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# Comparison of bootstrap survival function with the Kaplan-Meier survival function under the influence of different percentage of censoring

Qamruz Zaman

Department of Medical Statistics, Informatics and Health Economics, Innsbruck Medical University, Department of Statistics, University of Peshawar, Pakistan.

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**ABSTRACT**

If survival data follows a specific survival distribution (weibull, exponential), survival probabilities can be estimated by using the specific survival function. Alternate easy and assumptions free methods for computing the survival probabilities are Kaplan-Meier and Bootstrap survival functions. The aim of present study is to compare the two non-parametric methods under the influence of different percentage of censoring presented in four different data sets "Leukaemia data set, Stanford Heart Transplant data set, Thalassaemia data set and Lung cancer data set". Results of analysis show that the performance of Kaplan-Meier survival function is better than the Bootstrap survival function. This is due to the easy concept, less time, less time, easily availability as well as in terms of survival probabilities.

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## Introduction

Survival analysis is considered as the backbone of medical research and is based on the observed time of event.

The event of interest may for instance be death or recovery from treatment. Survival analysis is based on three techniques i) parametric ii) Semi-parametric and iii) Non-parametric.

Non-parametric technique is more commonly used technique (Fleming & Harrington, 1984), due to relax conditions about the assumptions of distributions.

Kaplan-Meier survival function (1958) is the most famous and commonly used non-parametric technique of survival analysis. To define the function we proceed as:

Let the survival times $X_1, X_2, \ldots, X_n$ be independently identically distributed according to the distribution function F (x).

Similarly, let $Y_1, Y_2, \ldots, Y_n$ be independently identically distributed censoring times according to G(y). In addition, the survival times $X_i$ and censoring times $Y_i$ are assumed to be independent (Miller and Rupert, 1983).

The observable random variables are $T_i = \min\{X_i, Y_i\}$ and $\delta_i = I(X_i \le Y_i)$ indicates whether the survival time is uncensored or censored. Let $T_1 < \ldots < T_n$ denote the ordered observed survival times, and let $\delta_1, \ldots, \delta_n$ be their corresponding (unordered) indicator values.

Let the number of individuals who are alive just before time $t_i$, including those who are about to die at this time, be denoted by $r_i$ and $e_i$ denotes the number who die at this time.

Using these notations, the Kaplan- Meier estimator is defined as

$$\hat{S}_{KM}(t) = \prod_{i=1}^{n}\left(\frac{r_i - e_i}{r_i}\right)$$

Another non-parametric similar approach for calculating the survival function is the Bootstrap survival function.

A brief introduction of the function is defined below:

## Bootstrap Method

The Bootstrap (Effron, 1979) is a method for calculating the approximated biases, standard deviations, confidence intervals etc. Except these applications, Bootstrap also doing a reasonable job under a variety of situations. e.g. in survival analysis, one can use the Bootstrap to estimate the survival probabilities (as by Kaplan-Meier, 1958).

Sampling scheme for Bootstrapping censored data was introduced by Efron for 'Bootstraping individual' k, sample a survival time and censoring indicator pair $(t_i, \delta_i)$ with replacement from the data set $\{(t_i, \delta_i), i=1, \ldots, n\}$. If n Bootstrap individuals are generated, a Bootstrap replicate can be found by applying the Kaplan-Meier estimator to the Bootstrap data set. We take M of these replicates and order them as

$$\hat{S}^{B}_{[1]}(t^*) \le \ldots \le \hat{S}^{B}_{[M]}(t^*)$$

The procedure is describe as

Draw Bootstrap sample of the pair (ti, $\delta_i$), and note $m_i = \#$ times $(t_i, \delta_i)$ appears in the Bootstrap sample, so $m = (m_1, m_2, \ldots, m_n)$ is an n-category multinomial, n draws, probability 1/n for each category: $m \sim mult(n, 1/n)$

Define

$$M_j = \sum_{i=j}^{n} m_i \,, \quad j = 1, 2, \ldots, n$$

Where

$M_1 = n$, $M_2 = n - m_1$ and so forth.

