

addresses, and dates of birth. Patients who had one or both implants reported as ruptured by one or both radiologists were counseled and offered bilateral explantation and implant replacement.

Statistical Analysis Plan

Data for the time from augmentation to MRI and whether or not the implant was determined by the MRI to be ruptured were analyzed in order to estimate the cumulative rupture rate function at both the patient and the implant level using the method of maximum likelihood (see technical appendix). Overt ruptures would have been included in these analyses as well had there been any such ruptures. Because it was known in advance of the analysis that there were no overt ruptures, no provision was made for their inclusion.) Patients were excluded from the analysis if the patient had a missing value for the MRI date. At the patient level, patients who had an explantation of an implant prior to the MRI date were excluded from the analysis. At the implant level, implants were excluded from the analysis if an explantation of the implant was performed prior to the MRI date. Using the estimated cumulative rupture rate function, estimates were obtained of the cumulative rupture rate at annual timepoints after the augmentation date (to obtain an estimate of change in rupture rate over time). The jackknife procedure² was used to estimate the standard errors of these estimates, which were then used to calculate 95% confidence intervals for the estimates. Rates of change over time in the rupture rate were estimated using conditional probability. A second set of analyses (patient level and implant level) were performed in which an MRI determination of rupture was overridden if, based upon physical examination of the explanted device, the device was determined to be intact (*i.e.*, confirmed ruptures). These analyses were performed in the same manner as the first set of analyses.

Potential Health Consequences of Rupture

The subset of women in the MRI study who had at least one ruptured implant determined by MRI and who subsequently underwent surgical explantation and confirmation of implant rupture were invited to participate in an observational study to assess potential health consequences of rupture of Mentor's silicone gel-filled breast implants. Women who agreed to participate underwent a blinded and standardized rheumatological assessment. The primary objective of the study was to examine the incidence of rheumatologist-diagnosed/confirmed rheumatologic disease among patients with ruptured silicone gel-filled breast implants. Secondary objectives included examination of the number of findings in a rheumatologic physical examination and the number of reported rheumatologic symptoms among patients with ruptured silicone gel-filled breast implants.

2. Efron and Gong, "A leisurely look at the bootstrap, the jackknife, and cross-validation," The American Statistician, 1983.

Results and Discussion

Information concerning the cohort evaluated in this study is provided below.

Number of NHS women with cosmetic subglandular Mentor Siltex silicone gel-filled breast implants	204
Number of NHS women with cosmetic subglandular Mentor Siltex silicone gel-filled breast implants who underwent MRI examination included in the patient level analysis	101
Number of women who underwent MRI examination, but were excluded from patient level analysis because one of their implants was removed prior to the MRI examination, but their remaining implant was included in the implant level analysis	2
Number of implants evaluated by MRI and included in implant-level analysis	204
Mean age at implantation	30.6±5.6 years
Mean age at MRI examination	40.0±6.1 years
Mean implant duration	8.8±2.5 years
Mean implant size	
Right	225±35 cc
Left	221±35 cc

The results of the MRI evaluation are presented below:

	Patient	Implant
Number of MRI-identified silent ruptures	12 (11.9%)	19 (9.3%)
Number of ruptures confirmed at surgery	9 (8.9%)	11 (5.4%)
Mean age of implants at MRI-identified rupture (excluding implants confirmed as intact)		9.2±1.5 years
Mean age of implants at confirmed rupture		9.1±1.6 years
Number of extracapsular ruptures	0	0

Results of the analyses to estimate the cumulative rupture rate over time by patient and implant for MRI-identified and confirmed ruptures are provided in Tables 1-4 below.

Of the patients with at least one ruptured implant who underwent rheumatological examination, only one woman reported possible rheumatological effects (one possible episode of “myalgic

encephalitis”), which was not considered by the evaluating rheumatologist to be implant related. Blood analyses revealed no abnormal findings.

In this study, the confirmed (by explantation) overall rupture rate was 8.9% (by patient) and 5.4% (by implant). No ruptures were observed until approximately 7 years after implantation, and, based on the modeling conducted, the rupture rate slowly increased thereafter until, at 12 years, the rate was approximately 12%. The average age of the implant at confirmed rupture was 9.1 ± 1.6 years, which demonstrates the durability of Mentor’s silicone gel-filled implants. Importantly, of the confirmed ruptures, none were extracapsular, and none of the women with ruptured implants experienced adverse health consequences associated with their breast implants.³

As shown in the table below, the third generation silicone gel-filled breast implant rupture rate and trends found in the present study conducted by Drs. Sharpe and Collis compare favorably to those reported in the literature.

Reference	Implant Generation	Implant Duration (years)	Rupture Rate (%)		Type of Rupture
			(Women)	(Devices)	
Sharpe & Collis	Third	Mean = 8.8 (4-12) years	8.9 (9/101)	5.4 (11/204)	Silent
Gabriel et al. 1997 (Prevalence study)	Women implanted 1964-1991	Mean = 7.8 (0-25.8)	5.7 (43/749)	3.3 56/1,703	Overt
Hölmich et al. 2003 (Incidence study)	Third generation: 62% of total studied	2-11	6 (12/197)	NA	Silent and Overt
Brown et al. 2000 (Prevalence study)	Third generation: 2% of total studied	Mean = 7.4	16.7 (1/6)	8.3 (1/12)	Silent

Determining an accurate estimate of device rupture rate has been a key element of many clinical investigations of silicone gel-filled breast implants over the years. Although a very broad range of incidence rates for rupture has been published, most reports suffer from limitations in the underlying studies. Some of these studies, for example, focused on highly selected, and, therefore, highly statistically biased, patient groups such as case series of explanted patients (e.g., Marotta et al. 2002),⁴ that include solely patients with complications or have decided to have

^{3/} One woman, as noted above, was diagnosed with myalgic encephalitis not considered by the evaluating rheumatologist to be implant related

^{4/} Marotta, J.S., et al. 2002. Silicone gel breast implant failure: evaluation of properties of shells and gels for explanted prostheses and meta-analysis of literature rupture data. *Ann Plast Surg* 49:227-242

their implants removed. Others focused on device designs that pre-date the current third generation of silicone gel-filled breast implants that Mentor Corporation has manufactured since 1985 (e.g., Robinson et al. 1995).⁵ First generation implants, which were marketed from the early 1960s through the early to mid-1970s, had a thick elastomeric wall enclosing a firm gel. Second generation implants, marketed between the mid-1970s through the mid-1980s, had thinner shells and a less viscous gel, and third generation “low-bleed” implants, marketed from the mid-to late-1980s to the present, had a multi-layer shell with a barrier layer to reduce the diffusion of silicone gel (see, e.g., Collis and Sharpe 2000). Mentor’s PMA devices represent a third generation design. Second generation devices have been associated in a number of studies with substantially higher rates of rupture (e.g., Robinson et al. 1995, Brown et al. 2000,⁶ Hölmich et al. 2003,⁷ Peters et al. 1996,⁸ and Collis and Sharpe 2000⁹) than either the first or third generation devices.

