A Case Study for Community of Practice: GSK's Graphics Team

Susan Duke, MS, MS
Associate Director,
Biostatistics Development Partners

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Invited Session

Overview

- The Problem (2004)
  - Statisticians rank near the top as one of the busier functional groups in drug development because their skills for turning raw data into interpreted results are needed for many drug development tasks.
  - Results from a 2004 graphics survey
    - Too few graphs were being produced
    - Graphs took too long to create
    - Existing graphs were sometimes of poor quality
      - Lack of graphical design knowledge
      - Software, macros, etc less than ideal for graphics use

Overview

- The Solution (2004-present)
  - Providing statisticians with easy-to-use, quality graphics and software has had a noticeable impact on drug development
  - Graphics facilitate better science and more effective communication through exploratory analysis, submissions, presentations and publications

Graphics Objective: *Promote more effective understanding, decision making and communication of data via the use of quality graphics.*

- Graphics Team is still an entity
  - What are we doing now? Why are we still together?
  - Graphics Team as a “Community of Practice”

Where We Are Now: 10 Graphs for Safety Review

PHARMACEUTICAL STATISTICS
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(www.interscience.wiley.com) DOI: 10.1002/pst.254

Graphical Approaches to the Analysis of Safety Data from Clinical Trials

MAIN PAPER

Ohad Amit[1], Richard M. Heiberger[2,‡] and Peter W. Lane[3,*,†]
[1] *Oncology Medicine Development Center, GlaxoSmithKline, USA*
[2] *Department of Statistics, Temple University, USA*
[3] *Research Statistical Unit, GlaxoSmithKline, UK*

Patient safety has always been a primary focus in the development of new pharmaceutical products. The predominant method for statistical evaluation and interpretation of safety data collected in a clinical trial is the tabular display of descriptive statistics. There is a great opportunity to enhance evaluation of drug safety through the use of graphical displays, which can convey multiple pieces of information concisely and more effectively than can tables. Graphs can be used in an exploratory setting to help identify emerging safety signals, or in a confirmatory setting as a tool to elucidate known safety issues. We developed several graphical displays for routine safety data collected during a clinical trial, covering a broad range of graphical techniques, and illustrate here 10 specific graphical designs, many of which display the data along with statistics derived from them. Two are simple plots, comparing distributions in the form of boxplots or cumulative plots, and four more display data and summaries over time, comparing information from two groups in terms of distribution (with boxplots), cumulative incidence, hazard, or simply means with error bars. The other four are multi-panel displays: one-dimensional and two-dimensional arrays of scatterplots, a trellis of individual profiles, and a paired dotplot displaying risk together with relative risk. The displays focus on key safety endpoints in clinical trials including the QT interval from electrocardiograms, laboratory measurements for detecting hepatotoxicity, and adverse events of special interest. We discuss in detail the statistical and graphical principles underlying the production and interpretation of the displays.

Keywords: *graphics; dotplot; boxplot; trellis display; hepatotoxicity; QT interval; adverse experience*

