Andreas Krause
Michael O'Connell *Editors*

A Picture is Worth a Thousand Tables

Graphics in Life Sciences

Springer

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ISBN 978-1-4614-5328-4 ISBN 978-1-4614-5329-1 (eBook)
DOI 10.1007/978-1-4614-5329-1
Springer New York Heidelberg Dordrecht London

Library of Congress Control Number: 2012950035

Printed on acid-free paper

Springer is part of Springer Science+Business Media (www.springer.com)

Foreword

The graphical display of data in medical research is a key component of communicating one's findings, yet sadly over the years little attention is paid to how to make such graphics truly effective and non-distortive.

For statisticians, clinicians, or other scientists there is virtually no training in the art and science of successful and reliable graphics, so the end result is that we all tend to muddle by as best we can. We resort to certain stereotypes of graph, and displays that distort research findings, e.g., by exaggerating true effects or not conveying statistical uncertainty, are quite common.

Hence, this book is an exciting contribution in explaining in a practical setting how graphics can be used best in medical research. The breadth of topics is particularly suited to the whole spectrum of pharmaceutical research, and the editors are to be congratulated on gathering such a well-informed and insightful set of experts to tackle each topic. Also noteworthy is that the book is an attractive read, illustrating the value of color for better perception of graphics. Whether it is for in-house and personal insights to data, publications in scientific journals, or conveying findings in regulatory submissions, this book's content carries a wealth of ideas that both statisticians and the broader realm of research scientists need to avidly absorb. Indeed, besides aiming at statisticians, modelers, and quantitative people the book's content should be appreciated by MDs, pharmacologists, managers, and decision makers, i.e., the key recipients of data analyses and their visualization. The hope is that in future we can all do a better job in utilizing graphics to convey the essence of our research findings.

London, UK — Stuart Pocock

Preface

Graphics are an essential means of communication for humans, from prehistoric cave painting to modern computer graphics. A graphic can often summarize and visualize information much more efficiently than tables or words.

A difference between verbal and graphical communication is that verbal communication is largely direct, the sender and the recipient of the message can exchange information. If necessary, in multiple iterations.

Graphics on the other hand are frequently an asynchronous means of communication: the creator of the graphic is not present to elucidate on what is being shown, to help understanding and facilitate correct interpretation. The graph has to speak for itself, deliver a clear message, and avoid misinterpretation.

Nowadays, graphs are often created to extract and reveal the information contained in a data set, reminding of the fact that having collected data is not equal to having generated knowledge. The knowledge must be distilled from the data and displayed in ways that make interpretation easy, accurate, and correct.

The life sciences and the pharmaceutical industry generate a wealth of data. A clinical study that aims to quantify the effects of a newly tested drug in humans, collects data from many domains: demographics, dosing, pharmacokinetics and pharmacodynamics, laboratory measurements, adverse events, ECG and vital signs, concomitant medications, medical history, and more; at many different time points in many different subjects, healthy volunteers, and treated patients. Data regarding the operations of the clinical trial, e.g., sites and investigators, are also voluminous, as are data generated in chemistry and biology research, and preclinical studies leading to the clinical trials. Other functional areas in pharmaceutical companies are also highly data-driven, e.g., post-marketing areas such as epidemiology and sales and marketing.

Clinical trial data are analyzed in various ways: by examining the raw data listings, aggregating the data in summary statistics, in tables and graphics. Tables, listings, and figures are used to summarize the data in clinical study reports and submissions to regulatory agencies at the conclusion of the clinical trials. They are also used to review the study data during clinical trials.

Wikipedia defines Graphics as follows:

> Graphics (from Greek γραφικός graphikos) are visual presentations on some surface, such as a wall, canvas, computer screen, paper, or stone; to brand, inform, illustrate, or entertain. Examples are photographs, drawings, Line Art, graphs, diagrams, typography, numbers, symbols, geometric designs, maps, engineering drawings, or other images. Graphics often combine text, illustration, and color. Graphic design may consist of the deliberate selection, creation, or arrangement of typography alone, as in a brochure, flier, poster, Web site, or book without any other element. Clarity or effective communication may be the objective, association with other cultural elements may be sought, or merely, the creation of a distinctive style.
>
> Graphics can be functional or artistic. […]
>
> Wikipedia entry on Graphics (Jan 23, 2012)

The Wikipedia entry states that graphics can be functional or artistic. The philosophy of this book is that efficient graphics are both functional and artistic. It takes a good amount of creativity on how to display the data, in order for the information in the data to be visualized effectively to the reader of the graph.

