Published in final edited form as:

J Stat Plan Inference. 2009 September 1; 139(9): 3329–3339. doi:10.1016/j.jspi.2009.03.007.

A Mass Redistribution Algorithm for Right Censored and Left Truncated Time to Event Data

Xu Zhang,

Department of Mathematics and Statistics, Georgia State University, Atlanta, GA 30303, USA,
matxxz@langate.gsu.edu, Phone: +1 404 413 6404, Fax: +1 404 413 6403

Mei-Jie Zhang, and

Division of Biostatistics, Department of Population Health, Medical College of Wisconsin,
Milwaukee, WI 53226, USA

Jason Fine

Department of Statistics, University of Wisconsin, Madison, WI 53792, USA

Abstract

Failure times are often right-censored and left-truncated. In this paper we give a mass redistribution algorithm for right-censored and/or left-truncated failure time data. We show that this algorithm yields the Kaplan-Meier estimator of the survival probability. One application of this algorithm in modeling the subdistribution hazard for competing risks data is studied. We give a product-limit estimator of the cumulative incidence function via modeling the subdistribution hazard. We show by induction that this product-limit estimator is identical to the left-truncated version of Aalen-Johansen (1978) estimator for the cumulative incidence function.

Keywords

Cumulative incidence function; subdistribution hazard; truncation

1 Introduction

Efron (1967) proposed a redistribution-to-the-right (RTR) algorithm to be used to estimate the survival function of the failure time with right censored data. This algorithm removes the mass of a censored subject and redistributes this mass equally to all subjects who fail or are censored at later times. Efron suggested that the survival function at t can be estimated by the mass of all subjects to the right of t , and such an estimate agrees with the Kaplan-Meier estimate. Another mass redistribution algorithm for right censored failure time data was discussed by Robertson and Uppuluri (1984). For this algorithm, the mass is redistributed equally to the failed items only. Such an algorithm yields the maximum entropy estimator of the survival function. Utilizing the idea of self-consistency (Efron, 1967), Turnbull (1976) developed an iterative procedure to estimate the survival function with arbitrarily grouped, censored and truncated data.

Correspondence to: Xu Zhang.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Extension of RTR algorithm has been studied by Malani (1995) and Gooley et al. (1999). Malani proposed a modified RTR algorithm with the presence of disease markers, and clarified that a mass associated with an individual at t can be used as a weight in estimating the survival function, as well as in the log-rank test or a regression model. Gooley et al. extended the RTR algorithm to the competing risks data. They suggested estimating the cumulative incidence function of cause 1, $F_1(t)$, by the mass of the subjects who fail from cause 1 no later than t . Gooley et al. adopted an iterative procedure to calculate the mass.

In medical studies left truncation may occur through delayed entry (Klein and Zhang, 1996). Kaplan and Meier (1958) stated that late entrance (also known as left truncation) is allowed in calculating the risk sets of their estimator of the survival function. Asymptotic properties of the left-truncated version Kaplan-Meier estimator has been studied by Woodroffe (1985), Keiding and Gill (1990), Wang, Jewell and Tsai (1986), as well as Lai and Ying (1991). There has been no discussion on how to redistribute the mass for left-truncated and right-censored failure time data. In this paper we propose a mass redistribution algorithm which can be applied to left-truncated (and/or right-censored) data, and show that the proposed algorithm yields identical estimates as the left-truncated version Kaplan-Meier estimator.

Efron's algorithm is closely related with the inverse probability of censoring weighting (IPCW) technique (Robins, 1993). The IPCW technique has been utilized to analyze the censored competing risks data through modeling the subdistribution hazard of a competing risk (Fine and Gray, 1999) or directly modeling the cumulative incidence function (Scheike et al. 2008). In this paper we demonstrate that the proposed mass redistribution algorithm can be applied to the left-truncated and/or right-censored competing risks data. We propose a nonparametric estimator of the subdistribution hazard function using the proposed weighting technique, and a product-limit estimator of the cumulative incidence function. We give a proof in the Appendix that this product-limit estimator is identical to the left-truncated version of the Aalen-Johansen (1978) estimator.

The outline of the remainder of this paper is as follows. In Section 2, we review RTR algorithm for right-censored only data and propose a new mass redistribution algorithm for left-truncated and/or right-censored data. In Section 3.1 we review the nonparametric estimators of the cumulative incidence function with right censored competing risks data. In Section 3.2 we propose a product-limit estimator of the cumulative incidence function for left-truncated and/or right-censored competing risks data, using a weight derived from the mass redistribution algorithm. A Monte Carlo study is presented in Section 4. Bone marrow transplant data is analyzed in Section 5. Concluding remarks are given in Section 6.

2 The mass redistribution algorithms

First we briefly show that Efron's RTR algorithm can be interpreted as IPCW technique with right censored failure time data. Next we introduce a new mass redistribution algorithm which can be applied to analyze the left-truncated and/or right-censored failure time data.

2.1 The redistribution-to-the-right algorithm

For right censored failure time data, we observe $X_i = \min(T_i, C_i)$ and $\delta_i = I\{T_i < C_i\}$ for $i = 1, \dots, n$, where T_i and C_i are failure time and censoring time, respectively. The RTR algorithm can be summarized as follows. For a sample of size n , each item has an initial mass of $1/n$. Starting from the first censored item, its mass is redistributed equally to all items to its right. Then redistribute the mass of the second censored item in the same way. Repeat the process until the last censored item.