Where We Are Now: 10 Graphs for Safety Review

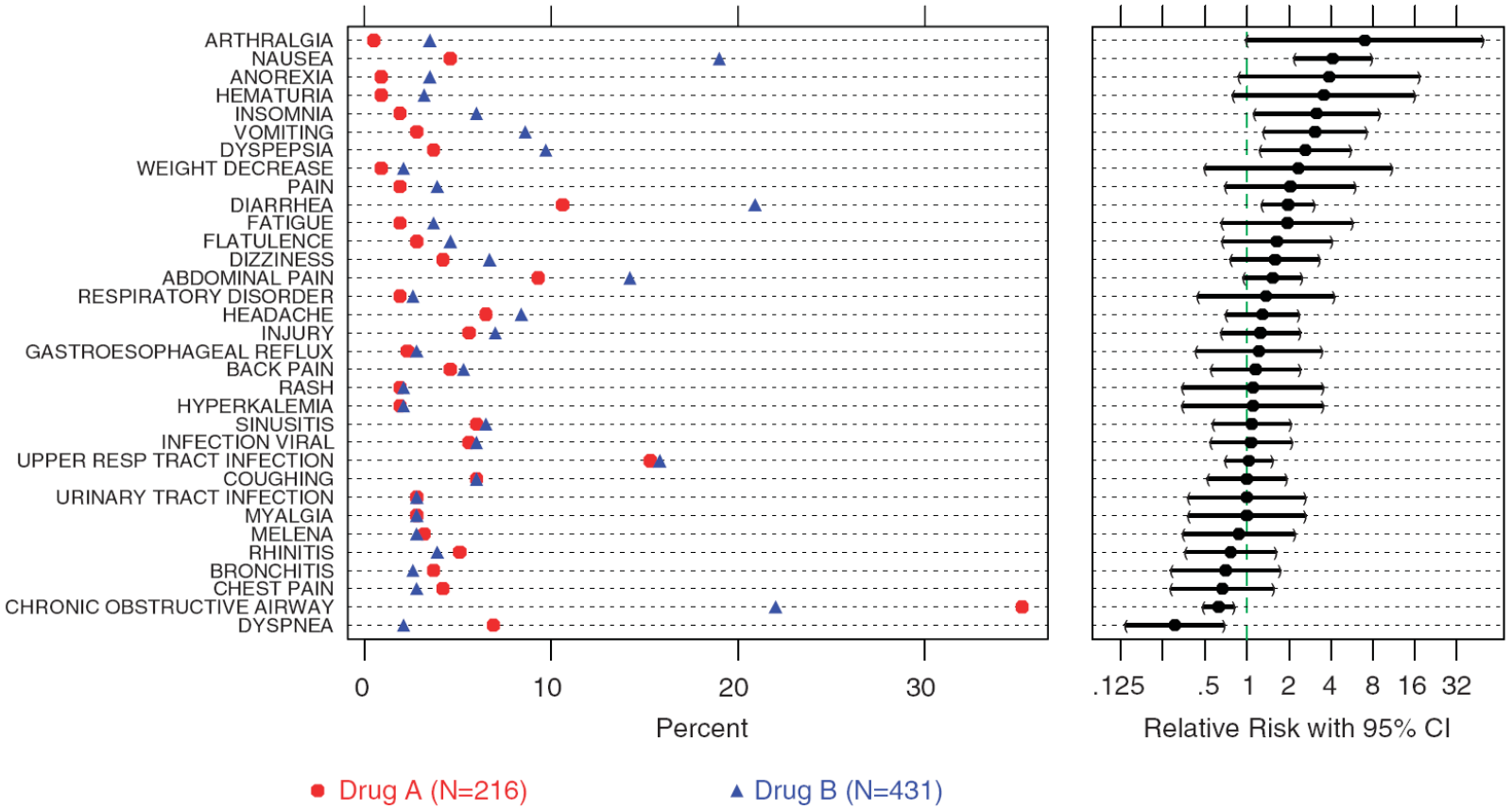

Figure 9. Most frequent on-therapy adverse events sorted by relative risk.

Where We Are Now: Graphics Catalogue

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BDS Graphical Catalogue

Contents of the Catalogue

BDS Graphical Catalogue

Title Contents of the BDS Graphics Catalogue
Category Introduction
Author Peter Lane
Date 7 September 2005, latest revision 22 April 2009

The BDS Graphics Catalogue is a collection of graphical information brought together to help people produce good graphics. It is provided by individuals and groups across BDS, and depends on their expertise and enthusiasm. Information is included only for graphics produced using the software recommended generally for statistical graphics, S-Plus and SAS. Entries are reviewed and edited by members of the Graphics Team to try to ensure consistency and accuracy.

This listing is one way to find information in the Catalogue, in addition to the Index of Graphical Terms, the Search mechanism of the BDS Library, and its hierarchical file structure. The Contents lists the entries in the Catalogue that illustrate specific types of graph, in simple categories based on the type of graph rather its application area. Each listing includes a brief description and a thumbnail graph, links to the entries in the Catalogue, and information about the applicability of the graph.

The Catalogue was released in September 2005, starting with a nucleus of entries arising mostly from the Graphics Team and Graphics Competition winners in 2004. We add and refine entries continually to improve the resource, particularly as BDS acquires more experience with S-Plus as well as SAS for producing graphics. Please contact the circulation list R&D_BDS-Graphics-Catalogue to discuss or submit potential entries, or to suggest any improvements to this resource.

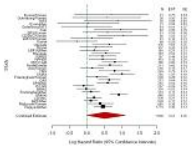
Latest changes

- 9.3 Matrix plot of residuals from repeated measurements, using SAS (22 April 2009)
- 6.3 Two, Three and Four Way Venn Diagrams, using SAS (11 February 2008)

Each thumbnail is constructed to be as clear as possible in a small area, but using a maximum of 10KB to avoid the size of this index becoming too large. Click on "Entry in Catalogue" beneath the thumbnail to open the entry that shows how to draw it, which includes a larger version of the graph; the entry will open in a new frame