Creativity requires inspiration. This book aims at providing that inspiration. We have assembled a group of life science graphics experts who have described graphics principles, techniques, and case studies to provide inspiration and for you, to incorporate graphical best practices into your work.

Many of the visualization principles that hold for life science data are also encountered in daily life. For example, the map you use to orient yourself on the London Underground ("The Tube") has only limited similarity to the actual geographical positions of train tracks and stops. The simplification to largely horizontal, vertical, and diagonal lines improves the interpretation and the usefulness enormously.[1]

The London underground map does not only simplify the layout by reducing the geographical layout to straight lines, but it also actually distorts the geography substantially: if you take the underground—the Piccadilly line—from the city to Heathrow airport, you will probably be surprised by how quickly the inner city stations follow one another and then by how long it takes to arrive at Heathrow airport. If the tube map would be scaled according to geography, the inner city part, the part most used by travelers, would shrink and become illegible. So leave early for the outer stations!

Garland (1994) gives a historical account of the development of the tube "map," highlighting the interactions that improved its usefulness to the user of the London tube system. The book highlights prominently that the use of the word map is actually inappropriate because the geographical reality is not—or not accurately—mapped onto paper ("Though not strictly speaking a map, this term is almost universally used by people when referring to the London Underground *Diagram* […]," p. 2, italics added).

[1] The simplification was taken too far in 2009 when it was suggested that the River Thames should not be shown on the tub map any longer (BBC London, "Thames reunited with tube map", http://news.bbc.co.uk/local/london/hi/people_and_places/newsid_8259000/8259435.stm).

	Relative survival rate, % (SE)			
	5 years	10 years	15 years	20 years
Cancer site				
Oral cavity and pharynx	56·7 (1·3)	44·2 (1·4)	37·5 (1·6)	33·0 (1·8)
Oesophagus	14·2 (1·4)	7·9 (1·3)	7·7 (1·6)	5·4 (2·0)
Stomach	23·8 (1·3)	19·4 (1·4)	19·0 (1·7)	14·9 (1·9)
Colon	61·7 (0·8)	55·4 (1·0)	53·9 (1·2)	52·3 (1·6)
Rectum	62·6 (1·2)	55·2 (1·4)	51·8 (1·8)	49·2 (2·3)
Liver and intrahepatic bile duct	7·5 (1·1)	5·8 (1·2)	6·3 (1·5)	7·6 (2·0)
Pancreas	4·0 (0·5)	3·0 (0·5)	2·7 (0·6)	2·7 (0·8)
Larynx	68·8 (2·1)	56·7 (2·5)	45·8 (2·8)	37·8 (3·1)
Lung and bronchus	15·0 (0·4)	10·6 (0·4)	8·1 (0·4)	6·5 (0·4)
Melanomas	89·0 (0·8)	86·7 (1·1)	83·5 (1·5)	82·8 (1·9)
Breast	86·4 (0·4)	78·3 (0·6)	71·3 (0·7)	65·0 (1·0)
Cervix uteri	70·5 (1·6)	64·1 (1·8)	62·8 (2·1)	60·0 (2·4)
Corpus uteri and uterus, NOS	84·3 (1·0)	83·2 (1·3)	80·8 (1·7)	79·2 (2·0)
Ovary	55·0 (1·3)	49·3 (1·6)	49·9 (1·9)	49·6 (2·4)
Prostate	98·8 (0·4)	95·2 (0·9)	87·1 (1·7)	81·1 (3·0)
Testis	94·7 (1·1)	94·0 (1·3)	91·1 (1·8)	88·2 (2·3)
Urinary bladder	82·1 (1·0)	76·2 (1·4)	70·3 (1·9)	67·9 (2·4)
Kidney and renal pelvis	61·8 (1·3)	54·4 (1·6)	49·8 (2·0)	47·3 (2·6)
Brain and other nervous system	32·0 (1·4)	29·2 (1·5)	27·6 (1·6)	26·1 (1·9)
Thyroid	96·0 (0·8)	95·8 (1·2)	94·0 (1·6)	95·4 (2·1)
Hodgkin's disease	85·1 (1·7)	79·8 (2·0)	73·8 (2·4)	67·1 (2·8)
Non-Hodgkin lymphomas	57·8 (1·0)	46·3 (1·2)	38·3 (1·4)	34·3 (1·7)
Multiple myeloma	29·5 (1·6)	12·7 (1·5)	7·0 (1·3)	4·8 (1·5)
Leukaemias	42·5 (1·2)	32·4 (1·3)	29·7 (1·5)	26·2 (1·7)

Rates derived from SEER 1973–98 database (both sexes, all ethnic groups).[12]
NOS=not otherwise specified.

