whereas the reduction in the mortality rate ratio from the time-independent Cox model was 28% in the original report, it is 26% in the updated data report.

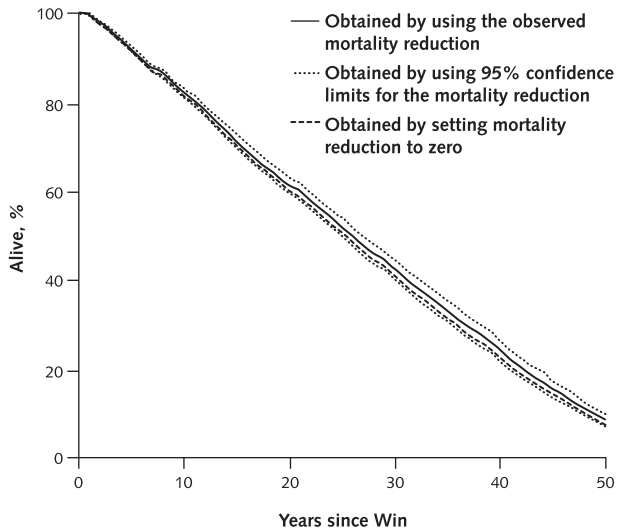
We began our reanalyses with the comparison of winners versus nonwinners. In the original report, winners' life expectancy was 3.6 years longer (99 deaths in 235 persons; $P = 0.013$) than that of nonwinners (221 deaths in 527 persons); the mortality rate reduction, estimated from a proportional hazards model in which status was static, was 25% (95% CI, 5% to 41%). In the updated data set, by the same analyses, we obtained an additional life expectancy of 3.3 years ($P = 0.024$) and a mortality rate reduction of 23% (CI, 3% to 39%).

We reanalyzed the data on these 766 winners and nominees in 2 ways. First, we used a time-dependent Cox proportional hazards model, with age in years as the time axis (that is, risk sets constructed at each age in years at death) and sex and year of birth as covariates. Each performer's status (already a winner or not) was updated at each successive risk set; those who had not yet been nominated by that age at death were excluded from that risk set. The estimated reduction in mortality rate was 18% (CI, −4% to 35%; $P = 0.104$). We represented status as the number of years since winning, with nonwinners assigned zero years, but again, status was not statistically significant, even when the number of years was represented by just a linear term or by linear and quadratic terms.

Second, following guidance in an article by Efron (11), we treated the 21 546 postnomination performer-years as 21 546 separate observations. Winning status was at the time of the observation, and death in the performer-year was treated as a Bernoulli random variable, with logit link. With sex, age, and calendar year as covariates, the mortality rate reduction was 18% (CI, −4% to 36%; $P = 0.100$).

From the fitted coefficients of this model, we calculated the expected total number of years alive in the period between winning and the end of follow-up (2001) in a hypothetical group of 238 performers of the same age in years, sex, and birth year as the 238 winning performers (**Appendix Figure**). We did this under 2 scenarios: 1) if the mortality rate in the 238 were the same as in those who did not win and 2) if the mortality rate were reduced by 18%, by the lower limit of −4% and by the upper limit of 36%. To illustrate this, we take the example of the remaining life expectancy, until the year 2001, for a man born in 1921 who won in 1960 at 39 years of age. From the actuarial life table constructed from the fitted regression coefficients, we calculated that his remaining life expectancy would be 33.3 years if winning did not reduce mortality rates; 34.4 years (a gain of 1.1 years) if it reduced them by 18%; 35.6 years (a gain of 2.3 years) if rates were reduced by 36% (95% upper limit); and 33.0 years (a loss of 0.3 year) if rates were increased by 4% (95% lower limit). The 238 winners would have lived an expected total of 5967.6 years if winning did not reduce mortality rates. The total would be 6194.2 years, 6451.3 years, and 5922.9 years if the mortality rate reductions were 18%, 36%, and −4%, respectively. Thus, the point estimate of the average longevity advantage was $(6194.2 - 5967.6)/238 = 1.0$ years (CI, −0.2 to 2.0 years). In the actual data set, the observed years lived by the 238 winners in