Generation-specific rupture rates are available from two sources: from explant studies and from the broader population-based epidemiological studies that rely on MRI to identify ruptures (i.e., silent ruptures). As noted above, explant studies are highly selected with respect to rupture rates, as they include solely patients with complications or who have decided to have their implants removed. Nonetheless, explant studies do provide information on relative rupture rates across implant generations.

In an explant series on overt rupture reported by Collis and Sharpe (2000), the majority of first generation implants (67%) remained intact out to 28 years of implantation; and the vast majority of third generation implants (91%) remained intact through 15 years of implantation. Importantly, in this review of third generation implants, 1,136 of 1,738 (65%) implanted were Mentor devices. Sharpe and Collis reported implanting 55 Mentor smooth gel-filled devices between 1989 and 1990: no ruptures were found in 17 explants that had been implanted for 1-3 years (mean 2.1 years; 0.8 SD). Between 1989 and 1997, 1,081 Mentor textured gel-filled implants were implanted: no ruptures were found in 81 explants that had been implanted 0.1 to 7 years (mean 2.5 years, 2.0 SD). By contrast, the majority of the second generation implants (65%) ruptured after 10 to 20 years of implantation.

5. Robinson, O.G., Jr., et al. 1995. Analysis of explanted silicone implants a report of 300 patients. *Ann Plast Surg*. 34(1):1-6.

6. Brown, S.L., et al. 2000. Prevalence of rupture of silicone gel breast implants revealed on MR imaging in a population of women in Birmingham, Alabama. *Am. J. Roentgenol* 175(4):1057-1064.

7. Hölmich, L.R., et al. 2003. Self-reported diseases and symptoms by rupture status among unselected Danish women with cosmetic silicone breast implants. *Plast Reconstr. Surg.* 111:723-732.

8. Peters, W.J., et al. 1996. Failure properties of 352 explanted silicone-gel breast implants. *Canadian J Plastic Surg* 4(1):55-58.

9. Collis, N. and Sharpe, D.T. 2000. Silicone gel-filled breast implant integrity. A retrospective review of 478 consecutively explanted implants. *Plast. Reconstr Surg* 105:1979-1985.

Additional estimates of rupture rates are provided by a series of recent population-based epidemiology studies, such as those published by Gabriel et al. (1997),¹⁰ Karlson et al. (1999),¹¹ Kjølner et al. (2002),¹² and Hölmich et al. (2003).

Gabriel et al. (1997) reported an overt rupture rate of 5.7% among 749 patients (3.29% among 1,703 devices), with a mean follow-up of 7.8 years (and up to a maximum of 26 years). Karlson et al. (1999) reported an overt rupture rate of 12% among a randomly selected subset of women with silicone breast implants (with a median follow-up of 12 years) from the Nurse's Health Study. More recently, Kjølner et al. (2002) reported a 0.53% rate of overt rupture among 754 patients (0.25% rate among 1,572 devices), with an average follow-up of 7 years (and up to a maximum of 23 years).¹³

Hölmich et al. (2003) reported an MRI-based incidence rate of overt and silent rupture among a randomly selected subset of the Kjølner et al. (2002) study population. Consistent with previous reports in the literature, Hölmich and colleagues observed a statistically significant 3- to 5-fold higher rate of rupture (definite and possible) among second generation devices as compared with third generation devices. The rupture (definite and possible) incidence rate for second generation devices was likewise higher than for first generation devices, also consistent with previous reports. Using Kaplan-Meier analyses, the study authors reported that "for modern implants intact 3 years after implantation, we estimated rupture-free survival of 98% at five years and 83% to 85% at ten years" for silent and overt ruptures.¹⁴

In addition to MRI data from Mentor's Core Study and the Sharpe and Collis study, other data demonstrate that third generation implants remain intact with essentially no ruptures, several years after implantation. In particular, using data prospectively obtained from the Danish Registry for Plastic Surgery of the Breast ("DPB"), Henriksen et al. (2003)¹⁵ reported no overt ruptures in 971 women (1,913 implants) within 2 years postoperatively of receiving third

10/ Gabriel, S.E., et al. 1997. Complications leading to surgery after breast implantation. *N Engl J Med* 336(10):677-682.

11/ Karlson, E.W., et al. 1999. Association of silicone breast implants with immunologic abnormalities: a prospective study. *Am J Med*. 106:11-19.

12/ Kjølner, K., et al. 2002. Epidemiological investigation of local complications after cosmetic breast implant surgery in Denmark. *Ann Plast Surg* 48(3):229-237.

13/ In an unpublished subanalysis focusing on third-generation implants by authors of the Kjølner et al. (2002) study, J. Fryzek and J. McLaughlin, only 2 of 509 third generation implants (0.4%) in 2 of 241 women (0.8%) ruptured by 5 years.

14/ Although a fifth epidemiology study by Brown et al. (2000) also recently assessed rupture status of silicone breast implants with MRI, it included almost exclusively second generation implants (94%). Because the Brown et al. (2000) study included only twelve third generation implants (only one of which had ruptured), its relevance to Mentor's third generation devices is limited. See Brown, S.L., et al., 2000. Prevalence of rupture of silicone gel breast implants revealed on MR imaging in a population of women in Birmingham, Alabama. *Am J Roentgenol* 175(4):1057-1064.

15/ Henriksen, T.F., et al. 2003. Incidence and severity of short-term complications after breast augmentation. *Ann Plast Surg* 51(6):531-539.

generation implants. Importantly, it has been reported that approximately 56% of the women included in the DPB are implanted with Mentor devices¹⁶ (Personal Communication, J. McLaughlin, February 2004). The DPB, established in 1999, contains prospectively collected pre-, peri-, and postoperative data for women undergoing breast implantation, breast reduction surgery, or mastopexy. Although participation in the Registry has been voluntary for both clinics and patients, 80% or more of Danish plastic surgery centers currently are registered. Additionally, patient follow-up is greater than 90%. Data collected and maintained in the Registry include: preoperative information on health; demographic, and lifestyle factors; surgical procedures and implant characteristics; and follow-up findings and adjuvant treatment, if any. To facilitate meaningful retrospective review, all information and data have been collected via standardized questionnaires and forms.

