Understanding Kaplan-Meier and Survival Statistics

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Purpose: This paper aims to explore the mathematics of Kaplan-Meier and survival statistics, explain how the mathematics are relevant for prosthodontic treatment planning, and provide advice for future presentation of such data. ***Materials and Methods:*** The mathematics of the Kaplan-Meier and related survival statistic formulas were explored with hypothetical data consisting of 100 prostheses, reviewed yearly for 10 years. The hypothetical impact of failures (n = 1, 2, 9, or 0) and censored data (n = 5, 9, or 10) were reviewed across three life tables and survival curves. Actual published data of 304 porcelain veneers, reviewed regularly for 16 years, were similarly utilized. The impact of changing the number of failures and censored data on the estimated cumulative survival (ECS) and the standard error (SE) was reviewed across two life tables and survival curves. ***Results:*** The ECS and SE are calculated from two data figures: the number of failures that occurred during an interval and the number of prostheses at risk during that same interval. The ECS reduces and its SE enlarges when prostheses fail. These results can also change if prostheses are lost from the study (censored). However, the number of failures is in the numerator of the equation. Therefore, if no failures occur, loss of prostheses from the study cannot change the ECS or the SE. This can dramatically affect the calculated ECS and SE if a prosthesis becomes lost to follow-up rather than presenting as a failure. The hypothetical and actual data were used to explore these concepts. ***Conclusion:*** Current techniques for analysis of time-to-event data are imperfect and can be misleading. It therefore behooves authors to strive to improve reporting transparency, journals to support such industry, and readers to remain mindful that the cumulative survival is an estimate, ie, a reflection of reality. *Int J Prosthodont 2013;26:218–226. doi: 10.11607/ijp.3406*

Prosthodontic research commonly explores longitudinal outcomes of prostheses as they age. These may be experimental studies such as randomized or controlled clinical trails that follow the performance of clinical interventions within patients enrolled for the research. They may also be observational studies such as prospective or retrospective cohort studies that follow the performance of interventions provided to patients. Analyses of these studies can use time-to-event statistical techniques, such as Kaplan-Meier,[1,2] to calculate the estimated cumulative survival (ECS). In such analyses, common endpoints (events) are "survival" and "failure."

A handsearch of the 50 leading dental journals, classified by citation factor, for 2008 was completed by this author. Continued analysis of these data is underway. The search revealed that 1.3% of all articles employed time-to-event statistics. Of articles in prosthodontic and implant journals (*Gerodontology, International Journal of Prosthodontics, Journal of Adhesive Dentistry, Journal of Oral Rehabilitation, Journal of Prosthetic Dentistry, Clinical Implant Dentistry and Related Research, Clinical Oral Implants Research, Implant Dentistry, International Journal of Oral & Maxillofacial Implants, International Journal of Periodontics and Restorative Dentistry*), 6% employed time-to-event statistics, and of those reporting outcome of dental treatment over time in human subjects, 54% employed time-to-event statistics.

The quality of reporting varied, with 70% failing to report the survival rate as an estimate, 71% failing to include a life table, and 50% failing to include a survival curve.

The ECS of prosthodontic prostheses forms the keystone of treatment planning. Clinicians rely on these survival outcomes to compare competing treatment options. Unfortunately, the statistic can be poorly reported and remains poorly understood.

This article aims to explore the mathematics of Kaplan-Meier and survival statistics, explain how the mathematics are relevant for prosthodontic treatment planning, and provide advice for future presentation of such data.

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Materials and Methods

The Data

Longitudinal studies provide two parallel types of data: the prosthesis outcome and the time at which that outcome occurred. In realistic clinical studies, it takes time to enroll patients and to perform treatments. Therefore, it is rare for all patients to be enrolled in the study at its immediate inception. Also, as studies progress with time, censorship (such as loss to follow-up) can occur. In other words, not all patients will remain in the study until its conclusion, and not all patients are necessarily enrolled at its inception. At each time interval within the study (such as year 1, year 2, year 3), patients and their prostheses are assessed and could be defined as surviving, failed, or censored. This definition can change as the study proceeds, with surviving prostheses possibly becoming failed or censored with time.

Consequently, not all data points are present for the entire study period. The Kaplan-Meier and survival analyses methods allow researchers to calculate an "estimated" cumulative survival rather than an "actual" percentage. The outcome of the prostheses within the study contributes to the mathematical calculations and the ECS. If prostheses become censored, they are removed from further direct calculations and do not contribute to the percentage survival of each future individual interval. However, their previous outcomes continue to contribute indirectly to the ECS through the mathematical formula. This will be explained in more detail below.

ECSs are commonly reported, but they are unfortunately poorly understood. It is often unclear that the calculated percentage is an estimate rather than a reality. Authors compound this problem by using incorrect nomenclature and often failing to report the "survival" as the "estimated cumulative survival" or the "estimated survival rate."

Mathematics is employed to combine disparate outcomes, such as surviving, failed, and censored prostheses, over a period of time. As these outcomes vary between different time periods, the results use previous "known data" to estimate the outcome at the current point in time. As patients and prostheses are lost from the studies, less data become available (that is, there are fewer prostheses at risk) and the "estimated" cumulative survival becomes less robust. This loss and censorship confounds our understanding.