Appendix Figure. **Selected post-win survival of a group of 238 persons of the same sex, birth year, and age at win as performers who won.**



Survival calculated actuarially from the coefficients of a logistic model (with age, sex, year, and status) fitted to the performer-years after each winner's and each never-nominated performer's first film. Status (already a winner and nonwinner), age, and year were updated yearly. Curves obtained by setting the mortality rate reduction to zero (*dashed line*), the point estimate of the reduction parameter (*solid line*), and the upper and lower 95% limits of this (*dotted lines*) are shown. Calculation for each individual terminated at the year 2001, or age 110 years, whichever came first.

the years between when they won and the year 2001 was 6223 years.

Guided by information provided in an article by Turnbull and colleagues (12), we directly estimated the magnitude of the immortal time bias. We calculated a set of conditional probabilities of a first win from the observed number of years between the first nomination and the first win (some won the same year, others much later, and some never). For example, 20.7% of actresses won the year they were first nominated; 2.6% of those who did not win immediately won the next year. Then, for each performer, regardless of whether he or she won an Oscar, we used these conditional probabilities and the number of postnomination years the performer lived to generate a random (hypothetical) age in years at a performer's first win. In each simulation, a majority of performers in each data set died before they could win, and those who did win these computer-generated awards (13) were not aware that they had won. Methods that treated group membership as dynamic recovered the null mortality rate ratio. However, across the simulated data sets, not accounting for immortal time produced an artifactual longevity advantage of 0.8 year (reduction in mortality rates, 6%) for those who won the randomly generated awards over those who did not survive long enough to win them.

We repeated these analyses with the winners versus controls. The initial report showed an additional life expectancy of 3.9 years and a mortality rate reduction of 28% ($P = 0.003$) for winners. In the updated data, the additional life expectancy was 3.7 years and the mortality rate reduction was 26% ($P = 0.006$). When we corrected for the winners' immortal time and took account of sex and year of birth, the mortality rate reduction was 15% (CI, −5% to 32%; $P = 0.129$) using a time-dependent Cox model and 15% (CI, −6% to 32%; $P = 0.161$) in the performer-years analysis. The 15% mortality rate reduction implies an average advantage of 0.7 year (CI, −0.3 to 1.6 years). Our simulations with randomly generated prizes suggested that not accounting for the immortal time—now more substantial—between the year of a winning performer's first film and the year he or she first won would produce an artificial longevity advantage of 1.7 years and a mortality rate reduction of 13%.

There are several references that are relevant to our analysis. Wagoner and colleagues (14) explain why, when particular workers' duration of exposure to vinyl chloride was classified according to what it was at the end of follow-up rather than dynamically, workers who had more than 15 years of exposure to vinyl chloride seemed to have lower mortality rates than those with fewer years of exposure. In a book by Breslow and Day (15), the authors revisit the analysis criticized by Wagoner and colleagues (14) and set out the correct way to make mortality-rate comparisons, that is, by using time-dependent cumulative exposure classifications.

In another relevant reference, Mantel and Byar (16) show how to form "Kaplan–Meier-like" life tables in which persons can move from one "exposure" status to another, for example, when patients move from "waiting-for-a-transplant" status to "post-transplant" status. If patients are inappropriately classified only by their final status (received transplant or not), the time they spend on the list waiting for a transplant is incorrectly credited to the transplant. Those patients who lived long enough received a transplant, but (because these were the earliest patients to receive transplants and transplantation techniques were still in their infancy) their post-transplantation survival was no better than that of those who were alive at the time of the transplantation but did not undergo the procedure.

Abel and Kruger (17) asked a question about baseball players similar to the one Redelmeier and Singh asked about performers. Abel and Kruger focused on players who were inducted into the Baseball Hall of Fame while they were still alive. In contrast to Redelmeier and Singh's study, Abel and Kruger's study "started the clock" at the time a player was inducted and used other players who were alive and who were same age as the inductee for comparison.