The Henriksen study was authored and published in the same year, and by the same core investigators who conducted the Hölmich study (Hölmich, Friis, Fryzek, McLaughlin, Kjølner, and Olsen). The two studies taken together permit the conclusion that silent and overt rupture-free survival of 98% at five years and 83% to 85% at ten years could be expected for Mentor's PMA devices. Other published explant and epidemiological reports discussed above consistently provide evidence of the low long-term (*i.e.*, 7-18-year) overt rupture rates for Mentor and other "third generation" implants.

The lack of rheumatological or other systemic findings in the small number of women with silent ruptures in the Sharp and Collis study is consistent with the overall body of well-designed, connective tissue disease ("CTD") and related population-based epidemiology studies that have evaluated this issue. These studies consistently found no association between systemic health consequences, such as the development of connective tissue diseases ("CTD"), rheumatic diseases, and/or related symptoms and ruptured (or intact) silicone gel-filled breast implants. As concluded in a recent review by Lipworth et al. (2004),¹⁷ "... the most recent epidemiological investigations have been remarkably consistent with earlier epidemiologic studies in finding no evidence of an excess of any individual connective tissue disease or all connective tissue diseases combined, including both established and atypical or undefined connective tissue disease, among women with cosmetic silicone breast implants."¹⁸

The MRI study conducted by Drs. Sharpe and Collis should be viewed as a part of the composite whole with regard to Mentor's clinical data and published literature supporting the Mentor PMA. The study provides valuable information on the rate of change of rupture over time, and the findings on rupture rate and potential health consequences are consistent with Mentor's own data and the published literature. It might be argued that selection concerns are presented by the study population, because it consisted of exclusively asymptomatic NHS augmentation patients

16/ By contrast, the Danish Registry contains implants that differ from the devices covered by the PMA of Inamed Corporation reviewed by the Advisory Panel in October 2003 (Personal Communication, J. McLaughlin, February 2004).

17/ Lipworth, L., et al. 2004. Silicone breast implants and connective tissue disease. An updated review of the epidemiologic evidence. *Ann. Plast Surg.* 52(6):598-601.

18/ *Id.*

from a single site, who were predominantly Caucasian, and had not undergone any surgical interventions since their original implantation surgery. Mentor believes, however, that these patient characteristics do not represent meaningful differences from the potential implant population as a whole. Moreover, the selection criteria used by Drs. Sharpe and Collis, and the resulting study cohort, serve to reduce the number of variables that might confound the results, while allowing the results obtained in this study to be extrapolated to the larger population implanted with Mentor's devices.

Use of only NHS patients does not raise a concern. As noted above, because the study was not supported by outside sources, NHS patients were exclusively included so that the cost of explant surgery would be reimbursed if the implants were found to be ruptured. Dr. Sharpe has stated that his NHS and private clinic patients are very similar, and that there are no apparent differences in demographics or socioeconomic status between them. In fact, the major reason given by Dr. Sharpe's patients for choosing a private clinic over the NHS system for their breast augmentation surgery was timing -- in the NHS system, women often have to wait a period of several months to a year to have their augmentation surgery approved, whereas there generally is no waiting period for private clinic surgeries. Additionally, a predominantly Caucasian population is representative of the Core study,¹⁹ and the women who seek breast implantation in the U.S.²⁰

Excluding women from the MRI study who sought surgical intervention after their implant surgery theoretically could introduce selection bias because these women might have higher silent rupture rates than asymptomatic women who required no intervention. However, Dr. Sharpe has indicated that only a "handful" of patients in his database had interventions (*i.e.*, approximately a dozen), and that all interventions were in patients who had capsular contracture and who underwent capsulectomy with explantation and reimplantation. Thus, these patients did not actually have the original implants remaining in place to be screened by MRI. No ruptures were noted in these women.

The use of a single site in the present study does not preclude extrapolation of these results to the U.S. implant population. Dr. Sharpe is a preeminent plastic surgeon who is widely published,²¹ and his practice represents a broad geographic catchment area. As noted above, the predominantly Caucasian population that constitutes Dr. Sharpe's breast implant practice is representative of the U.K. and the U.S. Core study populations. Moreover, the Sharpe and Collis cohort represents approximately 10.4% of all Mentor implants and approximately 15% of all implants sold in the U.K. per year, therefore, it can be assumed that the women drawn from their patient database are typical of implant recipients generally. Dr. Sharpe states that he also is able

19/ There were only 22 African Americans and 23 Asians out of a total of 1,007 women enrolled in Mentor's Core study for silicone gel-filled breast implants (*see* original PMA submission).

20/ *See* American Society of Plastic Surgeons 2003. 2003 Quick Facts. Cosmetic and Reconstructive Plastic Surgery, stating that "Hispanics made up 6 percent, African Americans made up 5 percent, and Asians made up 2 percent of all cosmetic plastic surgery patients." Available at: www.plasticsurgery.org.

21/ A list of selected publication by Dr. Sharpe is attached.

to achieve good patient follow-up because of lack of mobility of patient population, thereby obviating concerns with regard to selection bias because of poor follow-up.

The Sharpe and Collis study population consisted exclusively of cosmetic patients. Mentor believes that the data obtained in cosmetic patients are applicable to reconstruction patients because, given that reconstruction patients undergo regular check-up/breast screening, there is no reason to expect higher silent rupture rates in these patients than those seen in cosmetic patients

Drs. Sharpe and Collis only evaluated Mentor's Siltex silicone gel-filled devices in their MRI study, whereas Mentor's PMA devices include both smooth and Siltex implants. Mentor believes, however, that there is no reason to expect more than nominal differences between smooth and textured with respect to rupture rate based on findings from Mentor's complaint database (see Response 3), and the Cox Regression Analysis of the Core study data showed no correlation between rupture and implant surface.

The implants evaluated in the study by Drs. Sharpe and Collis were implanted subglandularly, and never via a periareolar insertion. In Mentor's Core study, submuscular placement was the most common surgical placement for all cohorts (42%, 61%, and 54% for Augmentation, Reconstruction, and Revision cohorts, respectively, and the periareolar approach was employed (23%, 21%, and 17% for the Augmentation, Reconstruction, and Revision cohorts, respectively). However, it is not likely that these differences in surgical approach and placement affect the rupture rate. Cox Regression analysis of the Core study data show no correlation between rupture and any operative variable (*i.e.*, surgical approach or placement).

Together with the published literature and Mentor's own data, Mentor believes that the data on silent ruptures collected by Drs. Sharpe and Collis, provide reasonable assurance of safety with respect to rupture rates, changes in rupture rate with time of, and health consequences associated with rupture of Mentor's silicone gel-filled breast implants, as well as sufficient information to inform doctors and their patients about these issues.

