In Kaplan-Meier plots, the event must be a one-time event. In other words, if relief from arthritis pain is found at two months into the trial, and found again in the same subject at three months into the trial, the event is only counted once (only the relief from pain occurring at two months is counted). Alternatively, where the event of interest is "relief from pain without relapse," and where relief is first detected at a scheduled assessment at two months, and where relief is again detected at a scheduled assessment at three months, then relief at both of these scheduled endpoints is mandated to trigger the endpoint (7). Where the goal of the investigator is to make a graph of events of a recurring nature, Kaplan-Meier plots are not used (8).

Where the Kaplan-Meier plot contains two curves, data used for plotting these curves are also used for calculating the P value and the hazard ratio (HR).

b. Examples of Kaplan-Meier plots – the Holm study

Holm et al. (9) conducted a clinical trial on breast cancer patients. The trial enrolled 564 subjects. All of the subjects received surgery followed by radiation in an attempt to eliminate the cancer. Of these, 276 subjects were then enrolled in arm A of the clinical trial and received tamoxifen, while 288 subjects were enrolled in arm B and received only placebo. The two arms are summarized below:

- **Arm A.** Tamoxifen.
- **Arm B.** Placebo.

Tamoxifen and placebo were administered for a period of two years. Subjects were observed for 15 years in all, starting from the day of assignment to arm A or arm B. During these years, subjects were periodically tested for recurrence of the cancer. Data that were collected took the form of an endpoint called recurrence-free survival.

For each of the subjects, the event of recurrence of the breast cancer, or the event of death from recurrence of the breast cancer, triggered this endpoint.

For each subject, when the event was triggered, the investigators placed a point on the survival curve, also known as the Kaplan-Meier plot (Fig. 9.1). This plot includes two survival curves, one for arm A and the other for arm B. The dots on the curves represent subjects who were censored. Each dot represents one subject. The Kaplan-Meier plot shown in Fig. 9.1 was simplified somewhat from the original diagram, for clarity in presentation. Subjects who are censored are usually represented by dots or tick marks, though some investigators choose not to indicate censored subjects. Censoring is defined below.

Visual inspection of the separation between the two curves can indicate the efficacy of the experimental treatment relative to the control treatment. While it is hoped

[7] The author thanks Dr. Jenna Elder for this suggestion.
[8] Motulsky H. *Intuitive Biostatistics*. New York, NY: Oxford Univ. Press; 1995;54.
[9] Holm C, Rayala S, Jirström K, Stål O, Kumar R, Landberg G. Association between Pak1 expression and subcellular localization and tamoxifen resistance in breast cancer patients. *J Natl Cancer Inst*. 2006;98:671–680.