1. Comparison of summary statistics

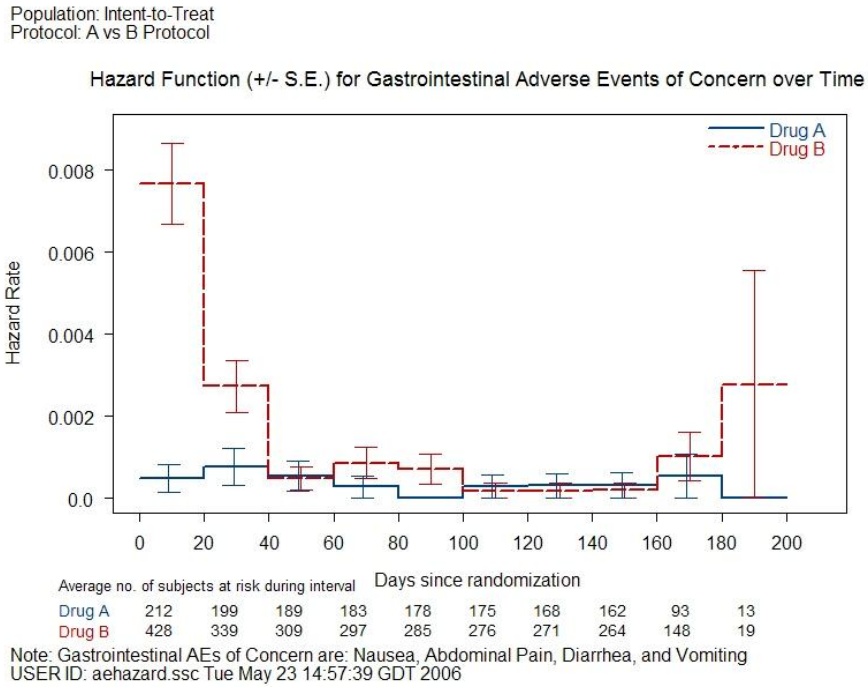
1.1 Forest plot, using S-Plus or SAS



This is a comparative display of a set of summary statistics with estimates of their variability, usually in the form of confidence intervals. The intervals are plotted as parallel lines, with the estimates marked with symbols in the centre of each; the symbols may vary in area in proportion to the number of observations contributing to each statistic.
Entry in Catalogue 15 June 05, S-Plus example added 29 Mar 06
Authors: Edit Kurali, Adrian Mander

Where We Are Now: Graphics Catalogue

Example of a Catalogue Entry



Each entry has:
Title, Category, Authors,
Date/Revision Dates,
Suitability (eg, Submission, Presentation),
Software used in the coding example,
Keywords,
Description,
Illustrative data,
Illustrative program

(This graph was drawn in S-Plus on-screen, exported in JPG format, and inserted directly into this Word document.)

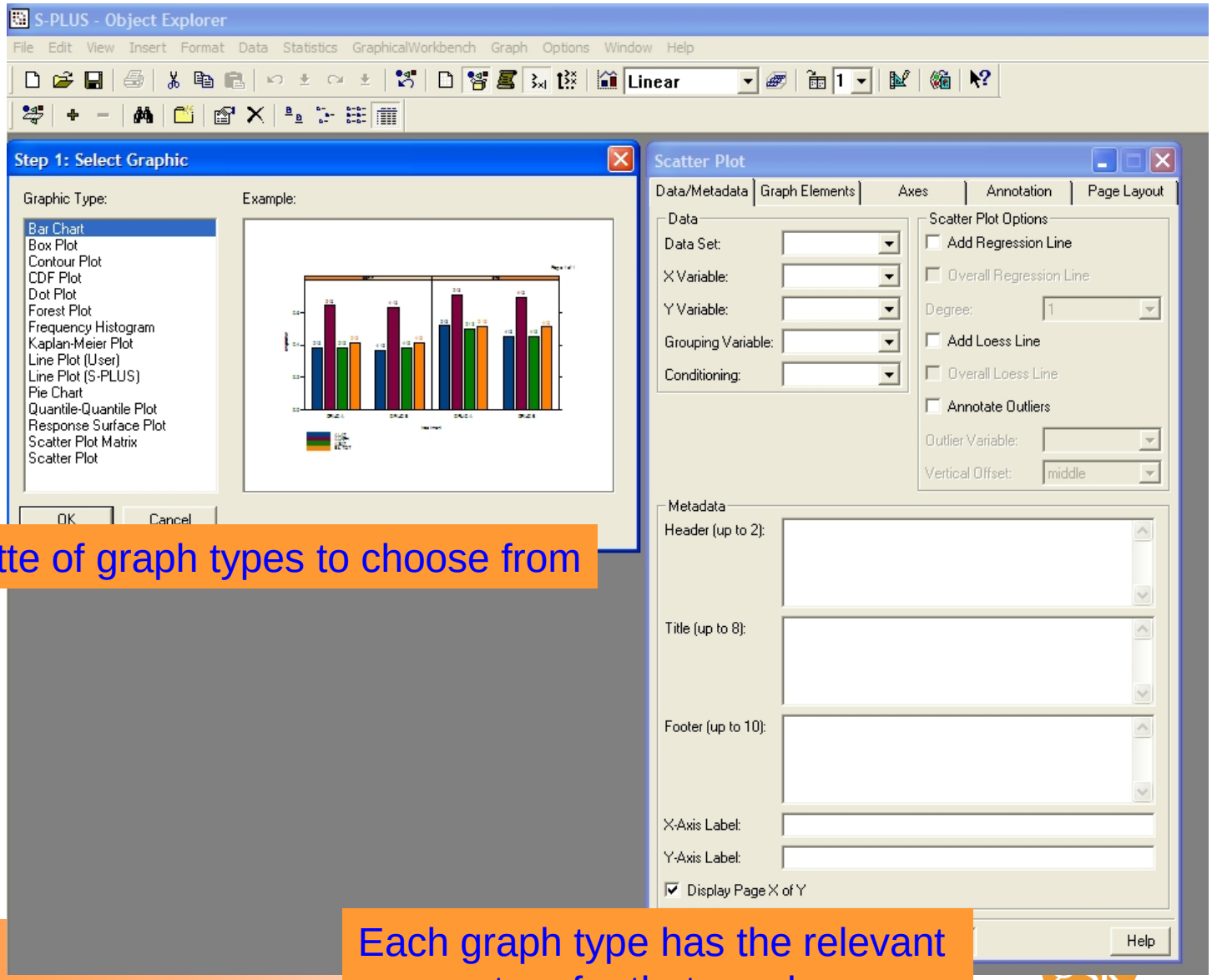
Title **AE hazard function, using S-Plus or SAS**
Category **Comparison of relationships, Lineplots**
Author **Michael Durante, Peter Lane**
Date **10 April 2006, latest revision 23 May 2006**
Suitability **Submission, Presentation**
Software **S-Plus or SAS script, example with S-Plus 7.0 and SAS 8.2**
Keywords **graphics, hazard, lineplot, safety, AE**
Description

This is a comparative lineplot of the hazard function over successive time intervals for adverse events (AEs) in a clinical trial. The example takes as input the estimated hazards and average numbers at risk, as output for example by the LIFETEST procedure in SAS.