SELECTED PUBLICATIONS BY DR. DAVID SHARPE

Sharpe and colleagues also have published extensively in peer-reviewed journals on analyses of a database containing the records of approximately 1,100 breast implant patients since 1985. Examples of the publications include:

- Collis N. and D.T. Sharpe, 2000. Silicone gel-filled breast implant integrity: A retrospective review of 478 consecutively explanted implants. *Plast. Reconstr. Surg.* 105:1979-1989.
- Collis N., D. Coleman, I.T.H. Foo and D.T. Sharpe, 2000. Ten-year review of a prospective randomized controlled trial of textured versus smooth subglandular silicone gel breast implants. *Plast. Reconstr. Surg.* 106:786-791.
- Collis N. and D.T. Sharpe, 2000. Recurrence of subglandular breast implant capsular contracture: Anterior versus total capsulectomy. *Plast. Reconstr. Surg.* 106:792-797.
- Malata C.M., L. Feldberg, D. Coleman, I.T.H. Foo and D.T. Sharpe, 1997. Textured or smooth implants for breast augmentation? Three year follow-up of a prospective randomised controlled trial. *British Journal of Plastic Surgery* 50:99-105.
- D. Coleman, I.T.H. Foo and D.T. Sharpe, 1991. Textured or smooth implants for breast augmentation? A prospective controlled trial. *British Journal of Plastic Surgery* 44:444-448.

Technical Appendix

Maximum Likelihood Estimators for Independent Observations on Cumulative Failures

The Problem: We have information on the sample cumulative failure rate at times $t_1 < t_2 < \dots < t_T$ for each of T independent samples of sizes n_1, n_2, \dots, n_T , respectively. The t 's need not be equally spaced. Let $x_i =$ observed number of failures in the i^{th} sample, $i=1,2,\dots,T$, and define

$$p_i = x_i/n_i = \text{observed cumulative failure rate for the } i^{\text{th}} \text{ sample, } i=1,2,\dots,T.$$

We wish to estimate π_i ($i=1,2,\dots,T$) where $\pi_i =$ the true cumulative failure rate at time t_i . No restrictions are imposed on the π_i 's except that $0 \leq \pi_1 \leq \pi_2 \leq \dots \leq \pi_T \leq 1$. We will assume that X_i , the random variable corresponding to x_i , has a Binomial (n_i, π_i) distribution, $i=1,2,\dots,T$. Then, since the X_i 's are independent, the log-likelihood function for $\underline{\pi} = (\pi_1, \pi_2, \dots, \pi_T)$ given

$\underline{p} = (p_1, p_2, \dots, p_T)$ is

$$(1) \quad L^*(\underline{\pi} | \underline{p}) = \sum_{i=1}^T L_i^*(\pi_i | p_i) \text{ where}$$

$$(2) \quad L_i^*(\pi_i | p_i) = \ln C_{n_i, p_i}'' + n_i [p_i * \ln \pi_i + (1-p_i) * \ln (1-\pi_i)], \quad i=1,2,\dots,T,$$

where C_k'' denotes the number of combinations of size k that can be formed from n distinct objects.

The maximum likelihood estimators $\hat{\underline{\pi}} = (\hat{\pi}_1, \hat{\pi}_2, \dots, \hat{\pi}_T)$ are obtained by maximizing $L^*(\underline{\pi} | \underline{p})$ subject to the constraints $0 \leq \pi_1 \leq \pi_2 \leq \dots \leq \pi_T \leq 1$. Thus,

$$(3) \quad L^*(\hat{\underline{\pi}} | \underline{p}) = \max L^*(\underline{\pi} | \underline{p}), \text{ given } 0 \leq \pi_1 \leq \pi_2 \leq \dots \leq \pi_T \leq 1.$$

Solution: The following proof demonstrates that the solution to Eqn. (3) may be computed as follows:

Step One: Define $p(m,n)$, $m \leq n$, as the observed proportion of failures among the samples m through n , inclusive. Then

$$(4) \quad p(m,n) = \frac{\sum_{i=m}^n x_i}{\sum_{i=m}^n n_i} = \frac{\sum_{i=m}^n n_i p_i}{\sum_{i=m}^n n_i}.$$

Step Two: Define $T_1, T_2, \dots, T_K = T$ sequentially as follows. Let

$$A_1 = \{\tau \in (1, 2, \dots, T): p(1, \tau) = \min p(1, j), j = 1, 2, \dots, T\} \text{ and}$$

$$(5) \quad T_1 = \text{largest element in } A_1 = \max A_1.$$

Continuing we define

$$(6) \quad T_2 = \text{largest element in } A_2 = \max A_2 \text{ where}$$

$$A_2 = \{\tau \in (T_1 + 1, \dots, T): p(T_1 + 1, \tau) = \min p(T_1 + 1, j), j = T_1 + 1, \dots, T\}$$

and

$$(7) \quad T_3 = \text{largest element in } A_3 = \max A_3 \text{ where}$$

$$A_3 = \{\tau \in (T_2+1, \dots, T): p(T_2+1, \tau) = \min p(T_2+1, j), j = T_2+1, \dots, T\}$$

and so on until $T_K = T$. The T_i 's are defined in terms of the largest minimizing τ in order to remove ambiguity in the case of ties. The smallest minimizing τ could have been used instead, but doing so would have made the proof and the calculations for $\hat{\pi}$ more difficult, despite yielding the same solution for $\hat{\pi}$.

Step Three: The solution to Eqn. (3) is given by

$$\hat{\pi}_i = p(1, T_1), i = 1, 2, \dots, T_1,$$

$$\hat{\pi}_i = p(T_1+1, T_2), i = T_1+1, \dots, T_2,$$

$$\hat{\pi}_i = p(T_2+1, T_3), i = T_2+1, \dots, T_3,$$

⋮

$$\hat{\pi}_i = p(T_{K-1}+1, T_K), i = T_{K-1}+1, \dots, T_K,$$

which can be written as

$$(8) \quad \hat{\pi}_j = p(T_{i-1}+1, T_i), j = T_{i-1}+1, \dots, T_i, i=1, 2, \dots, K, \text{ where } T_0 \equiv 0 \text{ and } T_K \equiv T.$$

The solution in Eqn. (8) requires computing at most $T(T+1)/2$ values of $p(i, j)$ and could be computed with 2 simple do loops.