The number of prostheses at risk can be defined differently across different studies. The life table actuarial method defines the number of prostheses at risk to be the number that enter an interval minus *half* the number that were censored (interval-censored data).

$$\hat{S}(t) = \prod_{t_i < t} \left(1 - \frac{d_i}{n_i}\right)$$

$$SE[\hat{S}(t)] = \sqrt{[\hat{S}(t)^2] \sum \frac{d_i}{n_i (n_i - d_i)}}$$

$\hat{S}$ = survival; t = time; d_i = number of events (failures) at t_i; n_i = number at risk at t_i.

Fig 1 The ECS function and Greenwood SE formulas.

This is based on the assumption that loss to follow-up occurs randomly across a time interval (such as a 1-year period).

The Kaplan-Meier product limit method defines the number of prostheses at risk as the number that have not yet failed. It uses exact failure dates and calculates the survival function each time an event (failure) occurs (right-censored data). Therefore, the intervals vary in length. If censorship is small in comparison to the numbers in the study, this is a more accurate way to estimate the cumulative survival than the actuarial method, but it relies on knowing exact failure dates. If censorship has occurred when an event has been registered, then censorship is considered to have occurred immediately *after* the event. In other words, the patients are all considered to be at risk for the survival calculation of that interval. However, if some subjects are only known to be failures when they present for a regular review (such as a 1-year period), the exact failure date cannot be known. In such instances, the method can be modified to accommodate a mixture of exact failure dates and interval-censored data. Although not specifically stated, it is likely that this method is employed in many prostheses outcome studies.

Data Exploration

The mathematics of calculating the ECS and its associated standard error (SE) were explored with hypothetical data sets and with data from an actual study.

The formulas for the ECS and Greenwood SE are outlined in Fig 1. The ECS and its SE are calculated from two variables: the number of events (such as failures) and the number of prostheses remaining at risk. It is important to note that the number of failures is in the numerator of the equation.

The hypothetical data consisted of 100 prostheses reviewed yearly for 10 years. The hypothetical impact of failures (n = 1, 2, 9, or 0) and censored data (n = 5, 9, or 10) were reviewed across three life tables and survival curves. The ECS was calculated with the ECS function (Fig 1), where the number of prostheses

Table 1 Hypothetical Data Where 100 Prostheses Were Followed up Yearly for 10 Years, 2 Failures Occurred (d_i) and 5 Prostheses Were Lost to Follow-up Each Year. The Worked Example Kaplan Meier Estimated Cumulative Survival Has Been Included. The Formula for the Standard Error Is More Complex, with the Final Figure Only Included. The Estimated Cumulative Survival at 10 Years Was 70.93% ± 5.78%

Time (y)	Number	Censored	Failed	Probability of survival (P_i) (per interval)		ECS	ECS (%)	SE (%)
0	100	0	0	NA	1.00	$P_0 = 1.00$	100.00	0.00
0–1	100	5	2	$1 - \frac{2}{100 - 2.5}$	0.9795	$P_0 \times P_1 =$ 1.00×0.9795	97.95	1.44
1–2	93	5	2	$1 - \frac{2}{93 - 2.5}$	0.9779	$P_0 \times P_1 \times P_2 =$ $1.00 \times 0.9795 \times 0.9779$	95.78	2.06
2–3	86	5	2	$1 - \frac{2}{86 - 2.5}$	0.9760	$P_0 \times P_1 \times \ldots P_3 =$ $1.00 \times 0.9795 \times \ldots 0.9760$	93.49	2.57
3–4	79	5	2	$1 - \frac{2}{79 - 2.5}$	0.9739	$P_0 \times P_1 \times \ldots P_4 =$ $1.00 \times 0.9795 \times \ldots 0.9739$	91.05	3.03
4–5	72	5	2	$1 - \frac{2}{72 - 2.5}$	0.9712	$P_0 \times P_1 \times \ldots P_5 =$ $1.00 \times 0.9795 \times \ldots 0.9712$	88.43	3.47
5–6	65	5	2	$1 - \frac{2}{65 - 2.5}$	0.9680	$P_0 \times P_1 \times \ldots P_6 =$ $1.00 \times 0.9795 \times \ldots 0.9680$	85.60	3.89
6–7	58	5	2	$1 - \frac{2}{58 - 2.5}$	0.9640	$P_0 \times P_1 \times \ldots P_7 =$ $1.00 \times 0.9795 \times \ldots 0.9640$	82.51	4.32
7–8	51	5	2	$1 - \frac{2}{51 - 2.5}$	0.9588	$P_0 \times P_1 \times \ldots P_8 =$ $1.00 \times 0.9795 \times \ldots 0.9588$	79.11	4.76
8–9	44	5	2	$1 - \frac{2}{44 - 2.5}$	0.9518	$P_0 \times P_1 \times \ldots P_9 =$ $1.00 \times 0.9795 \times \ldots 0.9518$	75.30	5.24
9–10	37	5	2	$1 - \frac{2}{37 - 2.5}$	0.9420	$P_0 \times P_1 \times \ldots P_{10} =$ $1.00 \times 0.9795 \times \ldots 0.9420$	70.93	5.78

ECS = estimated cumulative survival; SE = standard error.

at risk was considered to be the number entering the interval minus *half* the number censored. The Greenwood formula was used to calculate the SE.