Illustrative data

The datafile haz_info.sas7bdat has six columns of values and 20 rows, one for each combination

Where We Are Now: Easy-to-Use Quality Tool



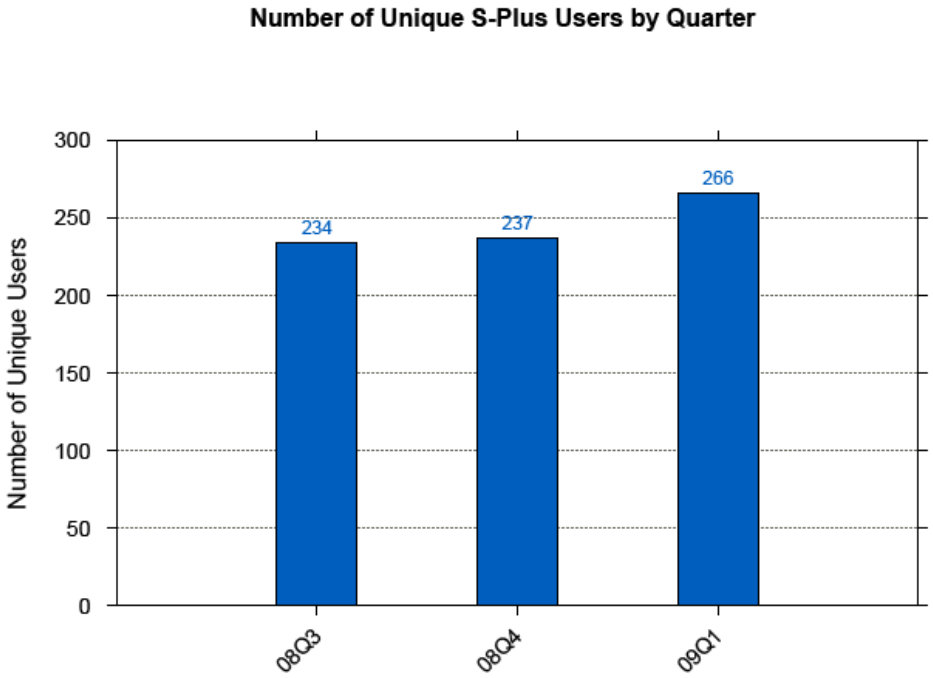
Palette of graph types to choose from

Each graph type has the relevant parameters for that graph

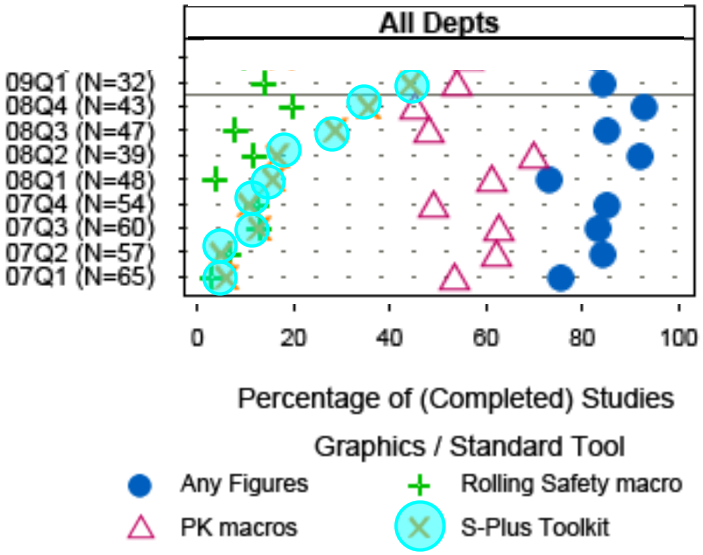
GlaxoSmithKline

Where We Are Now: Usage

- Steady growth in number of unique users



- Consistent and growing use in regulatory submissions



Standard Graphs Benefit a Recent Submission
Liver Toxicity: Baseline vs On-study

How this graph benefited the drug project team:

- *This graph made it very easy to detect toxicity issues*
  - *The outliers are clearly visible and the reference lines help spot values of potential critical concern*
  - *Data points appearing above the purple reference lines identify subjects with liver toxicity by glancing at the plot*
  - *Used as a data exploration graph to identify LFT related concerns*