Let $\hat{G}_C(t)$ be the Kaplan-Meier estimate of $P(C > t)$. In the RTR algorithm, the mass at the observed failure time t is $1/\{n\hat{G}_C(t)\}$ (Malani, 1995, p.517; Efron, 1967, p.843). The survival probability $S(t) = P(T > t)$ is estimated by the mass of all items to the right of t ,

$$\hat{S}(t) = \sum_{i=1}^n \frac{I\{X_i > t\}}{n\hat{G}_C(t)}. \quad (2.1)$$

It is known that this inverse probability of censoring weighting estimator is equal to the Kaplan-Meier estimator of $S(t)$ (Malani, 1995, p.517; Lin, Sun and Ying, 1999, p.61). Note that at time prior to t , $S(t^-)$ can be estimated by the mass of all items at t or to the right of t , that is,

$$\hat{S}(t^-) = \sum_{i=1}^n \frac{I\{X_i \geq t\}}{n\hat{G}_C(t)}. \quad (2.2)$$

2.2 A new mass redistribution algorithm for left-truncated and right-censored failure time data

Let T be the failure time, and let L and C be the left truncation time and the right censoring time, respectively. We assume that T is independent from (L, C) . Let $X = \min(T, C)$. For left-truncated and right-censored data, X is observable only if $L \leq X$. We assume that the observed data $\{L_i, X_i, \delta_i\}$ are independent and identically distributed for $i = 1, \dots, n$, where $\delta_i = I\{T_i \leq C_i\}$. At time t , the i th item is at risk if $I\{L_i \leq t \leq X_i\} = 1$. The risk set at t can be

defined as $\mathcal{R}(t) = \sum_{i=1}^n I\{L_i \leq t \leq X_i\}$. One problem exists if one directly carries over the RTR algorithm to the left-truncated and right-censored failure time data. In the RTR algorithm, the later events always obtain higher mass than the early events. However, with left truncated data, the early events need to be associated with higher weight to correct the selection bias caused by truncation (Woodroffe, 1985, p.169). To solve this problem, we propose a new mass redistribution algorithm. In this algorithm, the initial mass is set to be 1. The algorithm begins from time zero. Then

1. move the mass to the right until reaching a failure time.
2. equally distribute the mass to the items in the risk set; the mass associated with the failed item(s) stay at this failure time; the mass associated with the survivors is carried over to the right; and
3. return to 1 and stop after reaching the largest failure time.

It is important to note that redistribution is conducted at the distinct failure times only. At a failure time t , we let “mass $> t$ ” be the mass of the survivors at time t , and “mass $\leq t$ ” be the mass of the items failing at or before t . The mass of the survivors needs to be carried over to the next failure time. For tied observations, if an item is censored at a failure time t , the mass of the censored item needs to be placed in the “mass $> t$ ” category although its observed time is t .

We now use a psychiatric inpatients example to show how to prepare the data and apply the proposed algorithm. The data set was originally reported by Woolson (1981) and used as an example to illustrate left truncation by Tableman and Kim (2004). The sample consists of twenty-six patients who experienced psychiatric symptoms and were admitted to the University of Iowa hospitals during 1935–1948. The patients’ times to deaths, in terms of ages, were of study interested. The time to death was truncated by the age at which a patient was admitted to the hospital. The sample included 9 male patients and 15 female patients.

The gender specific survival curves need to be computed. The survival data on the 15 female patients is given in Table 1.

At each failure time, one needs to find the number of failures and the size of the risk set. Table 2 shows the distinct ordered failure times, together with the numbers of failed subjects and the sizes of risk sets. At time zero, the overall mass of the sample is set to be 1. At the first failure time 50, the overall mass is equally distributed among the 12 subjects in the risk set. We further divide the mass into two categories, “mass = 50” and “mass > 50”. The category “mass = 50” includes one failed subject only and obtains the value 0.083. The category “mass > 50” includes 11 survivors and is evaluated to be 0.917. The mass 0.917 should be carried over to the next failure time 52. At the failure time 52, the carried over mass 0.917, is equally distributed among the 12 subjects in the risk set. The category “mass = 52” consists of mass of two subjects failing at time 50 and 52, which is evaluated to be 0.159. The category “mass > 52” obtains the value 0.841 and this mass should be carried over to the next failure time. Such a procedure needs to be repeated until the last failure time. Figure 1 shows the mass redistribution procedure for the first three failure time points for this example.

Let $t_1 < t_2 < t_3 < \dots$ be the ordered failure times. Let d_j and n_j be the number of failures and number at risk at t_j , respectively. The general mass redistribution algorithm is summarized in Table 3.

We use “mass > t_j ” to estimate the survival function $S(t_j)$, which is the product of $(1 - d_j/n_j)$ and the mass carried over to t_j . The estimator is given by

$$\widehat{S}(t_i) = \{\text{mass carried over to } t_i\} \times \left(1 - \frac{d_i}{n_i}\right) = \widehat{S}(t_{i-1}) \left(1 - \frac{d_i}{n_i}\right) = \prod_{j:t_j \leq t_i} \left(1 - \frac{d_j}{n_j}\right),$$

which is exactly the Kaplan-Meier estimator (the right-censored and left-truncated version). At t_j , the individual mass is

$$\frac{\text{mass carried over to } t_i}{\# \text{ of items at risk at } t_i} = \frac{\widehat{S}(t_i - 1)}{\widehat{nb}(t_i)}, \quad (2.3)$$

where $\widehat{b}(t_i) = n_i/n$.

Note that, for the right-censored only failure time data, $\widehat{b}(t) = \sum_j I\{X_j \geq t\}/n$. Following equation (2.2), $\widehat{S}(t)/\{\widehat{nb}(t)\} = 1/\{\widehat{nG}_C(t)\}$. That is, the proposed weight reduces to the inverse probability of censoring weight (IPCW).

3 Nonparametric estimators of the cumulative incidence function with competing risks data

3.1 Right-censored competing risks data

For the i th individual, let T_i and C_i be the event time and censoring time, respectively, and assume that C_i is independent of T_i . Let $X_i = \min(T_i, C_i)$, $\delta_i = I\{T_i < C_i\}$ and $\epsilon_i \in \{1, \dots, K\}$ be the cause of failure. For right-censored competing risks data, we observe $(X_i, \delta_i, \epsilon_i)$ for $i = 1, \dots, n$. For simplicity, we assume that $K = 2$. The cumulative incidence function of type 1 failure is

$$F_1(t) = P(T_i \leq t, \epsilon_i = 1) = \int_0^t S(u^-) d\Lambda_1(u)$$

where $S(u)$ is the overall survival probability, $\Lambda_1(u) = \int_0^u \lambda_1(v) dv$, and $\lambda_1(t)$ is the cause-specific hazard function of cause 1. Define counting process $N_{i1}(t) = I\{X_i \leq t, \delta_i \epsilon_i = 1\}$ and $Y_i(t) = I\{X_i > t\}$. Let $N_{\bullet 1}(t) = \sum_{i=1}^n N_{i1}(t)$ and $Y_{\bullet}(t) = \sum_{i=1}^n Y_i(t)$. $F_1(t)$ is commonly estimated by the Aalen-Johansen (1978) estimator

$$\widehat{F}_1^{\text{AJ}}(t) = \int_0^t \widehat{S}(u^-) d\widehat{\Lambda}_1(u),$$

where $\widehat{S}(t)$ is the Kaplan-Meier estimator for all causes and $\widehat{\Lambda}_1(t) = \int_0^t \{Y_{\bullet}(u)\}^{-1} dN_{\bullet 1}(u)$ is the Nelson-Aalen estimator for cause 1.