Actual published data of 304 porcelain veneers, reviewed regularly for 16 years, were similarly used to explore the mathematics. In this study, the authors chose to use a strict definition for the number of prostheses remaining at risk. The ECS was calculated with the ECS function (Fig 1), where the number of prostheses at risk was considered to be the number entering the interval minus *all* (not half) the number censored. The impact of changing the number of failures and censored data on the ECS and the SE was reviewed across two life tables and survival curves.

Results

The Mathematics—Hypothetical Data

The hypothetical data consisted of 100 (n_i) prostheses reviewed yearly for 10 years (t). Hypothetically, two failures will occur each year (d_i), and five prostheses will become sequentially lost to follow-up. The ECS and SE are calculated from two data figures: the number of failures that occurred during an interval and the number of prostheses at risk during that same interval.

The life table for the hypothetical data is outlined in Table 1. Initially, the percentage survival is calculated for each individual interval (yearly). Each year could be considered to be a "separate," unrelated study. For example, the percentage survival at the end of year 1 = 97.95%, at the end of year 2 = 95.78%, and so forth. To combine the data together, the probability of survival of each interval is multiplied together (a product calculation). It becomes clear that data are removed from future equations if censorship occurs, but remain within the overall calculation via the product calculation.

Therefore, over 10 years, 20 prostheses have failed, 50 have become lost to follow-up (and were censored), and the ECS is 70.93%. This figure is calculated by multiplying the probability of survival of each intervening year.

$$\begin{aligned} \text{ECS} &= P_0 \times P_1 \times P_2 \times \ldots \times P_9 \times P_{10} \\ &= 1.00 \times 0.9795 \times 0.9779 \times \ldots \times 0.9518 \times 0.9420 \\ &= 0.7093\ (70.93\%) \end{aligned}$$

The formula for Greenwood SE is more complex and difficult to express in longhand. The calculation also relates to the number of failures that occurred during an interval and the number of prostheses at risk

Table 2 Hypothetical Data Where 100 Prostheses Were Followed up Yearly for 10 Years: If No Failures Were Observed (d_i) and 10 Prostheses Were Lost to Follow-up Each Year, the Estimated Cumulative Survival at 10 Years Would Be 100% ± 0%. Alternatively, If 1 of the 10 Prostheses During the 10th Year Was a Failure (d_i = 1, censored = 9), the Estimated Cumulative Survival at 10 Years Would Be 81.82% ± 16.45%

Time (y)	Number	Censored	Failed	Probability of survival (P_i) (per interval)		ECS	ECS (%)	SE (%)
0	100	0	0	NA	1.00	$P_0 = 1.00$	100.00	0.00
0–1	100	10	0	$1 - \frac{0}{100 - 5}$	1.00	$P_0 \times P_1 =$ 1.00 x 1.00	100.00	0.00
1–2	90	10	0	$1 - \frac{0}{90 - 5}$	1.00	$P_0 \times P_1 \times P_2 =$ $1.00 \times 1.00 \times 1.00$	100.00	0.00
2–3	80	10	0	$1 - \frac{0}{80 - 5}$	1.00	$P_0 \times P_1 \times \ldots P_3 =$ $1.00 \times 1.00 \times \ldots 1.00$	100.00	0.00
3–4	70	10	0	$1 - \frac{0}{70 - 5}$	1.00	$P_0 \times P_1 \times \ldots P_4 =$ $1.00 \times 1.00 \times \ldots 1.00$	100.00	0.00
4–5	60	10	0	$1 - \frac{0}{60 - 5}$	1.00	$P_0 \times P_1 \times \ldots P_5 =$ $1.00 \times 1.00 \times \ldots 1.00$	100.00	0.00
5–6	50	10	0	$1 - \frac{0}{60 - 5}$	1.00	$P_0 \times P_1 \times \ldots P_6 =$ $1.00 \times 1.00 \times \ldots 1.00$	100.00	0.00
6–7	40	10	0	$1 - \frac{0}{40 - 5}$	1.00	$P_0 \times P_1 \times \ldots P_7 =$ $1.00 \times 1.00 \times \ldots 1.00$	100.00	0.00
7–8	30	10	0	$1 - \frac{0}{30 - 5}$	1.00	$P_0 \times P_1 \times \ldots P_8 =$ $1.00 \times 1.00 \times \ldots 1.00$	100.00	0.00
8–9	20	10	0	$1 - \frac{0}{20 - 5}$	1.00	$P_0 \times P_1 \times \ldots P_9 =$ $1.00 \times 1.00 \times \ldots 1.00$	100.00	0.00
9–10	10	10	0	$1 - \frac{0}{10 - 5}$	1.00	$P_0 \times P_1 \times \ldots P_{10} =$ $1.00 \times 1.00 \times \ldots 1.00$	100.00	0.00
Alternative 10-year data								
9–10	10	9	1	$1 - \frac{1}{10 - 4.5}$	0.8182	$P_0 \times P_1 \times \ldots P_{10} =$ $1.00 \times 1.00 \times \ldots 0.8182$	81.82	16.45