In a review article relevant for its discussion of bias, van Walraven and colleagues (18) gave the immortal time bias a slightly different name because they covered a slightly broader spectrum of situations. In their review, they surveyed articles that contained survival analysis and that may have been subject to the same immortal time bias considered in our analysis. They defined a "baseline immeasurable" time-dependent variable as one that could not be measured at baseline and that indicated what happened to patients during observation. They illustrated what oc-

curs if time-dependent variables are analyzed as fixed variables. They used the following helpful example (18):

> Consider a hypothetic study determining prognosticators for patients who have a perforation of the sigmoid and undergo emergency hemicolectomy with colostomy. Patients who die in the first several months after the operation will never undergo closure of their colostomy. If this "baseline immeasurable time-dependent factor" ("Was colostomy closed?") is analyzed in a survival analysis as a fixed variable, one would associate no colostomy closure with a worse survival. This association is erroneous, because death results in the colostomy not getting closed, rather than vice versa.

Van Walraven and colleagues found that "52 survival analyses were susceptible to time-dependent bias. In 35 studies, the bias affected a variable highlighted in the study abstract and correction of the bias could have qualitatively changed the study's conclusion in over half of studies" (18). They concluded that "in medical journals, time-dependent bias is concerningly common and frequently affects key factors and the study's conclusion" (18). Of interest, one of the analyses they "cleared" of possible time-dependent bias was Redelmeier and Singh's (reference 32 in their survey).

Zhou and colleagues (19) use yet another name, "survival bias," for what is essentially the same bias as the immortal time bias. (Walker [2] and Suissa [3] call it immortal time bias, and Glesby and Hoover [10] refer to it as "survivor treatment selection bias.")

The abstract of the report by Zhou and colleagues (19) reads:

> The authors compared five methods of studying survival bias associated with time-to-treatment initiation in a drug effectiveness study using medical administrative databases (1996–2002) from Quebec, Canada. The first two methods illustrated how survival bias could be introduced. Three additional methods were considered to control for this bias. Methods were compared in the context of evaluating statins for secondary prevention in elderly patients post-acute myocardial infarction who initiated statins within 90 days after discharge and those who did not. Method 1 that classified patients into users and nonusers at discharge resulted in an overestimation of the benefit (38% relative risk reduction at 1 year). In method 2, following users from the time of the first prescription and nonusers from a randomly selected time between 0 and 90 days attenuated the effect toward the null (10% relative risk reduction). Method 3 controlled for survival bias by following patients from the end of the 90-day time window; however, it suffered a major loss of statistical efficiency and precision. Method 4 matched prescription time distribution between users and nonusers at cohort entry. Method 5 used a time-dependent variable for treatment initiation. Methods 4 and 5 better controlled for survival bias and yielded similar results, suggesting a 20% risk reduction of recurrent myocardial infarction or death events.

11. **Efron B.** The two-way proportional hazards model. Journal of the Royal Statistical Society, Series B. 2002;64:899-909.
12. **Turnbull BW, Brown BW, Hu M.** Survivorship analysis of heart-transplant data. Journal of the American Statistical Association. 1974;69:74-80.
13. **Leibovici L.** Effects of remote, retroactive intercessory prayer on outcomes in patients with bloodstream infection: randomised controlled trial. BMJ. 2001;323:1450-1. [PMID: 11751349]
14. **Wagoner JK, Infante PF, Saracci R.** Vinyl chloride and mortality? [Letter] Lancet. 1976;2:194-5. [PMID: 73810]
15. **Breslow NE, Day NE.** Statistical Methods in Cancer Research: Volume II: The Design and Analysis of Cohort Studies. New York: Oxford Univ Pr; 1994.
16. **Mantel N, Byar DP.** Evaluation of response-time data involving transient states—illustration using heart-transplant data. Journal of the American Statistical Association. 1974;69:81-6.
17. **Abel EL, Kruger ML.** The longevity of Baseball Hall of Famers compared to other players. Death Stud. 2005;29:959-63. [PMID: 16265814]
18. **van Walraven C, Davis D, Forster AJ, Wells GA.** Time-dependent bias was common in survival analyses published in leading clinical journals. J Clin Epidemiol. 2004;57:672-82. [PMID: 15358395]
19. **Zhou Z, Rahme E, Abrahamowicz M, Pilote L.** Survival bias associated with time-to-treatment initiation in drug effectiveness evaluation: a comparison of methods. Am J Epidemiol. 2005;162:1016-23. [PMID: 16192344]