Fig. 1 Cancer survival rates by cancer site and time from Brenner (2002)

Another fine example of highlighting information in data with graphics comes from Edward Tufte. Tufte has made a long and distinguished career by clearly displaying information from data. His book, "The Visual Display of Quantitative Information" was named one of the top 100 books of the twentieth century by Amazon.

In this particular example, Tufte used a table of relative cancer survival rates published in a landmark paper (Brenner, The Lancet, 2002) and showed how this display of data can be improved.

Figure 1 shows the original table. Each row gives the survival statistics for a particular type of cancer at 5, 10, 15, and 20 years, showing the relative survival rates and the associated standard errors. Figure 2 shows a simplified version: the font size of the standard errors is shrunk since they are arguably less important than the survival rates, and the rows are sorted by survival rate, the most likely measure of interest to the reader. The legibility of the information inside the data is improved considerably (Tufte 2007, p. 174).

Estimates of relative survival rates, by cancer site

	% survival rates and standard errors							
	5 year		10 year		15 year		20 year	
Prostate	98.8	0.4	95.2	0.9	87.1	1.7	81.1	3.0
Thyroid	96.0	0.8	95.8	1.2	94.0	1.6	95.4	2.1
Testis	94.7	1.1	94.0	1.3	91.1	1.8	88.2	2.3
Melanomas	89.0	0.8	86.7	1.1	83.5	1.5	82.8	1.9
Breast	86.4	0.4	78.3	0.6	71.3	0.7	65.0	1.0
Hodgkin's disease	85.1	1.7	79.8	2.0	73.8	2.4	67.1	2.8
Corpus uteri, uterus	84.3	1.0	83.2	1.3	80.8	1.7	79.2	2.0
Urinary, bladder	82.1	1.0	76.2	1.4	70.3	1.9	67.9	2.4
Cervix, uteri	70.5	1.6	64.1	1.8	62.8	2.1	60.0	2.4
Larynx	68.8	2.1	56.7	2.5	45.8	2.8	37.8	3.1
Rectum	62.6	1.2	55.2	1.4	51.8	1.8	49.2	2.3
Kidney, renal pelvis	61.8	1.3	54.4	1.6	49.8	2.0	47.3	2.6
Colon	61.7	0.8	55.4	1.0	53.9	1.2	52.3	1.6
Non-Hodgkin's	57.8	1.0	46.3	1.2	38.3	1.4	34.3	1.7
Oral cavity, pharynx	56.7	1.3	44.2	1.4	37.5	1.6	33.0	1.8
Ovary	55.0	1.3	49.3	1.6	49.9	1.9	49.6	2.4
Leukemia	42.5	1.2	32.4	1.3	29.7	1.5	26.2	1.7
Brain, nervous system	32.0	1.4	29.2	1.5	27.6	1.6	26.1	1.9
Multiple myeloma	29.5	1.6	12.7	1.5	7.0	1.3	4.8	1.5
Stomach	23.8	1.3	19.4	1.4	19.0	1.7	14.9	1.9
Lung and bronchus	15.0	0.4	10.6	0.4	8.1	0.4	6.5	0.4
Esophagus	14.2	1.4	7.9	1.3	7.7	1.6	5.4	2.0
Liver, bile duct	7.5	1.1	5.8	1.2	6.3	1.5	7.6	2.0

Fig. 2 Cancer survival rates by cancer site and time, adaptation by Tufte

Subsequently, Tufte took these survival rates and created a semi-graphic: Fig. 3 shows the same data but now the row and column structure has been broken up: vertical distances approximately represent numerical differences in survival rates instead of just another row. Interconnecting the values that correspond to the same type of cancer visually reveals trends in time: a negative slope indicates a decrease in survival rate with time.