The survival function based on Bootstrap data is

$$\hat{S}_m(t) = \prod_{j=1}\left(1 - \frac{m_j}{M_j}\right)^{\delta_i}$$

Tele:
E-mail addresses: ayanqamar@gmail.com

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**Aim**

"Bootstrap is a way to pull oneself up (from an unfavourable situation) by one's Bootstrap, to provide trustworthy answers despite of unfavourable Circumstances" (Efron, 1979).

The aim of the study is to judge the performance (in terms of bias) of the quote by comparing the curves as well as the survival probabilities of two nonparametric survival functions for four data sets. For small sample Kaplan-Meier gives downward bias results (Whittemore & Keller, 1986). The performance of the two methods will be evaluated through the probabilities and also through graphical presentation on four different data sets containing different percentage of censoring. For the analysis R- package (2004) is used.

Brief Introduction of Data Sets

**Leukaemia data set:**

The famous leukaemia data set conducted by Freireich (Freireich et. al. 1963), which was reviewed by Gehan (1965) and also used by Borkowf (2005). The data consisted of 21 patients, including 9 events and 12(57%) censored observations. The data set consists of weeks in maintenance of remission. We ignore the placebo controls (containing no censored observation) here.

The weeks in remission are: 6, 6, 6, 6+, 7, 9+, 10, 10+, 11+, 13, 16, 17+, 19+, 20+, 22, 23, 25+, 32+, 32+, 34+ and 35+.

Where + denotes a censored observation.

**Stanford Heart Transplant Data Analysis**

The second data set is the Stanford heart transplant data (Kalbflesch and Printice, 1980) .The data set contains 103 patients 75of were events and 28(27.2%) censored. The data set is given below

1, 2, 2, 2, 3, 3, 3, 5, 5, 6, 6, 8, 9, 11+, 12, 16, 16, 16, 17, 18, 21, 21, 28, 30, 31+, 32, 35, 36, 37, 39, 39+, 40, 40, 43, 45, 50, 51, 53, 58, 61, 66, 68, 68, 69, 72, 72, 77, 78, 80, 81, 85, 90, 96, 100, 102, 109+, 110, 131+, 149, 153, 165, 180+, 186, 188, 207, 219, 263, 265+, 285, 285, 308, 334, 340, 340+, 342, 370+, 397+, 427+, 445+, 482+, 515+, 545+, 583, 596+, 630+, 670+, 675, 733, 841+, 852, 915+, 941+, 979, 995, 1032, 1141+, 1321+, 1386, 1400+, 1407+, 1571+, 1586+, 1799+

Where + denotes a censored observation.

**An Application to a Lung Cancer Data**

A data set from the Veterans Administration lung cancer trial in which chemotherapy was given to males with advanced inoperable lung cancer (presented by Prentice (1973)). This data set was also used by Gupta (1999). The data set consists of 97 patients out of which 91 were events and 6(6.2%) were censored. The survival times are given in days:

| | | | | | | |
|---|---|---|---|---|---|---|
| 72 | 228 | 10 | 110 | 314 | 100* | 42 |
| | 144 | 30 | 384 | 4 | 13 | |
| 123* | 97* | 59 | 117 | 151 | 22 | 18 |
| | 139 | 20 | 31 | 52 | 18 | 51 |
| | 122 | 27 | 54 | 7 | 63 | 392 |
| 92 | 35 | 117 | 132 | 162 | 3 | 95 |
| | 162 | 216 | 553 | 278 | 260 | 156 |
| | 182* | 143 | 105 | 103 | | |
| 112 | 87* | 242 | 111 | 587 | 389 | 33 |
| 25 | 357 | 467 | 1 | 30 | | |
| 283 | 25 | 21 | 13 | 87 | 7 | 24 |
| 99 | 8 | 99 | 61 | 25 | 95 | 80 |
| 29 | 24 | 83* | 31 | 51 | 52 | 73 |
| 8 | 36 | 48 | 7 | 140 | 186 | 19 |
| | 45 | 80 | 52 | 53 | 15 | 133 |
| | 111 | 378 | 49 | | | |

Where + denotes a censored observation.