In the RTR algorithm, if failure of the i th subject is observed, its mass is $1/\{n\widehat{G}_C(X_i)\}$ (see Section 2.1). With competing risks data, $F_1(t)$ can be estimated by the mass of all items that failed from cause 1 before or equal to t ,

$$\widehat{F}_1^{\text{PCW}}(t) = \sum_{i=1}^n \frac{I\{X_i \leq t, \delta_i \epsilon_i = 1\}}{n\widehat{G}_C(X_i)}.$$

Gooley et al. (1999) introduced this inverse weighting estimator using an interactive procedure to calculate the mass. Recently, Scheike et al. (2008) derived $\widehat{F}_1^{\text{PCW}}(t)$ by directly modeling the cumulative incidence function. Note that $\widehat{S}(t^-)/Y_{\bullet}(t) = 1/\{n\widehat{G}_C(t)\}$ for right-censored failure time data (see Equation (2.2)). Thus, the Aalen-Johansen estimator can be expressed as

$$\begin{aligned} \widehat{F}_1^{\text{AJ}}(t) &= \sum_{i=1}^n \int_0^t \frac{\widehat{S}(u^-)}{Y_{\bullet}(u)} dN_{i1}(u) = \sum_{i=1}^n \frac{\widehat{S}(X_i^-)}{Y_{\bullet}(X_i)} I\{X_i \leq t, \delta_i \epsilon_i = 1\} \\ &= \sum_{i=1}^n \frac{I\{X_i \leq t, \delta_i \epsilon_i = 1\}}{n\widehat{G}_C(X_i)}. \end{aligned} \quad (3.1)$$

It follows that $\widehat{F}_1^{\text{AJ}}(t) = \widehat{F}_1^{\text{PCW}}(t)$.

An alternative nonparametric estimator of $F_1(t)$ is based on Gray's (1988) subdistribution hazards approach, where the subdistribution hazards of cause 1 is defined as

$$\begin{aligned} \lambda_1^*(t) &= \lim_{\Delta t \rightarrow 0} \frac{1}{\Delta t} P\{t \leq T \leq t + \Delta t, \epsilon = 1 | (T \geq t) \cup (T < t \cap \epsilon = 2)\} \\ &= -d \log \{1 - F_1(t)\} / dt. \end{aligned} \quad (3.2)$$

Gray stated that $\lambda_1^*(t)$ is the hazard function for the improper random variable T^* , where $T^* = T \times I\{\epsilon = 1\} + \infty \times I\{\epsilon = 2\}$. Fine and Gray (1999) proposed a regression model to directly assess effect of covariates on a subdistribution hazard function. Without covariates, the

cumulative subdistribution hazard function $\Lambda_1^*(t) = \int_0^t \lambda_1^*(u) du$ can be estimated by the Nelson-Aalen type estimator. Define the underlying counting process

$N_i^1(t) = I\{T_i \leq t, \epsilon_i = 1\}$ and $Y_i^1(t) = 1 - N_i^1(t^-) = I\{(T_i \geq t) \cup (T_i < t, \epsilon_i = 2)\}$. For the right-

censored competing risks data, $N_i^1(t)$ and $Y_i^1(t)$ are not observable for all t if the i th subject is censored. Let $r_i(t) = I\{C_i \geq (T_i \wedge t)\}$, then $r_i(t)N_i^1(t)$ and $r_i(t)Y_i^1(t)$ are fully computable. Note that $r_i(t)N_i^1(t) = N_{i1}(t)$ for all t . Fine and Gray suggested an IPCW, $\hat{w}_i(t) = r_i(t)/\hat{G}_C(X_i \wedge t)$, and proposed to estimate $\Lambda_1^*(t)$ by

$$\hat{\Lambda}_1^*(t) = \sum_{i=1}^n \int_0^t \frac{\hat{w}_i(u) dN_i^1(u)}{\sum_{j=1}^n \hat{w}_j(u) Y_j^1(u)}. \quad (3.3)$$

Then, $F_1(t)$ can be estimated by a product-limit estimator

$$\hat{F}_1^{\text{PL}}(t) = 1 - \prod_{u \leq t} \{1 - d\hat{\Lambda}_1^*(u)\}$$

In Appendix A we use RTR algorithm to show that $\hat{F}_1^{\text{AJ}}(t)$ and $\hat{F}_1^{\text{PL}}(t)$ yield identical estimates of $F_1(t)$.

3.2 Left-truncated and right-censored competing risks data

For left-truncated and right-censored competing risks data, $X_i = \min(T_i, C_i)$ is observable only if $L_i \leq X_i$. The observed data can be summarized as $\{L_i, X_i, \delta_i, \epsilon_i\}$, for $i = 1, \dots, n$.

Consider the counting process $N_{i1}^L(t) = I\{L_i \leq X_i \leq t, \delta_i \epsilon_i = 1\}$ and $Y_i^L(t) = I\{L_i \leq t \leq X_i\}$. Let $N_{\bullet 1}^L(t) = \sum_{i=1}^n N_{i1}^L(t)$ and $Y_{\bullet}^L(t) = \sum_{i=1}^n Y_i^L(t)$. The Aalen-Johansen estimator of $F_1(t)$ is,

$$\hat{F}_1^{\text{AJ}}(t) = \int_0^t \hat{S}(u^-) d\hat{\Lambda}_1(u), \quad (3.4)$$

where $\hat{\Lambda}_1(t) = \int_0^t dN_{\bullet 1}^L(u) / Y_{\bullet}^L(u)$ and $\hat{S}(t)$ are the corresponding left-truncated and right-censored version estimators. Asymptotic properties of $\hat{F}_1^{\text{AJ}}(t)$ have been studied by Huang and Wang (1995).