COMMENTS AND RESPONSES

Reanalysis of Survival of Oscar Winners

TO THE EDITOR: In this issue, Sylvestre and colleagues (1) correctly comment that survival statistics are fallible. The primary analysis in our study (2) was based on the Kaplan–Meier method because life expectancy is the preferred metric in medical decision analysis (3). Our article also provided 40 other secondary analyses to explore different models because no one statistic is ideal. Sylvestre and colleagues argue that the multivariate-adjusted Cox proportional hazards model with a time-varying step function is preferred over our primary analysis approach, do not discuss the limitations of such models, and intimate that other models give an unfair advantage. This position disagrees with us and with other reviews involving our work (4, 5).

We agree that time-varying functions are valuable for addressing a change in status from winning. One drawback with such models can be in assuming the same hazard for all winners following the first win; for example, Jodie Foster (who first won at age 25 years) and Judi Dench (who first won at age 62 years) are assigned identical hazards from age 63 years until death. However, we found that earlier wins were associated with greater advantages, contrary to this assumption. Adding fixed covariates that additionally model age (linear or quadratic) is no simple solution because the likelihood of winning is no simple function of age. The models also have limited power on small data sets, assume no unmeasured heterogeneity, and rarely capture complex trajectories (for example, multiple films, nominations, and wins) (6–9).

We thank many scientists for analyses of our database. We have also done an update to 29 March 2006 and observed 122 more individuals and 144 more deaths since our first publication. Our primary unadjusted analysis shows a smaller survival advantage of 3.6 years (79.7 years vs. 76.1 years; $P = 0.005$). Applying model 1 of Sylvestre and colleagues' Appendix so that winners are treated in a time-varying manner yielded a change in mortality of −8% (95% CI, −14% to 26%; $P = 0.455$). Modifying model 1 so that both winners and nonwinners are treated in a time-varying manner yielded a change in mortality of −15% (CI, −6% to 31%; $P = 0.140$). These estimates overlap earlier results. Apparently, the survival advantage depends on the analytic method chosen.

The statistical debate concerns inbuilt survival advantages that yield an immortality bias. We provided methods for addressing this bias, observed multiple findings suggesting this bias was not large in our cohort, and estimated the hidden confounding that would need to be postulated. We found no survival advantage when we compared individuals with many nominations and individuals with no nominations, for example, contrary to estimates of a large immortality bias. Moreover, we presumed that individuals not reported dead were alive, which is a different type of immortality bias that causes almost all of our analyses and Sylvestre and colleagues' analyses to underestimate survival differences.

Donald A. Redelmeier, MD
Sheldon M. Singh, MD
University of Toronto
Toronto, Ontario M4N 3M5, Canada

Potential Financial Conflicts of Interest: None disclosed.