**An Application to a Breast Cancer Data**

A large data set of 1207 breast cancer patient is obtained from SPSS, version 11.5 (SPSS, 2004) containing 1135 censored (94.3 %) and 72 events only.

**Method of Bootstrap Sample**

Software for the program is prepared in R-package. A Bootstrap of sample "10* size of data set" is drawn with replacement. Sample is selected with the point to give each time enough chances to be included in the sample.

**Results**

The results of leukaemia data set are shown in table 1 and in Figure 1. For heart transplant data, we prepared table 2 and Figure 2. Table 3 and Figure 3 represent the facts of lung cancer data set. For a very large breast cancer data set, we show the results through Figure 4 and not prepared table of probabilities, due to the same conclusion obtained from the previous data sets.

**Figure 1: Survival curves of Kaplan-Meier and Modified Kaplan-Meier for leukaemia data set**

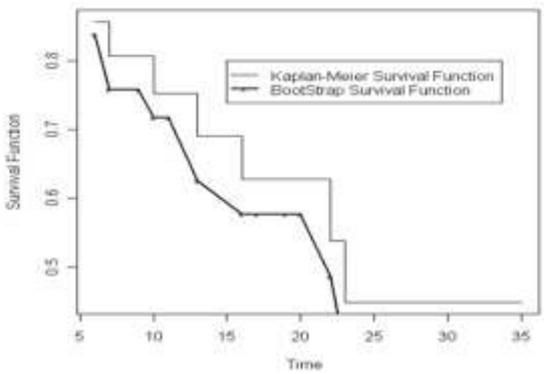
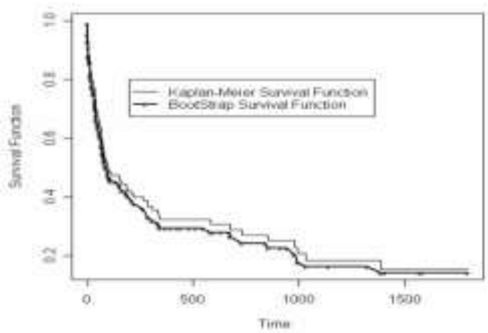



**Figure 2: Survival curves of Kaplan-Meier and Modified Kaplan-Meier for heart transplant data Set.**




Leukaemia data set containing 21 patients having 57% censored data. Stanford heart transplant data containing 27.2% censored data. Lung cancer data consists of 6.2% censored cases, while the breast cancer data 1207 patients having very high censoring (94.3%). The range of data sets is 21 to 1207 patients and the range of percentage censoring is 6.2 to 94.3. On the basis of these facts and also on the basis of 4 Figures and 3 Tables, we reach to the followings.

• Bootstrap function is a form of Kaplan-Meier survival function.

• Kaplan-Meier gives the underestimate (bias) results for small sample. By comparing the survival probabilities of given data sets and curves, we can say that Bootstrap function gives more bias results than Kaplan-Meier survival function.

• For large data set, Kaplan-Meier gives unbiased results (Maller and Zhou, 1996). If we compare the curves of breast cancer data, the Bootstrap still gives some bias.

• If the last observation is censored, one can not obtain the mean of survival function and the same result we obtained from the Bootstrap survival function.

• Both the survival functions have the same range i.e. 0 to 1.