In Section 2.2, we have shown that based on the new mass redistribution algorithm for the left-truncated and right-censored data, the individual mass at X_i is $\hat{S}(X_i^-) / \{nb(X_i)\}$ (see (2.3)). Thus, we can estimate $F_1(t)$ by the mass of all subjects who fail from cause 1 no later than t ,

$$\hat{F}_1^W(t) = \sum_{i=1}^n \frac{\hat{S}(X_i^-)}{nb(X_i)} I\{L_i \leq X_i \leq t, \delta_i \epsilon_i = 1\}. \quad (3.5)$$

Since

$$\hat{F}_1^{\text{AJ}}(t) = \sum_{i=1}^n \int_0^t \frac{\hat{S}(u^-)}{Y_{\bullet}^L(u)} dN_{i1}^L(u) = \sum_{i=1}^n \frac{\hat{S}(X_i^-)}{nb(X_i)} I\{L_i \leq X_i \leq t, \delta_i \epsilon_i = 1\}, \quad (3.6)$$

it is clear that the Aalen-Johansen estimator can be well explained by the proposed mass redistribution algorithm.

Here, we introduce an alternative estimator of $F_1(t)$ via the subdistribution hazard, $\Lambda_1^*(t)$ (Gray, 1988; Fine and Gray, 1999). In order to estimate $\Lambda_1^*(t)$ with the presence of left truncation, we define the observed process $Y_{i1}^L(t) = I\{(L_i \leq t \leq X_i) \cup (L_i \leq X_i < t, \delta_i \in \{2\})\}$. Let $Y_{\bullet 1}^L(t) = \sum_{i=1}^n Y_{i1}^L(t)$. Given t , $Y_{\bullet 1}^L(t)$ is the risk set at time t . Note that the subjects in the risk set do not possess the same mass due to censoring and truncation. According to the algorithm described in Section 2.2, the mass for one who is still under study at t is $\widehat{S}(t^-)/\widehat{b}(t)$, and the mass for the i th subject who has failed from the other cause before t but still remains in the risk set is $\widehat{S}(X_i^-)/\widehat{b}(X_i)$. Define the weight

$$\widehat{k}_i(t) = \begin{cases} \widehat{S}(t^-)/\widehat{b}(t), & X_i \geq t, \\ \widehat{S}(X_i^-)/\widehat{b}(X_i), & X_i < t, \end{cases}$$

which can be simplified as $\widehat{k}_i(t) = \widehat{S}(X_i^- \wedge t^-)/\widehat{b}(X_i \wedge t)$. With this proposed weight, we estimate $\Lambda_1^*(t)$ by

$$\tilde{\Lambda}_1^*(t) = \sum_{i=1}^n \int_0^t \frac{\widehat{k}_i(u) dN_{i1}^L(u)}{\sum_{j=1}^n \widehat{k}_j(u) Y_{j1}^L(u)}. \quad (3.7)$$

Then, $F_1(t)$ can be estimated by a product-limit estimator,

$$\widehat{F}_1^{\text{PL}}(t) = 1 - \prod_{u \leq t} \{1 - d\tilde{\Lambda}_1^*(u)\} \quad (3.8)$$

Another estimator of $F_1(t)$ can be derived from the relationship illustrated in Equation (3.2). It is given by $\widehat{F}_1^{\text{EXP}}(t) = 1 - \exp\{-\tilde{\Lambda}_1^*(t)\}$. It can be shown that the product-limit estimator in (3.8) yields identical estimates as the Aalen-Johansen estimator. A proof is given in Appendix B.

Remark 1—The question has been raised whether one could adopt an inverse probability of censoring weight with the presence of truncation. An intuitive weight is $1/\widehat{G}_C(X_i \wedge t)$, where $\widehat{G}_C(t)$ is the left-truncated version Kaplan-Meier estimate for the censoring distribution. The problem of using such weight with left-truncated data is that the weight of this type does not appropriately quantify the individual mass for the risk set at t . In a limited simulation study (Section 4) we show that this left-truncated version IPCW leads to a biased estimator.

Remark 2—For right-censored only competing risks data, following Equation (2.2), the proposed weight $\widehat{S}(X_i^- \wedge t^-)/\widehat{b}(X_i \wedge t)$ reduces to the inverse probability of censoring weight $1/\widehat{G}_C(X_i \wedge t)$.

Remark 3—Hudgens, Satten and Longini (2001) developed nonparametric estimation methods for a cumulative incidence function with a more general censoring and truncation pattern, using iterative procedures. We consider a restricted pattern with only right censoring and left truncation, and a one-step estimator (3.8) has been derived.

4 A Monte Carlo study

In this section we study the performance of the Aalen-Johansen estimator of cumulative incidence function for left-truncated and/or right-censored competing risks data. We consider the following underlying cumulative incidence functions

$$F_1(t)=0.6(1-e^{-t}) \quad \text{and} \quad F_2(t)=0.4(1-e^{-1.2t^{0.6}}).$$

According to the definition (3.2), the cumulative subdistribution hazard of cause 1 is

$$\Lambda_1^*(t)=-\log\{1-0.6(1-e^{-t})\},$$

which is estimated by

$$\sum_{i=1}^n \int_0^t \frac{\hat{\omega}_i(u) dN_{i1}^L(u)}{\sum_{j=1}^n \hat{\omega}_j(u) Y_{j1}^L(u)}, \quad (4.1)$$

where $\hat{\omega}_i(t)$ is one of the three weights:

1. $\hat{\omega}_i(t) \equiv 1$ (Equal weight);
2. $\hat{\omega}_i(t) = 1/\hat{G}_C(X_i \wedge t)$ (IPCW weight);
3. $\hat{\omega}_i(t) = \hat{S}(X_i^- \wedge t^-)/\hat{b}(X_i \wedge t)$ (New weight).

Note that $\hat{G}_C(t)$ is the left-truncated version Kaplan-Meier estimator of the censoring distribution. Three product-limit estimators of $F_1(t)$ are labeled as “equal weight”, “IPCW”, “new weight (A-J)”, respectively. In Appendix B we showed that the product-limit estimator of $F_1(t)$ with the weight $\hat{S}(X_i^- \wedge t^-)/\hat{b}(X_i \wedge t)$ agrees with the Aalen-Johansen estimator and is thus asymptotically unbiased. In this simulation study we want to find out whether the product-limit estimators of $F_1(t)$ with other weights give satisfactory results.