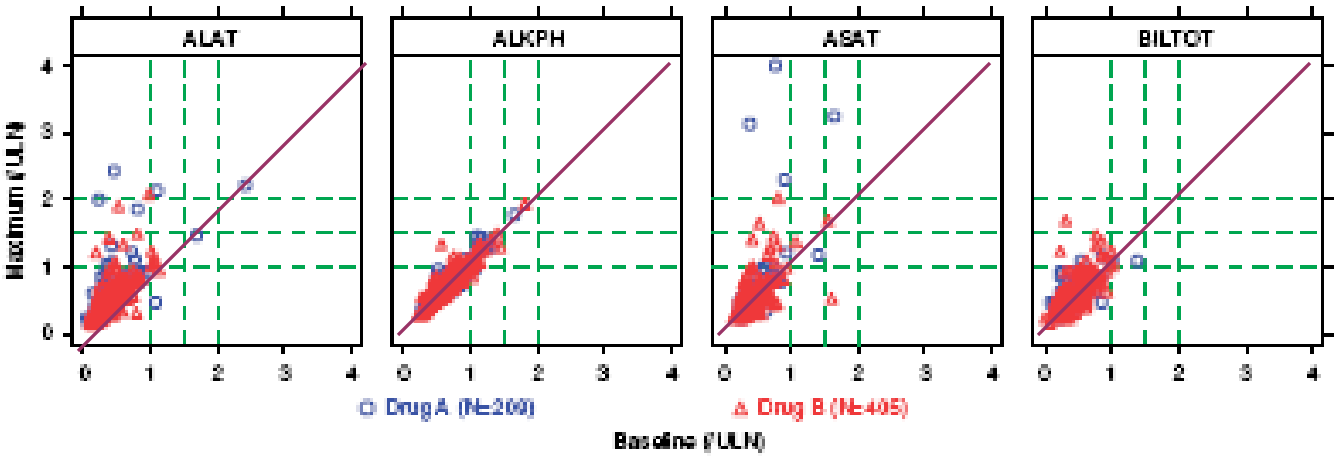


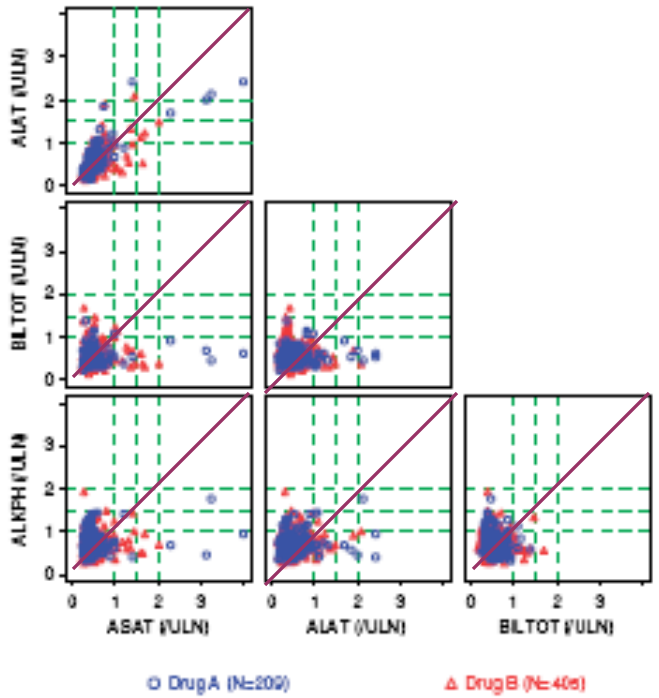
Figure 6. Trellis of LFT shifts from baseline to maximum by treatment.

Graphics benefits courtesy of Subha Jamburajan

Standard Graphs Benefit a Recent Submission
Liver Toxicity: Associations Across Parameters

How this graph benefited the drug project team:

- *This graph made it very easy to detect associations between liver function variables.*
  - *Values above toxicity grade 2 are clearly marked*
  - *Associations between all pairs of toxicity parameters are viewed on one*



For ALAT, ASAT and ALKPH, the Clinical Concern Level is 2 ULN;
For BILTOT, the CCL is 1.5 ULN; where ULN is the Upper Level of Normal Range

Figure 7. Matrix display of maximum LFT values.

Graphics benefits courtesy of Subha Jamburajan

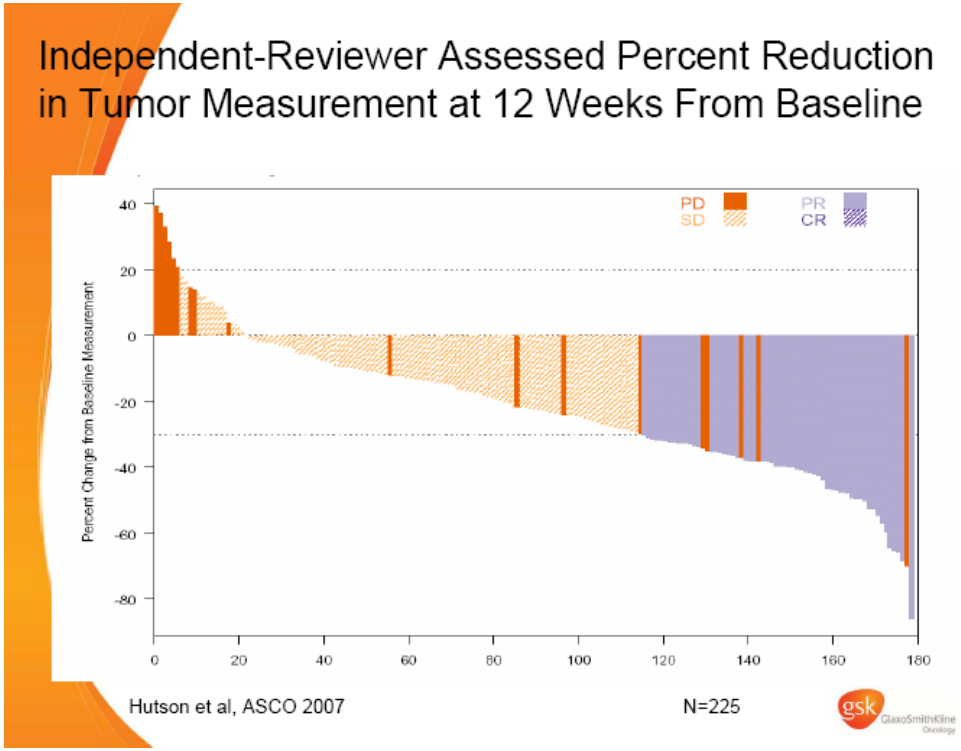
Pharmaceut. Statist. 2008; 7: 20–35
DOI: 10.1002/pst