**Figure 3: Survival curves of Kaplan-Meier and Modified Kaplan-Meier for lung cancer data set.**

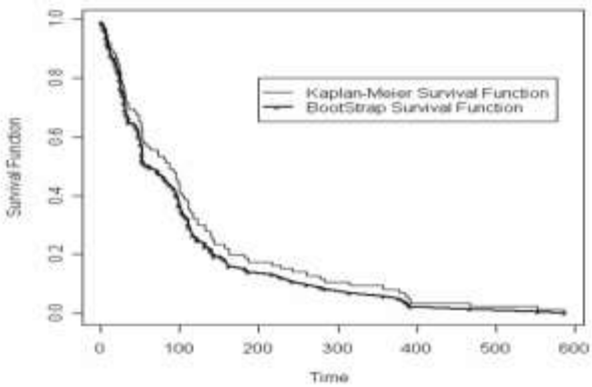
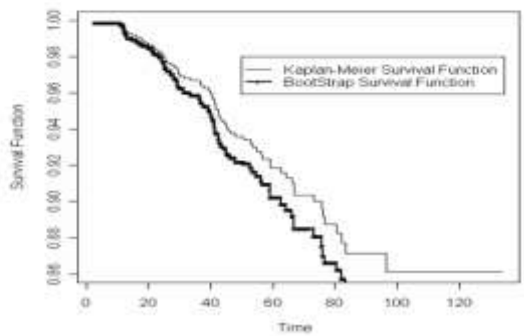



**Figure 4: Survival curves of Kaplan-Meier and Modified Kaplan-Meier for breast cancer data set (SPSS data directory).**




**Discussion and Conclusion**

Parametric approach produces better results, if we are able to find a specific parametric survival distribution (Exponential, Weibull etc.) that fits the data. As most of the survival data are skewed and some times, it is very difficult to find the appropriate distribution. The easiest way to avoid the possible error (which may occur due to the application of in appropriate distribution) is the non-parametric approach. The two non-parametric approaches for estimating the survival function are the Kaplan-Meier and Bootstrap approach.

In this article we compared the two approaches by applying them on different data sets and on the basis of analysis we reached to the conclusion that, Kaplan-Meier approach as compared to the Bootstrap approach is easy to understand and to apply. The Kaplan-Meier approach can be easily apply to different data sets by the help of packages e.g. SPSS, R, S, SPLUS, while for applying the Bootstrap technique, there is no option available in commonly used packages. In some situations Kaplan-Meier gives bias results, which are smaller than the results obtained by applying the Bootstrap survival function.

Bootstrap survival function in all the four data sets gives the smaller probabilities of survival (for every censoring percentage).

If comparatively large data set, having moderate censoring is available, then for estimating the probabilities and for drawing the survival curve, Kaplan-Meier is considered as the conventional, easy and less time consuming method.

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**Table 1. Estimated survival functions of Kaplan-Meier and Bootstrap for leukaemia data set**

| Time | Event | No. at risk | Kaplan-Meier Survival Function | Bootstrap Survival Function |
|---|---|---|---|---|
| 6 | 3 | 21 | 0.8571 | 0.8382 |
| 7 | 1 | 17 | 0.8067 | 0.7578 |
| 9 | 0 | 16 | 0.8067 | 0.7578 |
| 10 | 1 | 15 | 0.7529 | 0.7179 |
| 11 | 0 | 13 | 0.7529 | 0.7179 |
| 13 | 1 | 12 | 0.6902 | 0.6257 |
| 16 | 1 | 11 | 0.6275 | 0.5772 |
| 17 | 0 | 10 | 0.6275 | 0.5772 |
| 19 | 0 | 9 | 0.6275 | 0.5772 |
| 20 | 0 | 8 | 0.6275 | 0.5772 |
| 22 | 1 | 7 | 0.5378 | 0.4861 |
| 23 | 1 | 6 | 0.4482 | 0.3797 |
| 25 | 0 | 5 | 0.4482 | 0.3797 |
| 32 | 0 | 4 | 0.4482 | 0.3797 |
| 34 | 0 | 2 | 0.4482 | 0.3797 |
| 35 | 0 | 1 | 0.4482 | 0.3797 |