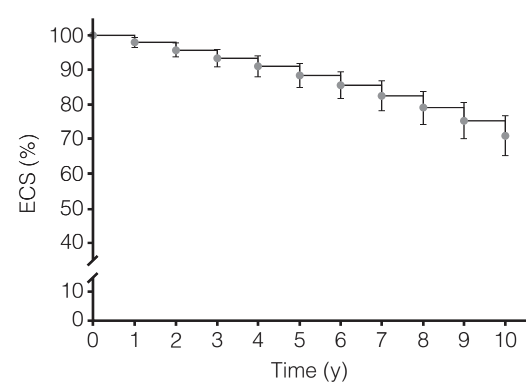
ECS = estimated cumulative survival; SE = standard error.

during that same interval. At 10 years, the ECS and its SE is 70.93% ± 5.78%. This can be seen in the survival curve (Fig 2).

Changes in the ECS and the SE are completely reliant on the “number of failures.” If no failures occur within a given interval, the probability of survival for that interval remains at 100% and its SE is 0%.

To explore the effect of the number of failures on survival probability calculations, a second set of hypothetical data was proposed (Table 2). The data consisted of 100 (n_i) prostheses reviewed yearly for 10 years (t). Hypothetically, no failures were observed during the yearly review (d_i), while 10 prostheses became sequentially lost to follow-up. Therefore, at 10 years, all prostheses had become censored and none remained in the study.

These hypothetical data show that the ECS remained at 100% with an SE of 0% (Table 2, Fig 3). Therefore, with no prostheses in the study, it can confidently be stated that there is a 10-year ECS of 100%! Within this data set, a further hypothetical change is proposed. What would happen if a single patient in the final year returned for continued care and presented as a failure? The survival probability for that single interval would decrease from 1.00 to 0.82, and the 10-year ECS would become 81.82% ± 16.45% (Table 2).



No. at risk at beginning of each 1-year interval and no. censored or failed within each 1-year interval

	0	1	2	3	4	5	6	7	8	9	10
Actual data											
N	100	100	93	86	79	72	65	58	51	44	37
C		0	5	5	5	5	5	5	5	5	5
D		0	2	2	2	2	2	2	2	2	2

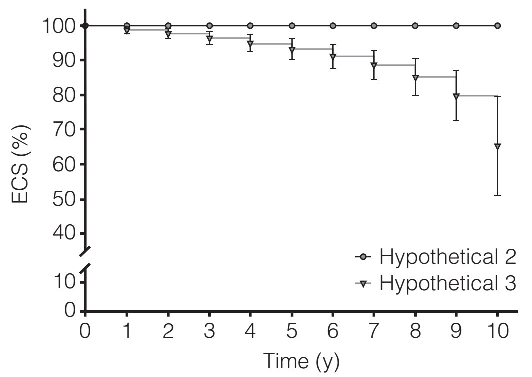
N = number; C = censored; D = failed.

Fig 2 Kaplan-Meier ECS curve and truncated life table for hypothetical data from Table 1. One hundred prostheses were followed over 10 years with two failed and five censored prostheses per year. The ECS at 10 years was 70.93% ± 5.78%.

Table 3 Hypothetical Data Where 100 Prostheses Were Followed up Yearly for 10 Years. The Estimated Cumulative Survival at 10 Years Became 65.22% ± 14.40% if 1 of the 10 Prostheses that Became Lost to Follow-up During Each Year Was Instead a Failure (d_i)

Time (y)	Number	Censored	Failed	Probability of survival (P_i) (per interval)		ECS	ECS (%)	SE (%)
0	100	0	0	NA	1.0000	$P_0 = 1.00$	100.00	0.00
0–1	100	9	1	$1 - \frac{1}{100 - 4.5}$	0.9895	$P_0 \times P_1 =$ 1.00×0.9895	98.95	1.04
1–2	90	9	1	$1 - \frac{1}{90 - 4.5}$	0.9883	$P_0 \times P_1 \times P_2 =$ $1.00 \times 0.9895 \times 0.9883$	97.80	1.54
2–3	80	9	1	$1 - \frac{1}{80 - 4.5}$	0.9868	$P_0 \times P_1 \times \ldots P_3 =$ $1.00 \times 0.9895 \times \ldots 0.9868$	96.50	1.99
3–4	70	9	1	$1 - \frac{1}{70 - 4.5}$	0.9847	$P_0 \times P_1 \times \ldots P_4 =$ $1.00 \times 0.9895 \times \ldots 0.9847$	95.03	2.45
4–5	60	9	1	$1 - \frac{1}{60 - 4.5}$	0.9820	$P_0 \times P_1 \times \ldots P_5 =$ $1.00 \times 0.9895 \times \ldots 0.9820$	93.31	2.94
5–6	50	9	1	$1 - \frac{1}{50 - 4.5}$	0.9780	$P_0 \times P_1 \times \ldots P_6 =$ $1.00 \times 0.9895 \times \ldots 0.9780$	91.26	3.52
6–7	40	9	1	$1 - \frac{1}{40 - 4.5}$	0.9718	$P_0 \times P_1 \times \ldots P_7 =$ $1.00 \times 0.9895 \times \ldots 0.9718$	88.69	4.26
7–8	30	9	1	$1 - \frac{1}{30 - 4.5}$	0.9608	$P_0 \times P_1 \times \ldots P_8 =$ $1.00 \times 0.9895 \times \ldots 0.9608$	85.21	5.33
8–9	20	9	1	$1 - \frac{1}{20 - 4.5}$	0.9355	$P_0 \times P_1 \times \ldots P_9 =$ $1.00 \times 0.9895 \times \ldots 0.9355$	79.72	7.29
9–10	10	9	1	$1 - \frac{1}{10 - 4.5}$	0.8182	$P_0 \times P_1 \times \ldots P_{10} =$ $1.00 \times 0.9895 \times \ldots 0.8182$	65.22	14.40

ECS = estimated cumulative survival; SE = standard error.