GlaxoSmithKline

Standard Graphs Benefit a Recent Submission Waterfall Plot

How this graph benefited the drug project team:

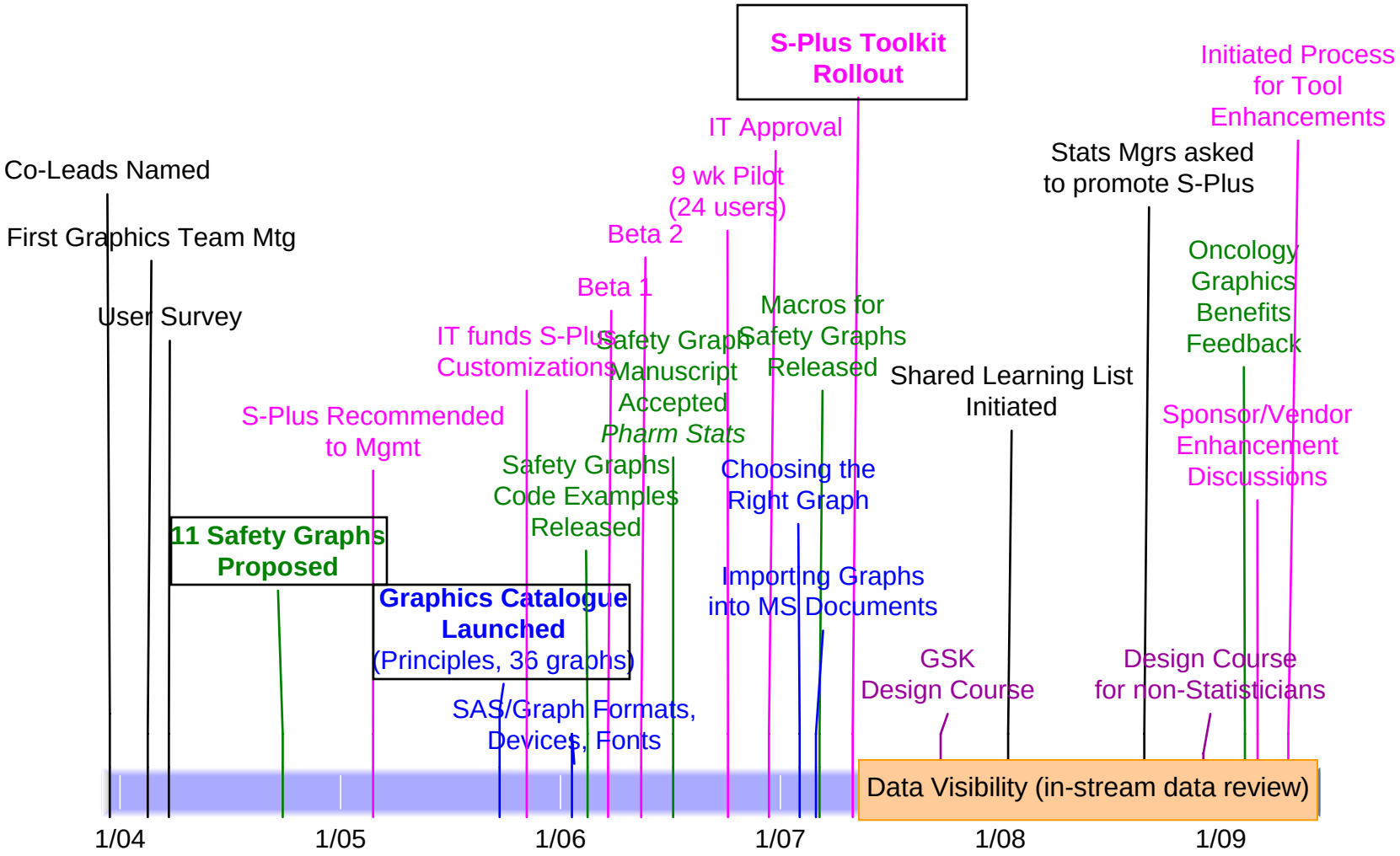
- *This graph shows the tumour response in percent change from baseline measurements. It Identifies the responders and provides a clear graphical view of the efficacy data.*



"The standard graphical displays and customized graphics software helped facilitate creation of information-rich graphs of key data in a short timeframe."