Proof of Eqn. (8): We will first prove that the $\hat{\pi}_j$'s in Eqn. (8) are a feasible solution, i.e. that

$0 \leq \hat{\pi}_1 \leq \hat{\pi}_2 \leq \dots \leq \hat{\pi}_T \leq 1$. Because the $\hat{\pi}_i$'s are proportions, we know that $0 \leq \hat{\pi}_i \leq 1$ for $i = 1, 2, \dots, T$. Now for $r=1, 2, \dots, K-1$ we have $\hat{\pi}_{T_r} = p(T_{r-1}+1, T_r) < p(T_{r-1}+1, k)$ for $k > T_r$ by definition of T_r . The inequality is strict because T_r was defined as the largest τ minimizing $p(T_{r-1}+1, \tau)$ for $\tau \geq T_{r-1}+1$. Thus, $p(T_{r-1}+1, T_r) < p(T_{r-1}+1, T_{r+1})$ for $r=1, 2, \dots, K-1$. Since $p(T_{r-1}+1, T_{r+1})$ can be written as a weighted average of $p(T_{r-1}+1, T_r)$ and $p(T_r+1, T_{r+1})$ we have

$$p(T_{r-1}+1, T_r) < a * p(T_{r-1}+1, T_r) + (1-a) * p(T_r+1, T_{r+1}) \text{ for some } a, 0 < a < 1. \text{ Thus,}$$

$$(1-a) * p(T_{r-1}+1, T_r) < (1-a) * p(T_r+1, T_{r+1}), \text{ so}$$

$$\hat{\pi}_{T_r} = p(T_{r-1}+1, T_r) < p(T_r+1, T_{r+1}) = \hat{\pi}_{T_{r+1}}, \quad r=1, 2, \dots, K-1, \text{ so that}$$

$$(9) \quad 0 \leq \hat{\pi}_{T_1} < \hat{\pi}_{T_2} < \dots < \hat{\pi}_{T_K} = \hat{\pi}_T \leq 1. \text{ Thus, by Eqn. (8) we have}$$

$$(10) \quad 0 \leq \hat{\pi}_1 = \dots = \hat{\pi}_{T_1} < \hat{\pi}_{T_1+1} = \dots = \hat{\pi}_{T_2} < \dots < \hat{\pi}_{T_{K-1}+1} = \dots = \hat{\pi}_{T_K} = \hat{\pi}_T \leq 1,$$

and the solution $\hat{\pi}$ is a feasible solution.

Now the solutions for the cases $T=2$ and $T=3$ will be derived. The solutions for these cases will then be used to prove the general case.

Solution for T=2: The solution for the $T=2$ case will be derived sequentially. We will start by maximizing $L^*(\underline{\pi} | \underline{p})$ with respect to π_1 . Taking the derivative of $L^*(\underline{\pi} | \underline{p})$ with respect to π_1 , setting this derivative equal to 0, and solving for π_1 , yields the unconstrained MLE solution

$\hat{\pi}_1 = p_1$ for π_1 . Since $\pi_1 \leq \pi_2$ this solution is feasible iff $p_1 \leq \pi_2$. Thus, the solution for $\hat{\pi}_1$ is

$$\hat{\pi}_1 = p_1 = \frac{x_1}{n_1}, \text{ if } p_1 \leq \pi_2$$

$$\hat{\pi}_1 = \pi_2, \quad \text{if } p_1 > \pi_2$$

or equivalently

$$\hat{\pi}_1 = p_1, \text{ if } p_1 < \pi_2$$

$$\hat{\pi}_1 = \pi_2, \text{ if } p_1 \geq \pi_2.$$

Now consider estimating π_2 . If $\hat{\pi}_1 = p_1$, maximizing $L^*(\underline{\pi} | \underline{p})$ with respect to π_2 reduces to maximizing $L_2^*(\pi_2)$ with respect to π_2 . The unconstrained maximum for $L_2^*(\pi_2)$ is obtained when $\hat{\pi}_2 = p_2$, which is feasible since $p_2 \leq 1$. If $\hat{\pi}_1 = \pi_2$, however, then the problem of maximizing $L^*(\underline{\pi} | \underline{p})$ with respect to π_2 reduces to the problem of maximizing

$L_1^*(\pi_2) + L_2^*(\pi_2)$ with respect to π_2 . Now

$$\begin{aligned} L_1^*(\pi_2) + L_2^*(\pi_2) &= \ln C_{n_1 p_1}^{n_1} + n_1^* [p_1^* \ln \pi_2 + (1-p_1)^* \ln (1-\pi_2)] \\ &\quad + \ln C_{n_2 p_2}^{n_2} + n_2^* [p_2^* \ln \pi_2 + (1-p_2)^* \ln (1-\pi_2)]. \end{aligned}$$

Taking the derivative of $L_1^*(\pi_2) + L_2^*(\pi_2)$ with respect to π_2 , setting the derivative equal to 0, and solving for π_2 yields the unconstrained solution

$$\hat{\pi}_2 = \frac{n_1 p_1 + n_2 p_2}{n_1 + n_2} = \frac{x_1 + x_2}{n_1 + n_2}.$$

This solution is feasible since $\hat{\pi}_2 \leq 1$. Thus, the solution for the T=2 case is

$$(10) \quad \hat{\pi}_1 = p_1, \hat{\pi}_2 = p_2, \text{ if } p_1 \leq p_2$$

$$\hat{\pi}_1 = \hat{\pi}_2 = \frac{n_1 p_1 + n_2 p_2}{n_1 + n_2}, \text{ if } p_1 > p_2,$$

or equivalently

$$\hat{\pi}_1 = p_1, \hat{\pi}_2 = p_2, \text{ if } p_1 < p_2$$

$$\hat{\pi}_1 = \hat{\pi}_2 = \frac{n_1 p_1 + n_2 p_2}{n_1 + n_2}, \text{ if } p_1 \geq p_2.$$

Solution for T=3: For the T=3 case the solution $\hat{\pi}_2$ in Equation (10) is feasible if $\hat{\pi}_2 \leq \pi_3$. Since the unconstrained solution $\hat{\pi}_1 = p_1$ can be either $\leq \hat{\pi}_2$ or $> \hat{\pi}_2$ and the unconstrained solution $\hat{\pi}_2$ can be either $\leq \pi_3$ or $> \pi_3$, the solution now has 4 possible cases.

$$(11a) \quad \hat{\pi}_1 = p_1, \hat{\pi}_2 = p_2, \text{ if } p_1 \leq p_2 \leq \pi_3,$$

$$(11b) \quad \hat{\pi}_1 = p_1, \hat{\pi}_2 = \pi_3, \text{ if } p_1 \leq \pi_3 < p_2,$$

$$(11c) \quad \hat{\pi}_1 = \hat{\pi}_2 = \frac{n_1 p_1 + n_2 p_2}{n_1 + n_2}, \text{ if } p_2 < \frac{n_1 p_1 + n_2 p_2}{n_1 + n_2} \leq \pi_3,$$

$$(11d) \quad \hat{\pi}_1 = \hat{\pi}_2 = \pi_3, \text{ if } p_1 > \pi_3 \text{ and } \frac{n_1 p_1 + n_2 p_2}{n_1 + n_2} > \pi_3.$$