References

1. Sylvestre M, Huszti E, Hanley JA. Do Oscar winners live longer than less successful peers? A reanalysis of the evidence. Ann Intern Med. 2006;145:361-3.
2. Redelmeier DA, Singh SM. Survival in Academy Award–winning actors and actresses. Ann Intern Med. 2001;134:955-62. [PMID: 11352696]
3. Sox HC, Blatt MA, Higgins MC, Marton KI. Medical Decision Making. Toronto: Butterworths; 1988:182-4.
4. Redelmeier DA, Singh SM. Longevity of screenwriters who win an academy award: longitudinal study. BMJ. 2001;323:1491-6. [PMID: 11751368]
5. Redelmeier DA, Singh SM. Association between mortality and occupation among movie directors and actors. Am J Med. 2003;115:400-3. [PMID: 14553877]
6. Fisher LD, Lin DY. Time-dependent covariates in the Cox proportional-hazards regression model. Annu Rev Public Health. 1999;20:145-57. [PMID: 10352854]
7. Therneau TM, Grambsch PM. Modeling Survival Data: Extending the Cox Model. New York: Springer; 2000:231-2.
8. Kalbfleisch JD, Prentice RL. The Statistical Analysis of Failure Time Data. 2nd ed. Hoboken, NJ: J Wiley; 2002:196-208.
9. Allison PD. Survival Analysis Using SAS: A Practical Guide. Cary, NC: The SAS Institute Inc.; 2004:111-84.

EDITORS' NOTE: The debate between Sylvestre and colleagues (1) and Redelmeier and Singh shows both the value and limitations of prepublication peer review and underscores the importance of review after publication. The original paper by Redelmeier on the survival of Oscar winners (2) underwent close in-house scrutiny and external methodologic review, which resulted in several new analyses, including the "time-varying covariate" model we discuss here. Because the editors felt that the methodologic issues were subtle, we also took what was at that time a somewhat unusual step to facilitate postpublication review. As a condition of publication, we required the authors to make the data set available to interested researchers. Unfortunately, various complications prevented its prompt dissemination, and it has taken almost 5 years for someone to come forward with a reanalysis of the data. We are glad to publish Sylvestre and colleagues' reanalysis, partly because the article affords a chance to amend a widely publicized result, but more so because the analytic methods at issue apply to many health care research questions.

The main purpose of this letter is to help the technically less sophisticated reader to understand the issues under discussion. The central issue is how best to analyze a sudden change in risk due to some life event (becoming ill, starting a high-risk behavior, or starting a treatment). In this case, the event is a salutary one: winning an important prize. The question is exactly when to "start the clock" in assessing whether the prize changes the winner's subsequent risk profile, and how to do that analytically. Redelmeier and Singh referred to this question in their original paper as the "time-zero" problem. Because Redelmeier and Singh matched winners and nonwinners on their age at the time the Oscar was won, their analysis appeared to start the clock at the right moment. However, their primary analysis did not maintain that matching; instead, it combined all winners into one group and all losers into another group and compared winners' and nonwinners' survival from birth. With this approach, winning the prize gets credit for how long the winner lived before winning the prize. This primary analysis produced a large and highly statistically significant advantage (a 3.9-year increase in life expectancy, equivalent to a 28% annual risk reduction), the outcome high-

lighted in the original paper and abstract and publicized in subsequent media reports.

As Sylvestre and colleagues make clear, the optimal methods of analysis involve starting the clock at the moment of winning the prize. In their 2001 paper, Redelmeier and Singh presented a number of secondary analyses that started the clock at different moments, including a Cox survival analysis in which the risk for subsequent death for winners and nonwinners could change at the instant of winning an Oscar. With this form of analysis, the putative risk modifier—in this case, winning the prize—would have no effect early in a prizewinner's life but would have an effect after the win. Winning the prize is, in statistical terminology, a "time-varying covariate." The Cox model suggested a 20% mortality risk reduction, with borderline statistical significance, and a range of uncertainty that just included the possibility of no survival benefit. Speaking for the *Annals* Editors, we regret that the original paper did not adequately emphasize this more equivocal but probably more correct result.

In the preceding letter, Redelmeier and Singh report the results of using the time-varying covariate modeling approach to analyze their most recently compiled data set of Oscar winners (updated to 2006). This analysis yields still weaker, now statistically nonsignificant evidence that winning an Oscar prolongs life: either an 8% survival advantage (with statistically compatible effects ranging from as low as 14% shorter survival to as high as 26% longer survival) or a 15% survival advantage (the uncertainty of which is compatible with a range of 6% shorter survival to up to 31% greater survival). The 2 estimates differ according to how the analysis handles the nonwinners.