**Table 2. Estimated survival functions of Kaplan-Meier and Bootstrap for heart transplant data set**

| Time | Event | No. at risk | Kaplan-Meier Survival Function | Bootstrap Survival Function |
|---|---|---|---|---|
| 1 | 1 | 103 | 0.9903 | 0.9874 |
| 2 | 3 | 102 | 0.9612 | 0.9500 |
| 3 | 3 | 99 | 0.9320 | 0.9247 |
| 5 | 2 | 96 | 0.9126 | 0.9062 |
| 6 | 2 | 94 | 0.8932 | 0.8788 |
| 8 | 1 | 92 | 0.8835 | 0.8697 |
| 9 | 1 | 91 | 0.8738 | 0.8616 |
| 11 | 0 | 90 | 0.8738 | 0.8616 |
| 12 | 1 | 89 | 0.8640 | 0.8515 |
| 16 | 3 | 88 | 0.8345 | 0.8164 |
| 17 | 1 | 85 | 0.8247 | 0.8066 |
| 18 | 1 | 84 | 0.8149 | 0.7968 |
| 21 | 2 | 83 | 0.7952 | 0.7738 |
| 28 | 1 | 81 | 0.7854 | 0.7633 |
| 30 | 1 | 80 | 0.7756 | 0.7510 |
| 31 | 0 | 79 | 0.7756 | 0.7510 |
| 32 | 1 | 78 | 0.7657 | 0.7448 |
| 35 | 1 | 77 | 0.7557 | 0.7297 |
| 36 | 1 | 76 | 0.7458 | 0.7155 |
| 37 | 1 | 75 | 0.7358 | 0.7084 |
| 39 | 1 | 74 | 0.7259 | 0.6933 |
| 40 | 2 | 72 | 0.7057 | 0.6756 |
| 43 | 1 | 70 | 0.6956 | 0.6616 |
| 45 | 1 | 69 | 0.6856 | 0.6519 |
| 50 | 1 | 68 | 0.6755 | 0.6449 |
| 51 | 1 | 67 | 0.6654 | 0.6361 |
| 53 | 1 | 66 | 0.6553 | 0.6256 |
| 58 | 1 | 65 | 0.6452 | 0.6159 |
| 61 | 1 | 64 | 0.6352 | 0.6045 |
| 66 | 1 | 63 | 0.6251 | 0.5940 |
| 68 | 2 | 62 | 0.6049 | 0.5766 |
| 69 | 1 | 60 | 0.5948 | 0.5662 |
| 72 | 2 | 59 | 0.5747 | 0.5474 |
| 77 | 1 | 57 | 0.5646 | 0.5423 |
| 78 | 1 | 56 | 0.5545 | 0.5346 |
| 80 | 1 | 55 | 0.5444 | 0.5219 |
| 81 | 1 | 54 | 0.5343 | 0.5159 |
| 85 | 1 | 53 | 0.5243 | 0.5040 |
| 90 | 1 | 52 | 0.5142 | 0.4955 |
| 96 | 1 | 51 | 0.5041 | 0.4819 |
| 100 | 1 | 50 | 0.4940 | 0.4700 |
| 102 | 1 | 49 | 0.4839 | 0.4615 |