The truncation and censoring times were generated from exponential distributions. The values of the distribution parameters were determined to yield the desired truncation and censoring rates. We used a sample size 200. For each setting, 1000 samples were generated.

Let $\hat{F}_1^{(i)}(t)$ denote the estimated value for the i th sample, given one estimator. We calculated the average of $\hat{F}_1^{(i)}(t)$'s, for $i = 1, \dots, 1000$, which is denoted by $\bar{F}_1(t)$. We report the average bias (BIAS), relative bias (RBIAS), empirical standard error (SE) and relative empirical standard error (RSE). Their explicit expressions are

$$\begin{aligned} \text{BIAS}(t) &= \bar{F}_1(t) - F_1(t), \\ \text{RBIAS}(t) &= \text{BIAS}(t)/F_1(t), \\ \text{SE}(t) &= \left[\frac{1}{1000-1} \sum_{i=1}^{1000} \left\{ \hat{F}_1^{(i)}(t) - \bar{F}_1(t) \right\}^2 \right]^{\frac{1}{2}}, \\ \text{RSE}(t) &= \text{SE}(t)/\bar{F}_1(t). \end{aligned}$$

The simulation results are given in Table 4. For four truncation and censoring settings, we further computed standardized biases by

$$\text{STD BIAS}(t) = \text{BIAS}(t) / \text{SE}(t),$$

and plotted them in Figure 2. The standardized bias is the ratio of the raw bias and the overall uncertainty in the estimated values. A standardized bias of larger than 100% means the raw bias falls beyond 1 standard error of the estimated parameter. The standardized bias of less than 50% in both directions has been considered as practically insignificant (Demirtas, 2004).

We have conducted simulations with the underlying cumulative incidence functions and with Uniform censoring times. The “new weight (A–J)” estimator is asymptotically unbiased, which is verified by this simulation study. The simulation also shows that the “IPCW” and the “equal weight” estimators are biased when the failure times are left truncated. The following is the summary of the simulation results.

1. The “equal weight” estimator performs well with the complete data (see the entry $(C\%, L\%) = (0, 0)$). With censored only or truncated only data, the bias is nonnegligible. With presence of both censoring and truncation, the higher mass in the early events due to truncation can be somehow balanced by the higher mass in the later events due to censoring. This explains that the performance of the “equal weight” estimator is acceptable for the settings like $(C\%, L\%) = (50, 30), (50, 50)$. In general, this estimator is still biased and should not to be practically recommended.
2. The “IPCW” estimator satisfactorily describes the cumulative incidence probabilities with right censored data (see the entry $(C\%, L\%) = (30, 0)$ and $(C\%, L\%) = (50, 0)$), but fails if truncation is present. Figure 2 shows that this is the worst estimator when censoring and truncation are both present.
3. The “new weight (A–J)” estimator, which is asymptotically unbiased, performs well in all settings. Figure 2 indicates that only this “new weight” estimator is practically unbiased in all these simulation settings.

5 An example

In this section, we analyze bone marrow transplant data to illustrate the impact of different weights on estimation of a cumulative incidence function. Children with initial acute leukemia are routinely treated with chemotherapy. Most of children will achieve complete remission following the chemotherapy treatment. Leukemia recurs in some children. For children in their second remission, bone marrow transplant is a treatment option to prevent leukemia recurrence. An early study (Barrett et al., 1994) compared the survival outcome of HLA-identical sibling bone marrow transplant and chemotherapy for children with acute lymphoblastic leukemia in second remission. For illustration purpose, we consider the transplant cohort only. The failure or follow-up times of 376 children who received bone marrow transplant in their second remission were reported by the International Bone Marrow Transplant Registry (IBMTR). IBMTR collects only the transplant cases. Children may die while waiting for their transplants. Thus, the survival times of the children with transplant treatment were left truncated by the transplantation times. Meanwhile, the survival times were subject to right censoring. The censoring times were observed on 148 patients, which accounts for 44% of the sample.

There are two competing risks, leukemia relapse and treatment related mortality (TRM). TRM is defined as death in complete remission. Graft-versus-host-disease is the major cause for TRM. The Aalen-Johansen estimator was utilized to compute the cumulative incidence

probabilities of relapse and TRM (Figure 3 and Figure 4). For the purpose of comparison, we also plotted in Figure 3 and Figure 4 the curves arising from the “equal weight” and “IPCW” estimators (see Section 4). For TRM, the cumulative incidence curves based on the three estimators are very close. For leukemia relapse, the cumulative incidence probabilities are over-estimated with the “equal weight” and “IPCW” estimators.

For this sample, light censoring was observed in the early period of study. For example, only 5% of the failure times occurring within the first six months were censored, which is much lower than the overall censoring rate 44%. As a result, the IPCW weights are very close to 1 for this period of time. Since the majority of the TRM failures (58%) occurred in the first 6 months, the cumulative incidence curves of TRM using the IPCW weight and the equal weight are close. Patients receiving bone marrow transplants usually remain leukemia free for some time. Much fewer leukemia relapse cases occurred during the first several months than TRM failures. Specifically, thirty-four TRM failures were observed during the first four months while only nine leukemia relapse cases were observed in the same period. For estimating the cumulative incidence of TRM, since most of the TRM failures occurred in the first six months while a relatively small number of leukemia relapse cases were observed, the cumulative incidence curve of TRM using the new weight is close to the curve using the equal weight.

6 Final Remarks

We have introduced a mass distribution algorithm with left truncated and right censored failure time data. Based on this algorithm, we proposed the weight, $\widehat{S}(X_i^- \wedge t^-)/\widehat{b}(X_i \wedge t)$, to model a subdistribution hazard with competing risks data. This weight is used to correct the bias caused by truncation and censoring. We have shown that the product integral of the proposed estimator of the subdistribution hazard coincides with the Aalen-Johansen estimator of the cumulative incidence function, and is hence asymptotically unbiased. The proposed weight can be further applied to model the subdistribution hazard and cumulative incidence function directly with the presence of covariates. In constructing a regression model on a subdistribution hazard, a stabilized weight, $\{\widehat{S}(X_i^- \wedge t^-)\widehat{b}(t)\}/\{\widehat{b}(X_i \wedge t)\widehat{S}(t^-)\}$, can be considered to reduce the high variation associated with the original weight. This idea follows from the stabilized inverse probability of censoring weight, which was first discussed by Robins (1993) and has been widely applied. For nonparametric estimation, the stabilized weight yields the identical estimates as the original weight. We used the original weight throughout in order to make a clear connection with the mass redistribution algorithm.