No. at risk at beginning of each 1-year interval and no. censored or failed within each 1-year interval

	0	1	2	3	4	5	6	7	8	9	10
Hypothetical 2											
N	100	100	90	80	70	60	50	40	30	20	10
C		0	10	10	10	10	10	10	10	10	10	10
D		0	0	0	0	0	0	0	0	0	0	0
Hypothetical 3											
N	100	100	90	80	70	60	50	40	30	20	10
C	0	9	9	9	9	9	9	9	9	9	9
D	0	1	1	1	1	1	1	1	1	1	1

N = number; C = censored; D = failed.
Hypothetical 2 = 0 failures and 10 censored; hypothetical 3 = 1 failure and 9 censored.

Fig 3 Kaplan-Meier ECS curve and truncated life table for hypothetical data from Tables 2 and 3. One hundred prostheses were followed over 10 years. When zero prostheses failed and 10 were censored per year, the 10-year ECS was 100% ± 0%. The ECS at 10 years became 65.22% ± 14.40% if one of the 10 prostheses that became lost to follow-up during each year was instead a failure.

Furthermore, what would happen if a single patient each year returned for continued care instead of becoming lost to follow-up and presented as a failure? The 10-year ECS would become 65.22% ± 14.40% (Fig 3, Table 3).

These examples illustrate the potential for misinterpretation of survival analyses.

The Mathematics—Real Data

The mathematics can have a dramatic effect on the interpretation of real data. To explore the impact of these formulas further, real data from research published by this author was considered.

The outcome of 304 feldspathic porcelain veneers over 16 years was published in 2007.[3] The formatting of the life table has been modified to align with the formatting used throughout this discussion paper.

Again, the ECS is related to the number of failures (d_i) and the number remaining at risk (n_i). However, for this paper, the author chose to use a strict definition for the number remaining at risk, ie, the number at risk was the number entering the interval minus *all* (not half) the number censored.

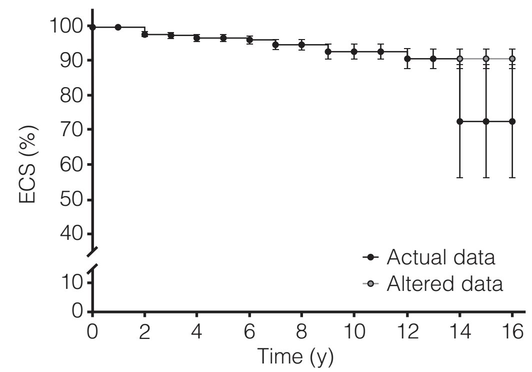
The paper reported an ECS of 92.91% ± 2.04% at 10 years and 90.80% ± 2.89% at 13 years. This survival dropped to 72.64% ± 16.41% at 14 years following the failure of one single veneer (Table 4, Fig 4).

Further details can be seen in Table 4. At the end of the 10th year, 91 veneers remained in the study,

Table 4 Life Table and Mathematical Calculations for 304 Feldspathic Porcelain Veneers In Situ for up to 16 Years. The Estimated Cumulative Survival at 16 Years Was 72.64% ± 16.41%