| 109 | 0 | 48 | 0.4839 | 0.4615 |
| 110 | 1 | 47 | 0.4736 | 0.4513 |
| 131 | 0 | 46 | 0.4736 | 0.4513 |
| 149 | 1 | 45 | 0.4631 | 0.4417 |
| 153 | 1 | 44 | 0.4526 | 0.4312 |
| 165 | 1 | 43 | 0.4426 | 0.4181 |
| 180 | 0 | 42 | 0.4421 | 0.4181 |
| 186 | 1 | 41 | 0.4313 | 0.4073 |
| 188 | 1 | 40 | 0.4205 | 0.4010 |
| 207 | 1 | 39 | 0.4097 | 0.3866 |
| 219 | 1 | 38 | 0.3989 | 0.3748 |
| 263 | 1 | 37 | 0.3882 | 0.3577 |
| 265 | 0 | 36 | 0.3882 | 0.3577 |
| 285 | 2 | 35 | 0.3660 | 0.3303 |
| 308 | 1 | 33 | 0.3549 | 0.3187 |
| 334 | 1 | 32 | 0.3438 | 0.3088 |
| 340 | 1 | 31 | 0.3327 | 0.3008 |
| 342 | 1 | 29 | 0.3212 | 0.2909 |
| 370 | 0 | 28 | 0.3212 | 0.2909 |
| 397 | 0 | 27 | 0.3212 | 0.2909 |
| 427 | 0 | 26 | 0.3212 | 0.2909 |
| 445 | 0 | 25 | 0.3212 | 0.2909 |
| 482 | 0 | 24 | 0.3212 | 0.2909 |
| 515 | 0 | 23 | 0.3212 | 0.2909 |
| 545 | 0 | 22 | 0.3212 | 0.2909 |
| 583 | 1 | 21 | 0.3059 | 0.2780 |
| 596 | 0 | 20 | 0.3059 | 0.2780 |
| 630 | 0 | 19 | 0.3059 | 0.2780 |
| 670 | 0 | 18 | 0.3059 | 0.2780 |
| 675 | 1 | 17 | 0.2879 | 0.2652 |
| 733 | 1 | 16 | 0.2699 | 0.2410 |
| 841 | 0 | 15 | 0.2699 | 0.2410 |
| 852 | 1 | 14 | 0.2507 | 0.2247 |
| 915 | 0 | 13 | 0.2507 | 0.2247 |
| 941 | 0 | 12 | 0.2507 | 0.2247 |
| 979 | 1 | 11 | 0.2279 | 0.2010 |
| 995 | 1 | 10 | 0.2051 | 0.1757 |
| 1032 | 1 | 9 | 0.1823 | 0.1622 |
| 1141 | 0 | 8 | 0.1823 | 0.1622 |
| 1321 | 0 | 7 | 0.1823 | 0.1622 |
| 1386 | 1 | 6 | 0.1519 | 0.1403 |
| 1400 | 0 | 5 | 0.1519 | 0.1403 |
| 1407 | 0 | 4 | 0.1519 | 0.1403 |
| 1571 | 0 | 3 | 0.1519 | 0.1403 |
| 1586 | 0 | 2 | 0.1519 | 0.1403 |
| 1799 | 0 | 1 | 0.1519 | 0.1403 |