Acknowledgments

Mei-Jie Zhang's work was partially supported by a grant (R01 CA54706-10) from the National Cancer Institute.

References

- Aalen OO, Johansen S. An empirical transition matrix for nonhomogeneous Markov chains based on censored observations. *Scandinavian Journal of Statistics*. 1978; 5:141–150.
- Barrett AJ, Horowitz MM, Pollock BH, Zhang MJ, Bortin MM, Buchanan GR, Camitta BM, Ochs J, Graham-Pole J, Rowlings PA, Rimm AA, Klein JP, Shuster JJ, Sobocinski KA, Gale RP. HLA-identical Sibling Bone Marrow Transplants versus Chemotherapy for Children with Acute Lymphoblastic Leukaemia in Second Remission. *The New England Journal of Medicine*. 1994; 331:1253–1258. [PubMed: 7935682]
- Demirtas H. Simulation-driven inferences for multiply imputed longitudinal datasets. *Statistica Neerlandica*. 2004; 58:466–482.

- Efron, B. The two sample problem with censored data. *Proceedings of the Fifth Berkeley Symposium On Mathematical Statistics and Probability*; Prentice-Hall; New York. 1967. p. 831-853.
- Fine JP, Gray RJ. A proportional hazards model for the subdistribution of a competing risk. *Journal of the American Statistical Association*. 1999; 94:496–509.
- Gooley TA, Leisenring W, Crowley J, Storer BE. Estimation of failure probabilities in the presence of competing risks: new representations of old estimators. *Statistics in Medicine*. 1999; 18:695–706. [PubMed: 10204198]
- Gray RJ. A class of K -Sample tests for comparing the cumulative incidence competing risk. *The Annals of Statistics*. 1988; 16:1141–1154.
- Huang Y, Wang MC. Estimating the occurrence rate for prevalent survival data in competing risks models. *Journal of the American Statistical Association*. 1995; 90:1406–1415.
- Hudgens MG, Satten GA, Longini IM. Nonparametric maximum likelihood estimation for competing risks survival data subject to interval censoring and truncation. *Biometrics*. 2001; 57:74–80. [PubMed: 11252621]
- Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. *Journal of the American Statistical Association*. 1958; 53:457–481.
- Keiding N, Gill RD. Random truncation models and Markov processes. *The Annals of Statistics*. 1990; 18:582–602.
- Klein, JP.; Zhang, MJ. Statistical Challenges in Comparing Chemotherapy and Bone Marrow Transplantation as a Treatment for Leukemia. In: NP, et al., editors. *Life Data: Models Reliability and Survival Analysis*. 1996. p. 175-185.
- Lai TL, Ying Z. Estimating a distribution function with truncated and censored data. *The Annals of Statistics*. 1991; 19:417–442.
- Lin DY, Sun W, Ying Z. Nonparametric estimation of the gap time distributions for serial events with censored data. *Biometrika*. 1999; 86:59–70.
- Malani HM. A modification of the redistribution to the right algorithm using disease markers. *Biometrika*. 1995; 82:515–526.
- Robertson JB, Uppuluri RR. A generalized Kaplan-Meier estimator. *The Annals of Statistics*. 1984; 12:366–371.
- Robins, JM. Information recovery and bias adjustment in proportional hazards regression analysis of randomized trials using surrogate markers. *Proceedings of the Biopharmaceutical Section, American Statistical Association; American Statistical Association; Alexandria, Virginia*. 1993. p. 24-33.
- Scheike TH, Zhang MJ, Gerds TA. Predicting cumulative incidence probability by direct binomial regression. *Biometrika*. 2008; 95:281–286.
- Tableman, M.; Kim, JS. *Survival Analysis Using S: Analysis of Time-to-Event Data*. CRC: Chapman & Hall; 2004.
- Turnbull BW. The empirical distribution function with arbitrarily grouped, censored and truncated data. *J. Roy. Statist. Soc. B*. 1976; 38:290–295.
- Wang MC, Jewell NP, Tsai WY. Asymptotic properties of the product limit estimate under random truncation. *The Annals of Statistics*. 1986; 14:1597–1605.
- Woodroffe M. Estimating a distribution function with truncated data. *The Annals of Statistics*. 1985; 13:163–177.
- Woolson RF. Rank tests and a one-sample log rank test for comparing observed survival data to a standard population. *Biometrics*. 1981; 37:687–696.

Appendix A

Proposition

For right-censored only competing risks data,

$$\widehat{F}_1^{\text{PL}}(t) = \widehat{F}_1^{\text{AJ}}(t), \quad \forall 0 \leq t \leq \tau,$$

where τ is the largest failure time.

Proof

Let $t_1 < t_2 < t_3, \dots$ be the ordered cause 1 failure times and set t_0 to 0. For simplicity, we assume that all failure times and censoring times are unique. By Equation (3.1), we have that $\widehat{F}_1^{\text{AJ}}(t_i) - \widehat{F}_1^{\text{AJ}}(t_{i-1}) = 1/\{n\widehat{G}_c(t_i)\}$.