Time (y)	Number	Censored	Failed	Probability of survival (P_i) (per interval)		ECS	ECS (%)	SE (%)
0	304	0	0	NA	1.0000	$P_0 = 1.00$	100.00	0.00
0–1	304	6	0	$1 - \frac{0}{304 - 6}$	1.0000	$P_0 \times P_1 =$ 1.00×1.00	100.00	0.00
1–2	298	0	6	$1 - \frac{6}{298 - 0}$	0.9799	$P_0 \times P_1 \times P_2 =$ $1.00 \times 1.00 \times 0.9799$	97.99	0.81
2–3	292	22	1	$1 - \frac{1}{292 - 22}$	0.9963	$P_0 \times P_1 \times \ldots P_3 =$ $1.00 \times 1.00 \times \ldots 0.9963$	97.62	0.89
3–4	269	18	2	$1 - \frac{2}{269 - 18}$	0.9921	$P_0 \times P_1 \times \ldots P_4 =$ $1.00 \times 1.00 \times \ldots 0.9921$	96.85	1.04
4–5	249	23	0	$1 - \frac{0}{249 - 23}$	1.0000	$P_0 \times P_1 \times \ldots P_5 =$ $1.00 \times 1.00 \times \ldots 1.0000$	96.85	1.04
5–6	226	46	1	$1 - \frac{1}{226 - 46}$	0.9944	$P_0 \times P_1 \times \ldots P_6 =$ $1.00 \times 1.00 \times \ldots 0.9944$	96.32	1.16
6–7	179	38	2	$1 - \frac{2}{179 - 38}$	0.9858	$P_0 \times P_1 \times \ldots P_7 =$ $1.00 \times 1.00 \times \ldots 0.9858$	94.95	1.49
7–8	139	14	0	$1 - \frac{0}{139 - 14}$	1.0000	$P_0 \times P_1 \times \ldots P_8 =$ $1.00 \times 1.00 \times \ldots 1.0000$	94.95	1.49
8–9	125	32	2	$1 - \frac{2}{125 - 32}$	0.9785	$P_0 \times P_1 \times \ldots P_9 =$ $1.00 \times 1.00 \times \ldots 0.9785$	92.91	2.04
9–10	91	14	0	$1 - \frac{0}{91 - 14}$	1.0000	$P_0 \times P_1 \times \ldots P_{10} =$ $1.00 \text{ x } 1.00 \times \ldots 1.0000$	92.91	2.04
10–11	77	21	0	$1 - \frac{0}{77 - 21}$	1.0000	$P_0 \times P_1 \times \ldots P_{11} =$ $1.00 \times 1.00 \times \ldots 1.0000$	92.91	2.04
11–12	56	12	1	$1 - \frac{1}{56 - 12}$	0.9773	$P_0 \times P_1 \times \ldots P_{12} =$ $1.00 \times 1.00 \times \ldots 0.9773$	90.80	2.89
12–13	43	22	0	$1 - \frac{0}{43 - 22}$	1.0000	$P_0 \times P_1 \times \ldots P_{13} =$ $1.00 \times 1.00 \times \ldots 1.0000$	90.80	2.89
13–14	21	16	1	$1 - \frac{1}{21 - 16}$	0.8000	$P_0 \times P_1 \times \ldots P_{14} =$ $1.00 \times 1.00 \times \ldots 0.8000$	72.64	16.41
14–15	4	0	0	$1 - \frac{0}{4 - 0}$	1.0000	$P_0 \times P_1 \times \ldots P_{15} =$ $1.00 \times 1.00 \times \ldots 1.0000$	72.64	16.41
15–16	4	1	0	$1 - \frac{0}{4 - 0}$	1.0000	$P_0 \times P_1 \times \ldots P_{16} =$ $1.00 \times 1.00 \times \ldots 1.0000$	72.64	16.41

ECS = estimated cumulative survival; SE = standard error.



No. at risk at beginning of each 2-year interval and no. censored or failed within each 2-year interval

	0	2	4	6	8	10	12	14	16
Actual data									
N	304	304	292	249	179	125	77	43	4
C	0	6	40	69	52	46	33	38	1
D	0	6	3	1	2	2	1	1	0
Altered data									
N	304	304	292	249	179	125	77	43	4
C	0	6	40	69	52	46	33	39	1
D	0	6	3	1	2	2	1	0	0

N = number; C = censored; D = failed; interval length = 2 years.

Fig 4 *(right)* Kaplan-Meier ECS curve and truncated life table for 304 feldspathic porcelain veneers followed for up to 16 years. The actual data represented an ECS at 16 years of 72.64% ± 16.41%. Hypothetically, changing the number of failures at the 14th year from 1 to 0 would result in an improved 16-year ECS of 90.80% ± 2.89%.

14 had failed, and 213 were censored (32 had failed to return for reviews, 181 veneers had been in situ for less than 10 years). This resulted in a 10-year ECS of 92.91% ± 2.04%. This cumulative survival is the product of the probability of survival for the first 10 years.

At the end of the 14th year, 21 veneers remained in the study, 16 veneers became lost to follow-up, and thus 5 remained at risk during the interval. At this time, 1 veneer failed. Therefore, the failure rate was 20% for that interval, the survival probability became 0.80, and the ECS was determined to be 72.64% ± 16.41%. A 16.41% SE equates to a 95% confidence interval [CI] spanning from approximately 40% to 100%!

Table 5 Life Table and Mathematical Calculations for 304 Feldspathic Porcelain Veneers In Situ for up to 16 Years. Hypothetically, Changing* the Number of Failures at the 14th Year from 0 to 1 Would Result in a 16-Year Estimated Cumulative Survival of 90.80% ± 2.89%