In the case of (11a) it is simply required to have $\hat{\pi}_3 \leq 1$, so

$\hat{\pi}_3 =$ unconstrained solution for $\pi_3 = p_3$

is obtained by maximizing $L_3^*(\pi_3)$ with respect to π_3 . In the case of (11b) the MLE solution for π_3 requires maximizing $L_2^*(\pi_3) + L_3^*(\pi_3)$ with respect to π_3 . This yields the solution

$$\hat{\pi}_3 = \frac{n_2 p_2 + n_3 p_3}{n_2 + n_3}.$$

In case (11c), $\hat{\pi}_3 =$ unconstrained solution for $\pi_3 = p_3$. Finally, in case (11d) the solution requires maximizing $L_1^*(\pi_3) + L_2^*(\pi_3) + L_3^*(\pi_3)$ with respect to π_3 . This yields the solution

$$\hat{\pi}_3 = \frac{n_1 p_1 + n_2 p_2 + n_3 p_3}{n_1 + n_2 + n_3}.$$

Thus, in the T=3 case we have the following ML solution:

$$(12a) \quad \hat{\pi}_1 = p_1, \hat{\pi}_2 = p_2, \hat{\pi}_3 = p_3, \text{ if } p_1 \leq p_2 \leq p_3,$$

$$(12b) \quad \hat{\pi}_1 = p_1, \hat{\pi}_2 = \hat{\pi}_3 = \frac{n_2 p_2 + n_3 p_3}{n_2 + n_3}, \text{ if } p_1 \leq \frac{n_2 p_2 + n_3 p_3}{n_2 + n_3} < p_2,$$

$$(12c) \quad \hat{\pi}_1 = \hat{\pi}_2 = \frac{n_1 p_1 + n_2 p_2}{n_1 + n_2}, \hat{\pi}_3 = p_3, \text{ if } p_2 < \frac{n_1 p_1 + n_2 p_2}{n_1 + n_2} \leq p_3,$$

$$(12d) \quad \hat{\pi}_1 = \hat{\pi}_2 = \hat{\pi}_3 = \frac{n_1 p_1 + n_2 p_2 + n_3 p_3}{n_1 + n_2 + n_3}, \text{ if } \min(p_1, \frac{n_1 p_1 + n_2 p_2}{n_1 + n_2}) > \frac{n_1 p_1 + n_2 p_2 + n_3 p_3}{n_1 + n_2 + n_3}.$$

It is clear that these solutions satisfy the requirement that $0 \leq \hat{\pi}_1 \leq \hat{\pi}_2 \leq \hat{\pi}_3 \leq 1$. In case (12a) we have $T_1=1$, $T_2=2$, and $T_3=3$, so from Eqn. (8)

$$\hat{\pi}_1 = p(1,1) = p_1, \hat{\pi}_2 = p(2,2) = p_2, \text{ and } \hat{\pi}_3 = p(3,3) = p_3.$$

In case (12b) we have $T_1=1$, $T_2=3$ so that

$$\hat{\pi}_1 = p(1,1) = p_1, \hat{\pi}_2 = \hat{\pi}_3 = p(2,3) = \frac{n_2 p_2 + n_3 p_3}{n_2 + n_3}.$$

In case (12c) we have $T_1=2$, $T_2=3$, so that

$$\hat{\pi}_1 = \hat{\pi}_2 = p(1,2) = \frac{n_1 p_1 + n_2 p_2}{n_1 + n_2}, \hat{\pi}_3 = p(3,3) = p_3.$$

In case (12d) we have $T_1=3$, so that

$$\hat{\pi}_1 = \hat{\pi}_2 = \hat{\pi}_3 = \frac{n_1 p_1 + n_2 p_2 + n_3 p_3}{n_1 + n_2 + n_3}.$$

Thus, the solutions from Eqn. (8) agree with the solutions in Eqns. (12a)-(12d).

General Case: Because the $\hat{\pi}_i$'s are restricted to be nondecreasing, we know that if $\hat{\pi}_i = \hat{\pi}_{i+k}$, then every $\hat{\pi}_j$ for $i \leq j \leq i+k$ must also equal $\hat{\pi}_{i+k}$. Hence every feasible solution to Eqn. (3) must be of the form:

$$(13) \quad \hat{\pi}_i = \hat{\pi}_{B_1}, \quad 1 \leq i \leq B_1,$$

$$\hat{\pi}_i = \hat{\pi}_{B_2}, \quad B_1+1 \leq i \leq B_2,$$

⋮

$$\hat{\pi}_i = \hat{\pi}_{B_R}, \quad B_{R-1}+1 \leq i \leq B_R \equiv T,$$

with $0 \leq \hat{\pi}_{B_1} < \hat{\pi}_{B_2} < \dots < \hat{\pi}_{B_R} \leq 1$ and $\{B_1, B_2, \dots, B_R\} \subseteq \{1, 2, \dots, T\}$ with $B_1 < B_2 < \dots < B_R \equiv T$. In words, feasible solutions partition the set $\{1, 2, \dots, T\}$ into distinct “intervals” $\{1, 2, \dots, B_1\}$,

$\{B_1+1, \dots, B_2\}, \dots, \{B_{R-1}+1, \dots, B_R\}$, and all of the time periods (corresponding to the T independent samples) falling into the same interval have the same ML solution.

Given the partition of Eqns. (13) and defining $B_0 \equiv 0$, the maximum likelihood problem is given by:

$$(14) \quad \text{Maximize } \sum_{i=1}^R \left[\left(\sum_{k=B_{i-1}+1}^{B_i} n_k p_k \right) * \ln \pi_{B_i} + \left(\sum_{k=B_{i-1}+1}^{B_i} n_k (1-p_k) \right) * \ln(1-\pi_{B_i}) \right]$$

such that $0 \leq \pi_{B_r} < \pi_{B_{r-1}} \leq 1$ for $r=1, 2, \dots, R-1$, where $B_0 \equiv 0$ and $B_R \equiv T$. The unconstrained solution to (14) is

$$(15) \quad \hat{\pi}_{B_r} = \frac{\sum_{k=B_{r-1}+1}^{B_r} n_k p_k}{\sum_{k=B_{r-1}+1}^{B_r} n_k} = p(B_{r-1}+1, B_r), \quad r=1, 2, \dots, R.$$

This solution is feasible if it meets the constraints in (14).