Following the RTR algorithm, we have that

$$n^{-1} \sum_{i=1}^n \frac{I(X_i \leq t, \delta_i \epsilon_i = 1)}{\widehat{G}_c(X_i)} + n^{-1} \sum_{i=1}^n \frac{I(X_i \leq t, \delta_i \epsilon_i = 2)}{\widehat{G}_c(X_i)} + n^{-1} \sum_{i=1}^n \frac{I(X_i > t)}{\widehat{G}_c(t)} = 1.$$

It follows that

$$1 - n^{-1} \sum_{i=1}^n \frac{I(X_i < t, \delta_i \epsilon_i = 1)}{\widehat{G}_c(X_i)} = n^{-1} \sum_{i=1}^n \frac{r_i(t) Y_i^1(t)}{\widehat{G}_c(X_i \wedge t)}.$$

Thus, we have $1 - \widehat{F}_1^{\text{AJ}}(t^-) = n^{-1} \sum_{i=1}^n \widehat{w}_i(t) Y_i^1(t)$. Assume that $\widehat{F}_1^{\text{PL}}(t_{i-1}) = \widehat{F}_1^{\text{AJ}}(t_{i-1})$. The increment of $\widehat{F}_1^{\text{PL}}$ at t_i can be expressed as

$$\begin{aligned} & \widehat{F}_1^{\text{PL}}(t_i) - \widehat{F}_1^{\text{PL}}(t_{i-1}) \\ &= (1 - \widehat{F}_1^{\text{PL}}(t_{i-1})) - \left[(1 - \widehat{F}_1^{\text{PL}}(t_{i-1})) \times \left\{ 1 - \left(\frac{1}{\widehat{G}_c(t_i)} \right) / \left(\sum_{j=1}^n \widehat{w}_j(t_i) Y_j^1(t_i) \right) \right\} \right] \\ &= (1 - \widehat{F}_1^{\text{PL}}(t_{i-1})) \times \left\{ \left(\frac{1}{\widehat{G}_c(t_i)} \right) / \left(\sum_{j=1}^n \widehat{w}_j(t_i) Y_j^1(t_i) \right) \right\} \\ &= (1 - \widehat{F}_1^{\text{PL}}(t_{i-1})) \times \left\{ \frac{1/\widehat{G}_c(t_i)}{n(1 - \widehat{F}_1^{\text{AJ}}(t_{i-1}))} \right\} = \frac{1}{n\widehat{G}_c(t_i)}. \end{aligned}$$

We have shown that $\widehat{F}_1^{\text{PL}}(t_i) - \widehat{F}_1^{\text{PL}}(t_{i-1}) = \widehat{F}_1^{\text{AJ}}(t_i) - \widehat{F}_1^{\text{AJ}}(t_{i-1})$ for all i . Therefore, the equivalence of $\widehat{F}_1^{\text{PL}}(t)$ and $\widehat{F}_1^{\text{AJ}}(t)$ follows by induction.

Appendix B

Proposition

For left-truncated and right-censored competing risks data,

$$\widehat{F}_1^{\text{PL}}(t) = \widehat{F}_1^{\text{AJ}}(t), \quad \forall 0 \leq t \leq \tau,$$

where τ is the largest failure time.

Proof

Let $t_1 < t_2 < t_3, \dots$ be the failure times. Let n_j be the number of subjects at risk at time t_j and let d_j and r_j be the number of failure from cause 1 and 2 at t_j , respectively.

By proposed mass redistribution algorithm and the fact of $\{\text{mass } t_p \text{ cause 1}\} + \{\text{mass } t_p \text{ cause 2}\} + \{\text{mass } > t_j\} = 1$ can be expressed by

$$\sum_{j:t_j \leq t_i} \widehat{S}_{(t_{j-1})} \frac{d_j}{n_j} + \sum_{j:t_j \leq t_i} \widehat{S}_{(t_{j-1})} \frac{r_j}{n_j} + \widehat{S}(t) = 1.$$

It follows that

$$\begin{aligned} 1 - \widehat{F}_1^{\text{AJ}}(t_{i-1}) &= n^{-1} \sum_{j:j \leq \{i-1\}} \frac{\widehat{S}(t_{j-1})}{n_j/n} r_j + n^{-1} \frac{\widehat{S}(t_{i-1})}{n_i/n} n_i \\ &= n^{-1} \sum_{j=1}^n \widehat{k}_j(t_i) Y_{j1}^L(t_i). \end{aligned}$$

By Equation (3.6), $\widehat{F}_1^{\text{AJ}}(t_i) - \widehat{F}_1^{\text{AJ}}(t_{i-1}) = \widehat{S}(t_{i-1}) d_i / n_i$. Assume $\widehat{F}_1^{\text{AJ}}(t_{i-1}) = \widehat{F}_1^{\text{PL}}(t_{i-1})$, then we have

$$\begin{aligned} &\widehat{F}_1^{\text{PL}}(t_i) - \widehat{F}_1^{\text{PL}}(t_{i-1}) \\ &= \left(1 - \widehat{F}_1^{\text{PL}}(t_{i-1})\right) - \left[\left(1 - \widehat{F}_1^{\text{PL}}(t_{i-1})\right) \times \left\{ 1 - \left(n \widehat{S}(t_{i-1}) d_i / n_i \right) / \left(\sum_{j=1}^n \widehat{k}_j(t_i) Y_{j1}^L(t_i) \right) \right\} \right] \\ &= \left(1 - \widehat{F}_1^{\text{PL}}(t_{i-1})\right) \times \left\{ \left(n \widehat{S}(t_{i-1}) d_i / n_i \right) / \left(\sum_{j=1}^n \widehat{k}_j(t_i) Y_{j1}^L(t_i) \right) \right\} \\ &= \left(1 - \widehat{F}_1^{\text{PL}}(t_{i-1})\right) \times \left\{ \frac{\widehat{S}(t_{i-1}) d_i / n_i}{1 - \widehat{F}_1^{\text{AJ}}(t_{i-1})} \right\} \\ &= \widehat{S}(t_{i-1}) d_i / n_i = \widehat{F}_1^{\text{AJ}}(t_i) - \widehat{F}_1^{\text{AJ}}(t_{i-1}). \end{aligned}$$

Then, $\widehat{F}_1^{\text{PL}}(t) = \widehat{F}_1^{\text{AJ}}(t)$ follows by induction.