Time (y)	Number	Censored	Failed	Probability of survival (P_i) (per interval)		ECS	ECS (%)	SE (%)
0	304	6	0	NA	1.0000	$P_0 = 1.00$	100.00	0.00
0–1	304	6	0	$1 - \frac{0}{304 - 6}$	1.0000	$P_0 \times P_1 =$ 1.00×1.00	100.00	0.00
1–2	298	0	6	$1 - \frac{6}{298 - 0}$	0.9799	$P_0 \times P_1 \times P_2 =$ $1.00 \times 1.00 \times 0.9799$	97.99	0.81
2–3	292	22	1	$1 - \frac{1}{292 - 22}$	0.9963	$P_0 \times P_1 \times \ldots P_3 =$ $1.00 \times 1.00 \times \ldots 0.9963$	97.62	0.89
3–4	269	18	2	$1 - \frac{2}{269 - 18}$	0.9921	$P_0 \times P_1 \times \ldots P_4 =$ $1.00 \times 1.00 \times \ldots 0.9921$	96.85	1.04
4–5	249	23	0	$1 - \frac{0}{249 - 23}$	1.0000	$P_0 \times P_1 \times \ldots P_5 =$ $1.00 \times 1.00 \times \ldots 1.0000$	96.85	1.04
5–6	226	46	1	$1 - \frac{1}{226 - 46}$	0.9944	$P_0 \times P_1 \times \ldots P_6 =$ $1.00 \times 1.00 \times \ldots 0.9944$	96.32	1.16
6–7	179	38	2	$1 - \frac{2}{179 - 38}$	0.9858	$P_0 \times P_1 \times \ldots P_7 =$ $1.00 \times 1.00 \times \ldots 0.9858$	94.95	1.49
7–8	139	14	0	$1 - \frac{0}{139 - 14}$	1.0000	$P_0 \times P_1 \times \ldots P_8 =$ $1.00 \times 1.00 \times \ldots 1.0000$	94.95	1.49
8–9	125	32	2	$1 - \frac{2}{125 - 32}$	0.9785	$P_0 \times P_1 \times \ldots P_9 =$ $1.00 \times 1.00 \times \ldots 0.9785$	92.91	2.04
9–10	91	14	0	$1 - \frac{0}{91 - 14}$	1.0000	$P_0 \times P_1 \times \ldots P_{10} =$ $1.00 \times 1.00 \times \ldots 1.0000$	92.91	2.04
10–11	77	21	0	$1 - \frac{0}{77 - 21}$	1.0000	$P_0 \times P_1 \times \ldots P_{11} =$ $1.00 \times 1.00 \times \ldots 1.0000$	92.91	2.04
11–12	56	12	1	$1 - \frac{1}{56 - 12}$	0.9773	$P_0 \times P_1 \times \ldots P_{12} =$ $1.00 \times 1.00 \times \ldots 0.9773$	90.80	2.89
12–13	43	22	0	$1 - \frac{0}{43 - 22}$	1.0000	$P_0 \times P_1 \times \ldots P_{13} =$ $1.00 \times 1.00 \times \ldots 1.0000$	90.80	2.89
13–14	**21**	**17**	**0**	$\mathbf{1 - \frac{0}{21 - 16}}$	**1.0000**	$\mathbf{P_0 \times P_1 \times \ldots P_{14} =}$ $\mathbf{1.00 \times 0.9799 \times \ldots 1.0000}$	**90.80**	**2.89**
14–15	**4**	**0**	**0**	$\mathbf{1 - \frac{0}{4 - 0}}$	**1.0000**	$\mathbf{P_0 \times P_1 \times \ldots P_{15} =}$ $\mathbf{1.00 \times 0.9799 \times \ldots 1.0000}$	**90.80**	**2.89**
15–16	**4**	**1**	**0**	$\mathbf{1 - \frac{0}{4 - 0}}$	**1.0000**	$\mathbf{P_0 \times P_1 \times \ldots P_{16} =}$ $\mathbf{1.00 \times 0.9799 \times \ldots 1.0000}$	**90.80**	**2.89**

ECS = estimated cumulative survival; SE = standard error.
*The changed data are highlighted in **bold**.

There are two conclusions that can be drawn from these data. First, the data uncertainty at 14 years is so high that the 14-year ECS for feldspathic porcelain veneers based on data from this research is unknown. Data certainty can only be reviewed when a failed event occurs, and it has been argued that clinical use of survival data should be confined within the dates of event occurrence. As the outcome is essentially "unknown" at year 14, data certainty was last calculated (and known) at year 12. Conclusions could therefore be truncated to a 12-year ECS of 90.80% ± 2.89%. The data simply cannot express a change in certainty until another failed event occurs, at which time (year 14) a clinically unreliable 95% CI of approximately 65% ensued.

Second, it is unlikely that data uncertainty with an approximate 95% CI of 12% at 13 years could have suddenly enlarged to 65% at 14 years simply because one veneer failed. It is more realistic that data uncertainty was increasing over the previous intervening years, but that this data uncertainty remained hidden. It remained hidden because the number of failures (d_i) was zero. However, this data uncertainty was realized in year 14, when a single veneer failed and the mathematical formulas had an opportunity to reflect the underlying numbers.

The impact of hidden data uncertainty can be exemplified further. What would happen if that single failed veneer, during the 14th year, had been recorded as a censored prosthesis? This may occur if that patient with the failed veneer chose not to return for continued care. The survival probability for that interval would change from 0.80 to 1.00, and the 14-year ECS would remain at 90.80% ± 2.89%, and the data uncertainty would remain completely undetected (Table 5, Fig 4)!

Discussion

The Mathematics—Summary Comments

As a study progresses, if the number of failures increases, the ECS decreases. Also, if patients become lost to follow-up and censored, the number of prostheses remaining at risk decreases and the ECS also decreases. If no failures occur, the survival for that period is 100%. Also, if no failures occur but patients become lost to follow-up, the survival for that period remains at 100%. This is because the number of failures is in the numerator of the equation and no amount of loss to follow-up can effect a change in the estimated survival.