Now consider any partition $\{B_1, B_2, \dots, B_R\}$ that yields a non-trivial feasible solution. We will show that the likelihood corresponding to the partition $\{T_1, T_2, \dots, T_K\}$ is at least as large as the likelihood corresponding to the partition $\{B_1, B_2, \dots, B_R\}$. We will do this by first showing that replacing the first break in the B-partition with T_1 yields a feasible solution with a likelihood that is greater than or equal to the likelihood associated with $\{B_1, B_2, \dots, B_R\}$. The same reasoning can then be applied seriatim to give the result for the entire partition.

Start with T_1 and suppose that $T_1 \neq B_1$. Then either $T_1 < B_1$ or $T_1 > B_1$. First suppose that $T_1 > B_1$. Then $B_m < T_1 \leq B_{m+1}$ for some m in $\{1, 2, \dots, R-1\}$. Suppose that $T_1 = B_{m+1}$. Since

$\hat{\pi}_{B_1} < \hat{\pi}_{B_2} < \dots < \hat{\pi}_{B_{m+1}}$ we must have $p(1, B_1) < p(B_1+1, B_2) < \dots < p(B_m+1, B_{m+1}) = p(B_m+1, T_1)$. However, $p(1, T_1)$ is a weighted average of $p(1, B_1)$, $p(B_1+1, B_2)$, ..., $p(B_m+1, T_1)$, so therefore $p(1, T_1) > p(1, B_1)$, which is a contradiction of the definition of T_1 . Thus, $T_1 \neq B_{m+1}$, so we must have $B_m < T_1 < B_{m+1}$.

Now consider the three probabilities formed by the partition $(B_{m-1}+1, B_m)$, (B_m+1, T_1) , (T_1+1, B_{m+1}) of the "interval" $(B_{m-1}+1, B_{m+1})$:

$$(16) \quad p'_1 = p(B_{m-1}+1, B_m), \quad p'_2 = p(B_m+1, T_1), \quad \text{and} \quad p'_3 = p(T_1+1, B_{m+1}).$$

If $m=1$ then $p(1, T_1)$ is a weighted average of $p'_1 = p(1, B_1)$ and p'_2 . Since $p(1, T_1)$ is a minimum, we know that $p'_1 \geq p(1, T_1)$ and therefore $p'_1 \geq p'_2$. Then using the result for the case $T=2$ [Eqn. (10)] with $p'_1 \geq p'_2$ we know that the likelihood must be at least as large if we replace the break at B_1 with a break at T_1 .

If $m>1$ then $p(1, T_1)$ is a weighted average of p'_1 , p'_2 , and $p(1, B_{m-1})$. Therefore, since $p(1, T_1)$ is a minimum, it can be shown that the weighted average of p'_1 and p'_2 cannot exceed $p(1, B_{m-1})$. However, $\hat{\pi}_{B_1} < \hat{\pi}_{B_2} < \dots < \hat{\pi}_{B_{m-1}} < \hat{\pi}_{B_m} = p'_1$ and $p(1, B_{m-1})$ is a weighted average of

$\hat{\pi}_{B_1}, \dots, \hat{\pi}_{B_m}$ so $p(1, B_{m-1}) < p'_1$. Therefore the weighted average of p'_1 and p'_2 is less than p'_1 , which implies that $p'_2 < p'_1$. Now $p'_1 = \hat{\pi}_{B_m} < \hat{\pi}_{B_{m+1}} = p(B_m+1, B_{m+1})$, which is a weighted

average of p'_2 and p'_3 . Therefore, since $p'_2 < p'_1$, this implies that $p'_2 < p'_1 < p'_3$. This satisfies the conditions of Eqn. (12c), so that partitioning the interval $(B_{m-1}+1, B_{m+1})$ at T_1 , rather than at B_m , maximizes the likelihood. Thus, the principle of maximum likelihood tells us to replace the break at B_m with a break at T_1 . Repeating the same reasoning we can in turn replace B_{m-1} by T_1 , B_{m-2} by T_1 , etc. until the first break in the partition is at T_1 .

Now suppose that $T_1 < B_1$ and consider the probabilities formed by the partition $(1, T_1)$,

(T_1+1, B_1) of the interval $(1, B_1)$. Since $p(1, T_1)$ is a minimum and $T_1 < B_1$, we know that

$p(1, T_1) < p(1, B_1)$. The inequality is strict since T_1 is the largest τ such that $p(1, \tau)$ is minimized. However, we can write $p(1, B_1)$ as a weighted average of $p(1, T_1) = p'_1$ and $p(T_1+1, B_1) = p'_2$ so

$$p(1, B_1) = a * p'_1 + (1-a) * p'_2, \text{ for some } a \text{ with } 0 < a < 1. \text{ Thus,}$$

since $p'_1 = p(1, T_1) < p(1, B_1)$ we have that $p'_1 < a * p'_1 + (1-a) * p'_2$, so $p'_1 < p'_2$. Using the result for the case $T=2$ [Eqn. (10)] with $p'_1 < p'_2$, we know that the likelihood will be at least as large if a partition is used with the first break at T_1 , rather than at B_1 .

We have shown that the maximum likelihood solution $\hat{\pi}$ must have its first break at T_1 . Now consider T_2 and partitions of the interval (T_1+1, T) . Applying the same reasoning used above for partitions of the interval $(1, T)$ to partitions of this interval shows that the likelihood is "maximized" by using a partition with its first two breaks at T_1 and T_2 . This process can be continued to show that no partition yields a larger likelihood than the T -partition defined by (5)ff with the corresponding estimated $\hat{\pi}$'s of Eqn. (8).

Generalization of the Proof to Exact Timepoints: Suppose there are n individuals with data, and for each individual the data consists of a measurement time and whether or not the individual had experienced a failure at or prior to that time. Then the data are of the form (t_i, y_i) , $i=1,2,\dots,n$ where

t_i = time of measurement for individual i , and

$y_i = 0$, if the individual did not have an event by time t_i

1, if the individual had an event by time t_i .

WLOG we will relabel the times so that $0 \leq t_1 \leq t_2 \leq \dots \leq t_n$. Now suppose that T of these n measurements are distinct and denote these times as $t_{(1)}, t_{(2)}, \dots, t_{(T)}$, where

$0 < t_{(1)} < t_{(2)} < \dots < t_{(T)}$ and n_i individuals have time $t = t_{(i)}$, $i=1,2,\dots,T$. Then $\sum_{i=1}^T n_i = n$ and

$0 < t_1 = t_2 = \dots = t_{n_1} = t_{(1)} < t_{n_1+1} = t_{n_1+2} = \dots = t_{n_1+n_2} = t_{(2)} < \dots < t_{n_1+n_2+\dots+n_{T-1}+1} = \dots = t_n = t_{(T)}$.