Sylvestre and colleagues point out that although this Cox "time-varying" result is closer to the truth than the result that Redelmeier and Singh reported as the primary analysis in their paper, it may not yet be optimal, for many of the same reasons that Redelmeier and Singh point out in their letter. Sylvestre and colleagues prefer the conceptually simpler approach of measuring life expectancy from the moment of winning the Oscar. This approach, outlined in their Web-only appendix, produces a result qualitatively consistent with the result from the time-varying model that Redelmeier and Singh report in their letter.

The debate about whether winning an Academy Award confers any survival advantage—and if it does, by how much—will continue in exchanges between interested scientists. To facilitate their participation in this discussion, we are posting on the *Annals* Web site the data set (updated to March 2006) that Redelmeier and Singh have provided and that Sylvestre and colleagues used in their analysis. The Editors invite people who want to contribute to the discussion to communicate their ideas as a Rapid Response letter about Sylvestre and colleagues' article. We hope that other members of the statistical community will take up the challenge of determining the most appropriate way to measure the effect of winning an Oscar and the statistical uncertainty around the result. Their efforts will inform the analysis of many similar phenomena in biomedicine.

When the dust settles, we expect that the estimated effect will be nonsignificant, and closer to Redelmeier and Singh's adjusted estimates and to the estimate of Sylvestre and colleagues than to the original estimate of 3.9 years (now 3.6 years, using the 2006 updated data set). Until then, we urge everyone to observe much greater caution about claiming the existence of an "Oscar effect" on life span. Granted, doing so may mean some tempering of joy among Academy Award winners. They will get their statuette, and the attention it brings, but we doubt that winning it will confer many—if any—more years to enjoy the fruits of their enhanced celebrity.

Steven Goodman, MD, PhD
Associate Editor

Harold C. Sox, MD
Editor

Potential Financial Conflicts of Interest: None disclosed.

References

1. Sylvestre M, Huszti E, Hanley JA. Do Oscar winners live longer than less successful peers? A reanalysis of the evidence. Ann Intern Med. 2006;145:361-3.
2. Redelmeier DA, Singh SM. Survival in Academy Award-winning actors and actresses. Ann Intern Med. 2001;134:955-62. [PMID: 11352696]

Cryptogenic Stroke and Patent Foramen Ovale

TO THE EDITOR: In their comprehensive and informative Update (1), Drs. Holloway and Józefowicz suggest using warfarin for secondary prevention of stroke in patients with atrial septal defect. The current literature has no strong evidence to support this view, and therefore the current guidelines from the American Academy of Neurology state that "the evidence is insufficient to determine whether aspirin or warfarin is superior in preventing recurrent stroke or death in patients with patent foramen ovale (PFO) alone" (2). However, the American Academy of Neurology does recommend warfarin therapy in patients with patent foramen ovale and evidence of deep venous thrombosis (2).

The rationale for aspirin therapy in patients with patent foramen ovale comes from a French study of 216 patients with a cryptogenic stroke (3). This trial reported that the incidence of recurrent stroke was only 2.3% after 4 years in patients who had patent foramen ovale alone and were taking aspirin, a value similar to the 4.2% risk in the control group. Support for the use of aspirin also comes from the Patent Foramen Ovale in Cryptogenic Stroke Study, which did not demonstrate a statistical difference between the effects of aspirin and warfarin on the risk for subsequent stroke or death among patients with cryptogenic stroke and patent foramen ovale (4). Although studies have favored warfarin over aspirin for secondary prevention of stroke in patients with patent foramen ovale and atrial septal defect, they included small numbers of patients, had limited statistical power, and were unblinded and retrospective (5). On the basis of currently available evidence, the American College of Chest Physicians also recommends aspirin over no therapy or warfarin therapy in patients with patent foramen ovale (6).

Ashok K. Malani, MD
Hussam Ammar, MD
Heartland Regional Medical Center
St. Joseph, MO 64506

Potential Financial Conflicts of Interest: None disclosed.