The mathematics for the SE works in a similar manner. If the number of failures increases, the SE (and confidence range) enlarges. Also, if patients become lost to follow-up and censored, the SE will increase. However, if no failures occur but patients become lost to follow-up, the SE does not change. It cannot change because the numerator remains at zero. This is of particular concern.

The Impact of Data Uncertainty

In statistics, data certainty is expressed with a measure of variance. Common measures include the SE and the 95% CI (often equal to 1.96 $\times$ the SE). As data uncertainty increases, the measure of variance should also enlarge.

Clearly, a decrease in the number of prostheses at risk increases the uncertainty within the sample. However, given the discussion above, it is equally clear that the mathematics does not necessarily reflect this increased uncertainty by increasing the SE.

Certainty of clinical outcomes is central to clinical decisions. Research outcomes are used to estimate outcomes that may occur when treating other similar populations. The SE allows a 95% CI to be calculated, providing clinicians with the range within which 95% of survival outcomes would be expected if a similar study, or similar treatment, were to be undertaken. If the 95% CI does not accurately reflect the uncertainty in the study sample, it cannot reflect the uncertainty within the population and the calculated results remain theoretically accurate but clinically useless.

This problem will be compounded when ECSs containing hidden data uncertainty are included in meta analyses. Meta-analytic methodology cannot account for such bias.[4] The resulting summary figure would again remain theoretically accurate but provide clinically useless data and possibly promote harmful management.

To be certain about conclusions, researchers should observe findings within a large number of patients. Clearly, conclusions should not be drawn about prostheses when few units remain in situ. However, this is not an uncommon occurrence in survival statistics. Clinicians often consider the number entering at year 1, eg, 304 veneers, and may not be presented with enough data by the researchers to recognize that the numbers, and thus the certainty, had reduced dramatically over the study period, eg, to only four in the final year.

Reporting Challenges

ECS data can be reported as a single figure for a particular time period, within a life table for interval time periods, or on a survival curve for all known time periods. Reporting the data with all three types of presentation is uncommon. However, inclusion of all data is vital to the interpretation by readers and future secondary researchers, especially when data are censored. Inclusion of the life table allows readers to identify censored data and to make their own decisions regarding the apparent accuracy of the predicted survival rate. Although journal publication space is limited, efforts should be made to provide journal page space for complete presentation of data or electronic access to additional data files.

Where space limits the inclusion of a life table in the printed manuscript, another form of presentation could be considered: a condensed version of a life table below the survival curve. While this presentation is truncated, it would serve to alert readers that censorship is occurring and indicate that they should review the full electronic life table, if available. An example of this alternative combined data is provided in Figs 2 to 4.

Some survival curves include censorship marks along the curve. These can be automatically generated by several statistical packages. However, many of these statistical packages do not allow for the addition of the SE to these same survival curves. Realistically, if both sets of data were included, the survival curves would become crowded and difficult to interpret.

The ECS is often reported as a single percentage figure without its associated statistical variance (such as its SE or 95% CI). These data are vital to the interpretation and must not be omitted.

The dental profession has embraced evidence-based methodology, but with this has come an increased reliance on the statistical genre. It is understandably impossible for practicing clinicians to be familiar with the nuances of individual formulas and in this specific situation to detect clinical uncertainty when the reported survival mathematics can appear to be so precise. It is also challenging for authors, experts in their scientific fields, to become experts in statistical reporting and ensure their manuscripts provide sufficient reporting detail.[5]

Conclusion

Current techniques for analysis of time-to-event data are imperfect and can be misleading. It therefore behooves authors to strive to improve reporting transparency, journals to support such industry, and readers to remain mindful that the cumulative survival is an estimate, ie, a reflection of reality.

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References

1. Kaplan E, Meier P. Nonparametric estimation form incomplete observations. J Am Stat Assoc 1958;53:457–481.
2. Gerds TA, Vogeler M. Endpoints and survival analysis for successful osseointegration of dental implants. Stat Methods Med Res 2005;14:579–590.
3. Layton D, Walton TR. An up to 16-year prospective study of 304 porcelain veneers. Int J Prosthodont 2007;20:389–396.
4. Thompson S, Pocock S. Can meta-analysis be trusted? Lancet 1991;338:1127–1130.
5. Fernandes-Taylor S, Hyun JK, Reeder RN, Harris AH. Common statistical and research design problems in manuscripts submitted to high-impact medical journals. BMC Res Notes 2011;4:304.

Literature Abstract

Tooth loss and osteoporosis: To assess the association between osteoporosis status and tooth number

This study aimed to investigate the link between the osteoporotic condition of patients and number of teeth. Confounding factors such as age, smoking status, alcohol consumption, and hormone replacement therapy were also taken into account. From March 2008 until June 2010, 359 patients from the Manchester region were recruited. Each patient had a dental panoramic tomograph taken and the number of teeth were counted during the dental charting. Data such as osteoperotic condition, smoking status, alcohol consumption, age, and use of hormone replacement therapy were collected. Complete data were obtained from 333 patients of which 90 patients were osteoporotic. Analysis using SPSS software (version 19) showed a significant relationship between molar tooth number and osteoporotic status ($P = .017$; 95% confidence interval, –1.339 to –0.137). The authors concluded that clinicians should educate osteoporotic patients of the higher risk of tooth loss and implement intensive preventive measures for them.

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