**Table 2. Estimated survival functions of Kaplan-Meier and Bootstrap for lung cancer data set**

| Time | Event | No. at risk | Kaplan-Meier Survival Function | Bootstrap Survival Function |
|---|---|---|---|---|
| 1 | 1 | 97 | 0.9897 | 0.9897 |
| 3 | 1 | 96 | 0.9794 | 0.9784 |
| 4 | 1 | 95 | 0.9691 | 0.9650 |
| 7 | 2 | 94 | 0.9485 | 0.9343 |
| 8 | 2 | 91 | 0.9276 | 0.9161 |
| 10 | 1 | 89 | 0.9172 | 0.9030 |
| 13 | 2 | 88 | 0.8963 | 0.8771 |
| 15 | 1 | 86 | 0.8859 | 0.8652 |
| 18 | 0 | 85 | 0.8859 | 0.8652 |
| 19 | 1 | 83 | 0.8753 | 0.8512 |
| 20 | 1 | 82 | 0.8646 | 0.8402 |
| 21 | 1 | 81 | 0.8539 | 0.8272 |
| 22 | 1 | 80 | 0.8432 | 0.8162 |
| 24 | 2 | 79 | 0.8219 | 0.7923 |
| 25 | 3 | 77 | 0.7899 | 0.7602 |
| 27 | 1 | 74 | 0.7792 | 0.7515 |
| 29 | 1 | 73 | 0.7685 | 0.7391 |
| 30 | 2 | 72 | 0.7472 | 0.7124 |
| 31 | 2 | 70 | 0.7258 | 0.6863 |
| 33 | 1 | 68 | 0.7151 | 0.6734 |
| 35 | 1 | 67 | 0.7045 | 0.6595 |
| 36 | 1 | 66 | 0.6938 | 0.6484 |
| 42 | 1 | 65 | 0.6831 | 0.6419 |
| 45 | 1 | 64 | 0.6724 | 0.6280 |
| 48 | 1 | 63 | 0.6618 | 0.6169 |
| 49 | 1 | 62 | 0.6511 | 0.5984 |
| 51 | 2 | 61 | 0.6298 | 0.5710 |
| 52 | 3 | 59 | 0.5977 | 0.5391 |
| 53 | 1 | 56 | 0.5871 | 0.5200 |
| 54 | 1 | 55 | 0.5764 | 0.5095 |
| 59 | 1 | 54 | 0.5657 | 0.5008 |
| 61 | 0 | 53 | 0.5657 | 0.5008 |
| 63 | 1 | 52 | 0.5548 | 0.4946 |
| 72 | 1 | 51 | 0.5440 | 0.4847 |
| 73 | 1 | 50 | 0.5331 | 0.4748 |
| 80 | 1 | 49 | 0.5222 | 0.4613 |
| 83 | 1 | 47 | 0.5111 | 0.4506 |
| 87 | 2 | 46 | 0.4889 | 0.4363 |
| 92 | 1 | 44 | 0.4778 | 0.4240 |
| 95 | 2 | 43 | 0.4555 | 0.4048 |
| 97 | 1 | 41 | 0.4444 | 0.3953 |
| 99 | 2 | 40 | 0.4222 | 0.3681 |
| 100 | 1 | 38 | 0.4111 | 0.3623 |
| 103 | 1 | 37 | 0.4000 | 0.3448 |
| 105 | 1 | 36 | 0.3889 | 0.3331 |
| 110 | 1 | 35 | 0.3778 | 0.3232 |
| 111 | 2 | 34 | 0.3555 | 0.2987 |
| 112 | 1 | 32 | 0.3444 | 0.2890 |
| 117 | 2 | 31 | 0.3222 | 0.2640 |
| 122 | 1 | 29 | 0.3111 | 0.2540 |
| 123 | 1 | 28 | 0.3000 | 0.2487 |
| 132 | 1 | 27 | 0.2889 | 0.2372 |
| 133 | 1 | 26 | 0.2778 | 0.2265 |
| 139 | 1 | 25 | 0.2667 | 0.2181 |
| 140 | 1 | 24 | 0.2555 | 0.2120 |
| 143 | 1 | 23 | 0.2444 | 0.2012 |
| 144 | 1 | 22 | 0.2333 | 0.1921 |
| 151 | 0 | 21 | 0.2333 | 0.1921 |
| 156 | 1 | 20 | 0.2217 | 0.1807 |
| 162 | 2 | 19 | 0.1983 | 0.1601 |
| 182 | 1 | 17 | 0.1867 | 0.1525 |
| 186 | 1 | 16 | 0.1750 | 0.1394 |
| 216 | 1 | 15 | 0.1633 | 0.1325 |
| 228 | 1 | 14 | 0.1517 | 0.1202 |
| 242 | 1 | 13 | 0.1400 | 0.1088 |
| 260 | 1 | 12 | 0.1283 | 0.0965 |
| 278 | 1 | 11 | 0.1167 | 0.0896 |
| 283 | 1 | 10 | 0.1050 | 0.0820 |
| 314 | 1 | 9 | 0.0933 | 0.0705 |
| 357 | 1 | 8 | 0.0817 | 0.0598 |
| 378 | 1 | 7 | 0.0700 | 0.0513 |
| 384 | 1 | 6 | 0.0583 | 0.0398 |
| 389 | 1 | 5 | 0.0467 | 0.0307 |
| 392 | 1 | 4 | 0.0350 | 0.0238 |
| 467 | 1 | 3 | 0.0233 | 0.0138 |
| 553 | 1 | 2 | 0.0117 | 0.0061 |
| 587 | 1 | 1 | 0.0000 | 0.0000 |