Figure 1.
The mass redistribution algorithm for the first three failure time points for the psychiatric inpatients example

Figure 2.
Standardized bias for four truncation and censoring settings

Figure 3.
Estimated cumulative incidence probabilities of relapse

Figure 4.
Estimated cumulative incidence probabilities of TRM

Table 1

The raw survival data for 15 female psychiatric patients

Age at admission	Age at death or end of follow-up	Status	Age at admission	Age at death or end of follow-up	Status
51	52	1	36	76	1
55	57	1	58	59	1
25	57	1	28	50	1
47	61	1	48	59	1
31	62	0	25	61	1
33	68	0	30	67	0
43	69	1	45	69	1
35	70	0			

Table 2

The redistributed mass for 15 female psychiatric patients

Failure time (<i>t</i>)	Number of failures	Number at risk	Mass t	Mass $> t$
50	1	12	0.083 $(= \frac{1}{12})$	0.917 $(= \frac{11}{12})$
52	1	12	0.159 $(= 0.083 + 0.917 \times \frac{1}{12})$	0.841 $(= 0.917 \times \frac{11}{12})$
57	2	12	0.299 $(= 0.159 + 0.841 \times \frac{2}{12})$	0.701 $(= 0.841 \times \frac{10}{12})$
59	2	11	0.426 $(= 0.299 + 0.701 \times \frac{2}{11})$	0.574 $(= 0.701 \times \frac{9}{11})$
61	2	9	0.554 $(= 0.426 + 0.574 \times \frac{2}{9})$	0.446 $(= 0.574 \times \frac{7}{9})$
69	2	4	0.777 $(= 0.554 + 0.446 \times \frac{2}{4})$	0.223 $(= 0.446 \times \frac{2}{4})$
76	1	1	1 $(= 0.777 + 0.223)$	0

Table 3
A mass redistribute algorithm for right censored and left truncated failure time data

Failure time (t)	t ₀	t ₁	t ₂	...	t _i
Number of failures		d ₁	d ₂	...	d _i
Number at risk		n ₁	n ₂	...	n _i
Mass t	0	$\frac{d_1}{n_1}$	$\frac{d_1}{n_1} + (1 - \frac{d_1}{n_1}) \frac{d_2}{n_2}$	...	$i \prod_{j=1}^{i-1} \{ \text{mass} > t_{j-1} \} \frac{d_i}{n_i}$
Mass > t	1	$1 - \frac{d_1}{n_1}$	$\left(1 - \frac{d_1}{n_1}\right) \left(1 - \frac{d_2}{n_2}\right)$	...	$\prod_{j=1}^{i-1} \left(1 - \frac{d_j}{n_j}\right)$

Table 4

Simulation results with $n = 200$

$(C\%, L\%)$	Estimator	$F_1(0.4) = 0.20$					$F_1(1.6) = 0.48$					$F_1(2.8) = 0.56$				
		BIAS	RBIAS	SE	RSE	BIAS	RBIAS	SE	RSE	BIAS	RBIAS	SE	RSE			
(0,0)	Equal weight	-0.00	-0.00	0.028	0.14	-0.00	-0.00	0.036	0.08	-0.00	-0.00	0.036	0.06			
	IPCW	Same as equal weight					Same as equal weight					Same as equal weight				
	New weight (A-J)	Same as equal weight					Same as equal weight					Same as equal weight				
(0,30)	Equal weight	0.02	0.09	0.059	0.28	0.07	0.15	0.046	0.08	0.09	0.17	0.039	0.06			
	IPCW	Same as equal weight					Same as equal weight					Same as equal weight				
	New weight (A-J)	0.00	0.01	0.061	0.31	0.00	0.01	0.064	0.13	0.01	0.01	0.066	0.12			
(0,50)	Equal weight	0.01	0.08	0.070	0.33	0.09	0.18	0.050	0.09	0.12	0.21	0.042	0.06			
	IPCW	Same as equal weight					Same as equal weight					Same as equal weight				
	New weight (A-J)	-0.00	-0.01	0.072	0.37	0.00	0.00	0.075	0.16	0.00	0.01	0.078	0.14			
(30,0)	Equal weight	-0.00	-0.01	0.029	0.15	-0.03	-0.07	0.040	0.09	-0.07	-0.12	0.042	0.08			
	IPCW	-0.00	-0.00	0.029	0.15	0.00	0.00	0.042	0.09	0.00	0.00	0.046	0.08			
	New weight (A-J)	Same as IPCW					Same as IPCW					Same as IPCW				
(50,0)	Equal weight	-0.00	-0.02	0.031	0.16	-0.09	-0.18	0.045	0.11	-0.15	-0.27	0.046	0.11			
	IPCW	0.00	0.01	0.032	0.16	0.00	0.00	0.056	0.12	-0.01	-0.01	0.076	0.14			
	New weight (A-J)	Same as IPCW					Same as IPCW					Same as IPCW				
(30,30)	Equal weight	0.02	0.10	0.059	0.27	0.05	0.10	0.049	0.09	0.04	0.07	0.047	0.08			
	IPCW	0.02	0.10	0.059	0.27	0.07	0.14	0.049	0.09	0.08	0.14	0.047	0.07			
	New weight (A-J)	0.00	0.02	0.061	0.30	0.01	0.01	0.064	0.13	0.01	0.01	0.068	0.12			
(30,50)	Equal weight	0.01	0.07	0.064	0.30	0.07	0.14	0.051	0.09	0.07	0.13	0.045	0.07			
	IPCW	0.01	0.07	0.064	0.30	0.08	0.17	0.051	0.09	0.11	0.20	0.045	0.07			
	New weight (A-J)	-0.00	-0.00	0.065	0.33	0.01	0.01	0.067	0.14	0.01	0.02	0.068	0.12			
(50,30)	Equal weight	0.02	0.08	0.049	0.23	0.00	0.01	0.048	0.10	-0.04	-0.08	0.050	0.10			
	IPCW	0.02	0.09	0.049	0.23	0.06	0.12	0.051	0.09	0.07	0.12	0.064	0.10			
	New weight (A-J)	0.00	0.02	0.050	0.25	0.01	0.02	0.059	0.12	0.01	0.01	0.073	0.13			

		$F_1(0.4) = 0.20$					$F_1(1.6) = 0.48$					$F_1(2.8) = 0.56$				
(C%, L%)	Estimator	BIAS	RBIAS	SE	RSE	BIAS	RBIAS	SE	RSE	BIAS	RBIAS	SE	RSE			
(50,50)	Equal weight	0.01	0.07	0.054	0.25	0.03	0.07	0.052	0.10	0.00	0.00	0.052	0.09			
	IPCW	0.02	0.08	0.054	0.25	0.08	0.16	0.053	0.10	0.10	0.18	0.060	0.09			
	New weight (A-J)	0.00	0.00	0.055	0.28	0.01	0.01	0.065	0.13	0.01	0.01	0.075	0.13			