Graphics benefits courtesy of Subha Jamburajan
Waterfall plot courtesy of Will Bushnell

Graphics Team Activities



The People Who Make Graphics Team Work

Graphics Sponsor: **Roger Liddle**, VP Discovery Biometrics
Executive Sponsor: **Frank Rockhold**, SVP Drug Development Sciences

Graphics Community Steering Team

- Co-Leaders:
  Mark K Jones* (BDP) Lead Graphics Expert, Business System Owner
  Jay Hilliard* (Integrated System Support) S-Plus Toolkit support, trainer for S-Plus Toolkit in RTP
  Susan Duke (BDP) Graphics Champion

- **Peter Lane** (RSU) creator and co-editor of the Graphics Catalogue, co-author of safety-graphics paper in *Pharmaceutical Statistics,* developer and co-presenter of the Graphics Design course
- **Max Cherny** (CVM MDC)
- **Jennifer Gauvin, Ian Dixon,* Andrew Nicholls, Andrew Miskell, Genqian Cai, June Ye** (Discovery Biometrics)
- **Michael Irizarry, Samantha St. Laurent, Nada Boudiaf** (Epidemiology)
- **Scott Burroughs** (Infectious Disease MDC)
- **Mark Hopton** (Neurosci MDC)
- **Mike Durante** (Onc MDC)
- **Lisa Willits, Steve Mallett** (Resp MDC)

- Special thanks to
  - **Ohad Amit** (Oncology, co-lead for initial phase, lead author of safety-graphics paper in *Pharmaceutical Statistics*) and Richard Heiberger (Temple University, co-author of *Pharmaceutical Statistics paper)*
  - **Subha Jamburajan** (Discovery Biometrics) for use of her study team's graphics benefits
  - Michael O'Connell and his colleagues at Tibco

*S-Plus Toolkit trainers (trainers not on GCST: Eric Simms, Nancy Hausser)

Why Graphics Team Works

- Strong support from sponsor and executive sponsor
- Broad-based graphics composed of people passionate about good graphics
- Right mixture of centralized-role and study project-role members

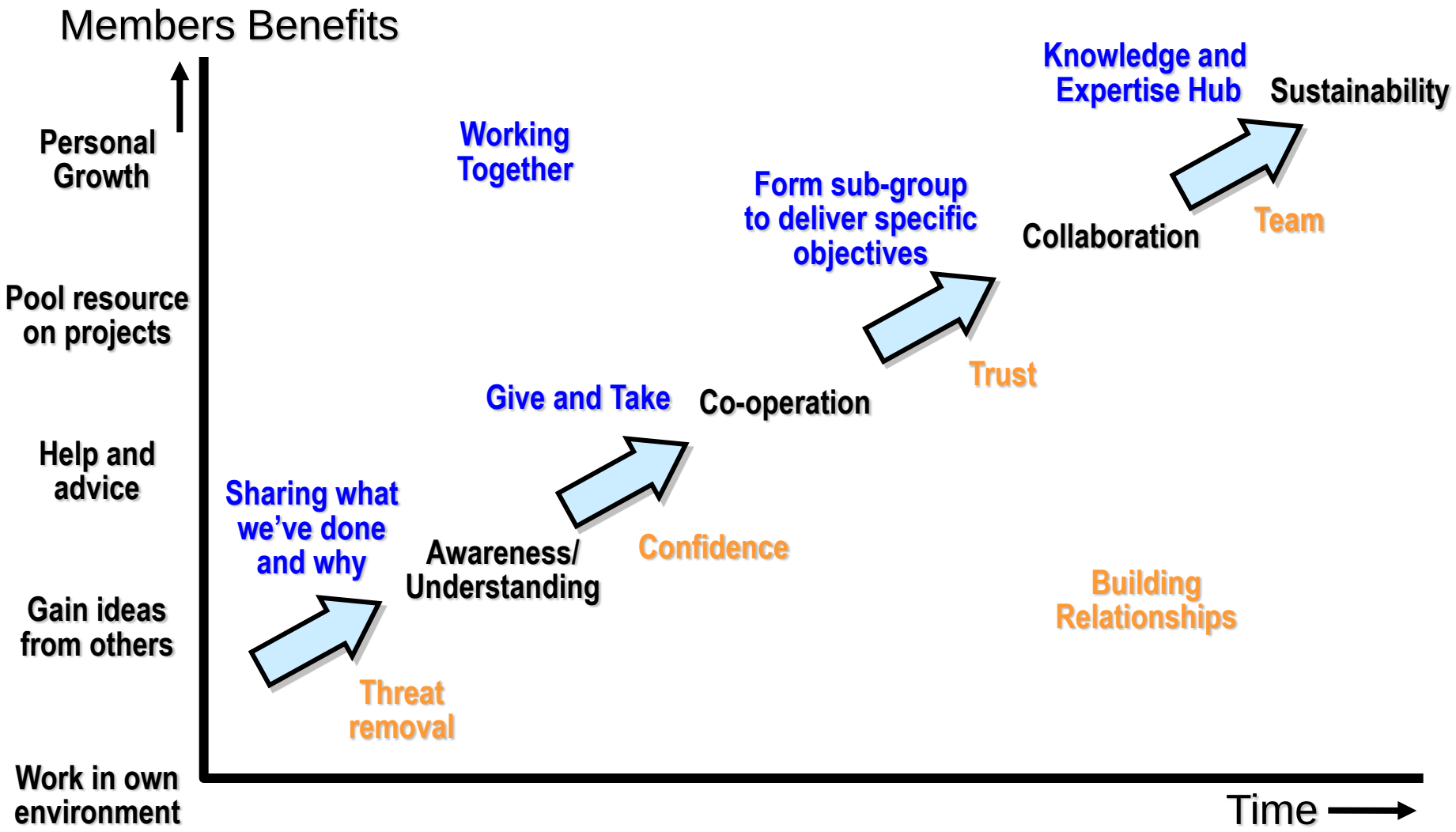
- Good collaboration between
  - GSK business & GSK IT
  - GSK & vendor
  - Statistics departments
    - Collaboration needed because our statistics function is decentralized