We can then apply the results of the ML proof above with these T distinct measurement times, sample sizes n_1, n_2, \dots, n_T , and

$$p_i = \frac{\sum y_i}{n_i} \text{ where the sum is over the } n_i \text{ individuals with time } t = t_{(i)},$$

to estimate $\pi_i =$ true cumulative failure rate at time $t_{(i)}$, $i=1,2,\dots,T$.

Using linear interpolation between the distinct timepoints, the cumulative failure rate function then becomes

$$\begin{aligned} \hat{\pi}(t) &= \hat{\pi}_1 * \left(\frac{t}{t_{(1)}}\right), 0 \leq t \leq t_{(1)}, \\ &= \hat{\pi}_1 + \frac{(\hat{\pi}_2 - \hat{\pi}_1)(t - t_{(1)})}{t_{(2)} - t_{(1)}}, t_{(1)} < t \leq t_{(2)}, \\ &= \hat{\pi}_2 + \frac{(\hat{\pi}_3 - \hat{\pi}_2)(t - t_{(2)})}{t_{(3)} - t_{(2)}}, t_{(2)} < t \leq t_{(3)}, \\ &\vdots \end{aligned}$$

$$= \hat{\pi}_{T-1} + \frac{(\hat{\pi}_T - \hat{\pi}_{T-1})(t - t_{(T-1)})}{t_{(T)} - t_{(T-1)}}, t_{(T-1)} < t \leq t_{(T)}.$$

In terms of the T_i 's we can write $\hat{\pi}(t)$ as

$$\begin{aligned} \hat{\pi}(t) &= \hat{\pi}_{T_k} + \frac{(\hat{\pi}_{T_{k+1}} - \hat{\pi}_{T_k})(t - t_{(T_{k+1})})}{t_{(T_{k+1}+1)} - t_{(T_k)}} , t_{(T_k)} < t < t_{(T_{k+1}+1)}, \\ &= \hat{\pi}_{T_k}, t_{(T_{k-1}+1)} \leq t \leq t_{(T_k)}, \end{aligned}$$

for $k=1,2,\dots,K$, where $T_0 \equiv 0$, $t_{(0)} = 0$, and $\hat{\pi}_0 = 0$.

Example: Suppose we have the following data (t_i, y_i) , $i=1,2,\dots,n$, for $n=20$ individuals:

(5,0), (6,0), (8,1), (8,0), (8,1), (9,0), (11,1), (12,0), (14,1), (16,1), (16,1), (17,1), (18,0), (18,1), (19,1), (20,0), (20,1), (20,1), (21,0), (22,1).

Then $T=14$ and $t_{(1)} = 5$, $t_{(2)} = 6$, $t_{(3)} = 8$, $t_{(4)} = 9$, $t_{(5)} = 11$, $t_{(6)} = 12$, $t_{(7)} = 14$, $t_{(8)} = 16$, $t_{(9)} = 17$,

$t_{(10)} = 18$, $t_{(11)} = 19$, $t_{(12)} = 20$, $t_{(13)} = 21$, $t_{(14)} = 22$. Also, $n_1 = 1$, $n_2 = 1$, $n_3 = 3$, $n_4 = 1$, $n_5 = 1$,

$n_6 = 1$, $n_7 = 1$, $n_8 = 2$, $n_9 = 1$, $n_{10} = 2$, $n_{11} = 1$, $n_{12} = 3$, $n_{13} = 1$, $n_{14} = 1$. It can be shown that $T_1 = 2$, $T_2 = 6$, $T_3 = 13$, and $T_4 = 14$. Therefore, from Eqn. (8) we have

$$\hat{\pi}_i = p(1, T_1) = p(1, 2) = 0, i = 1, 2,$$

$$\hat{\pi}_i = p(T_1+1, T_2) = p(3, 6) = 0.5, i = 3, 4, 5, 6,$$

$$\hat{\pi}_i = p(T_2+1, T_3) = p(7, 13) = 8/11 = 0.727, i = 7, 8, 9, 10, 11, 12, 13, \text{ and}$$

$$\hat{\pi}_i = p(T_3+1, T_4) = p(14, 14) = 1, i = 14.$$

Hence,

$$\hat{\pi}(t) = \hat{\pi}_2 * \left(\frac{t}{t_{(1)}}\right) = 0 * \left(\frac{t}{5}\right) = 0, 0 < t < t_{(1)} = 5,$$

$$= \hat{\pi}_2 = 0, t_{(1)} = 5 \leq t \leq t_{(2)} = 6,$$

$$= \hat{\pi}_2 + \frac{(\hat{\pi}_6 - \hat{\pi}_2)(t - t_{(2)})}{t_{(3)} - t_{(2)}} = 0 + \frac{0.5(t - 6)}{(8 - 6)} = 0.25 * t - 1.5, t_{(2)} = 6 < t < t_{(3)} = 8,$$

$$= \hat{\pi}_6 = 0.5, t_{(3)} = 8 \leq t \leq t_{(6)} = 12,$$

$$= \hat{\pi}_6 + \frac{(\hat{\pi}_{13} - \hat{\pi}_6)(t - t_{(6)})}{t_{(7)} - t_{(6)}} = 0.5 + \frac{(\frac{8}{11} - 0.5)(t - 12)}{(14 - 12)} = \frac{5}{44} * t - \frac{19}{22}, t_{(6)} = 12 < t < t_{(7)} = 14,$$

$$= \hat{\pi}_{13} = \frac{8}{11}, t_{(7)} = 14 \leq t \leq t_{(13)} = 21,$$

$$= \hat{\pi}_{13} + \frac{(\hat{\pi}_{14} - \hat{\pi}_{13})(t - t_{(13)})}{t_{(14)} - t_{(13)}} = \frac{8}{11} + \frac{(1 - \frac{8}{11})(t - 21)}{(22 - 21)} = \frac{3}{11} * t - 5, t_{(13)} = 21 < t < t_{(14)} = 22,$$

$$= \hat{\pi}_{1,2} = 1, t \geq t_{(1+)} = 22.$$

So,

$$\hat{\pi}(t) = 0, 0 < t \leq 6,$$

$$= 0.25 * t - 1.5, 6 < t < 8,$$

$$= 0.5, 8 \leq t \leq 12,$$

$$= \frac{5}{44} * t - \frac{19}{22}, 12 < t < 14$$

$$= \frac{8}{11}, 14 \leq t \leq 21,$$

$$= \frac{3}{11} * t - 5, 21 < t < 22$$

$$= 1, t \geq 22.$$