Graphics Team is an Example of Community of Practice

- "Communities of practice are groups of people who share a passion for something that they know how to do and who interact regularly to learn how to do it better" *E. Wenger*

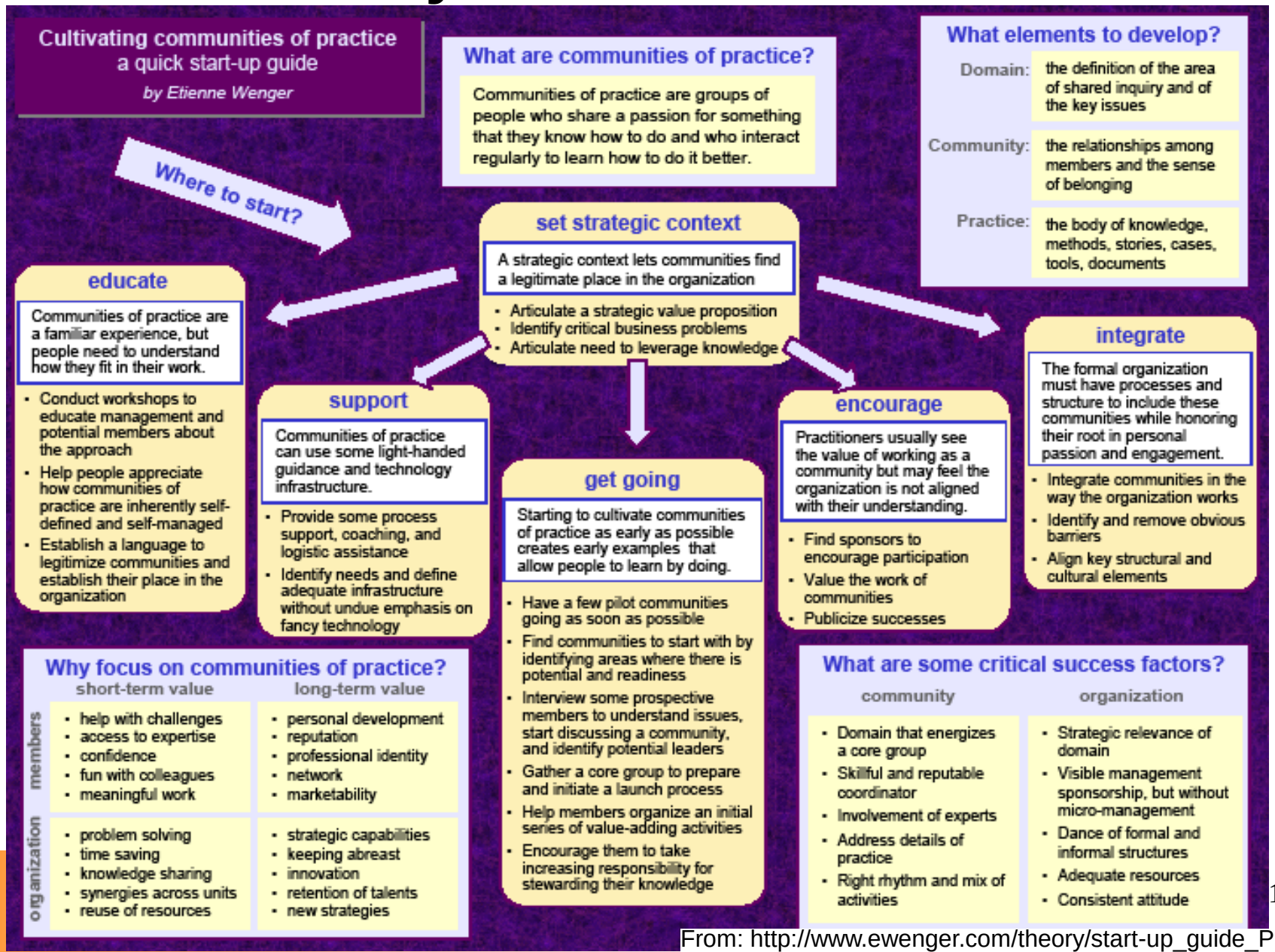
- Two basic elements are needed
  - A common location to keep the community's information
  - A group of people who trust each other to meet the needs of the community
    - Credible (relevant activities, quality output, credit where it is due)
    - Protect needs of the community (no place for big egos)
    - Meet monthly, continually getting things done

Developing the Community



Slide courtesy of John Riddell, GMS

Community of Practice in a Nutshell



From: http://www.ewenger.com/theory/start-up_guide_PDF.pdf

Conclusion

Graphics Objective: *Promote more effective understanding, decision making and communication of data via the use of quality graphics.*

- Community of Practice approach fits well with
  - Motivated, passionate individuals striving for a common goal
  - Topical areas that don't naturally fit within the existing organizational structure

- Trustworthiness required to make Community of Practice work well encourages the better nature in all of us