The left-hand side graph shows an artistically adapted version: for better legibility, the vertical dimension—the invisible *y*-axis—corresponds only roughly to the numerical values of the 5 year survival statistics. The cancer types are sorted vertically by 5 year survival statistics, and the slopes of the subsequent survival statistics of the particular cancer type correspond to the decrease in survival. A negative slope corresponds to a decline in survival over time. Note how the ease of interpretation is markedly improved over the original table (Tufte 2006, p. 176, originally published on the Internet in 2003).

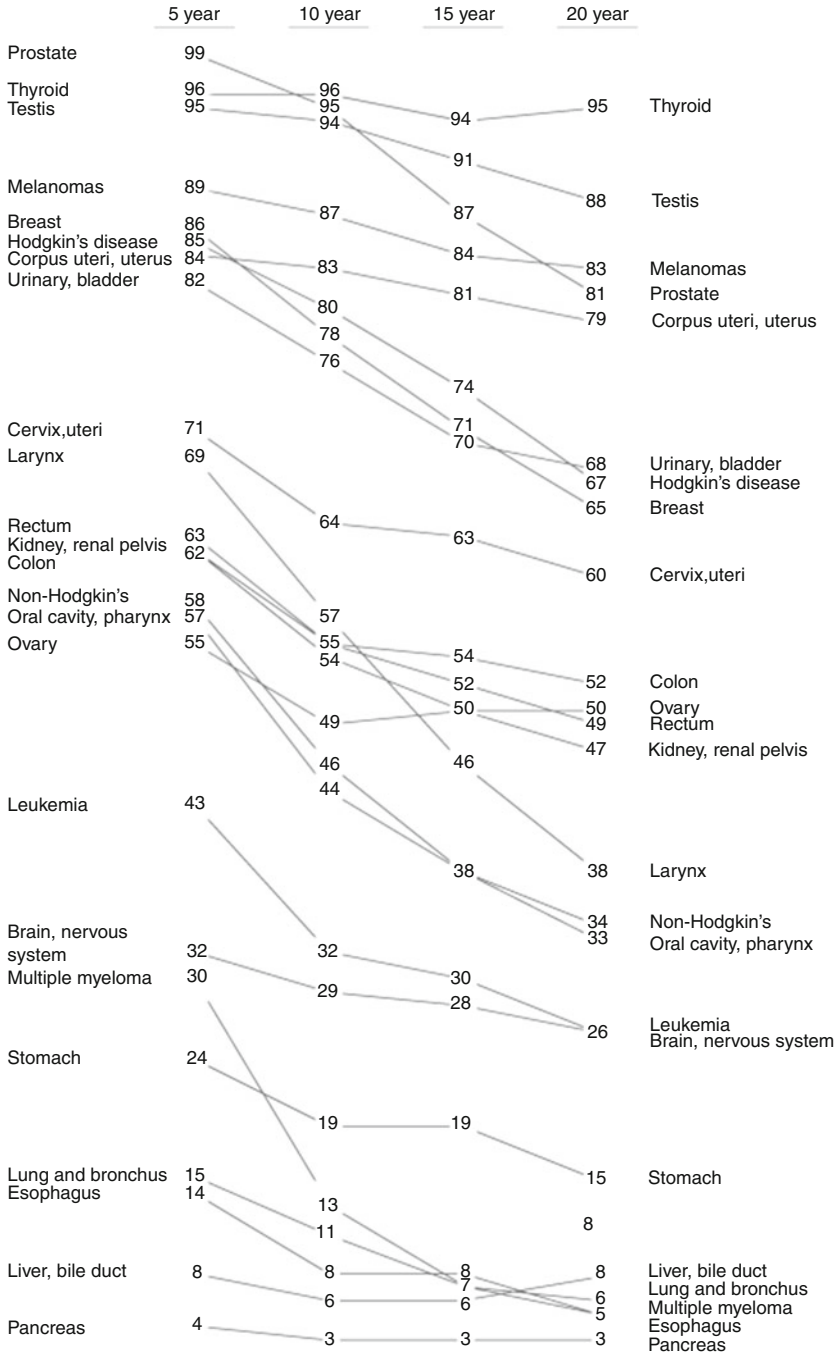

Fig. 3 Cancer survival rates by cancer site and time displayed as semi-graphic

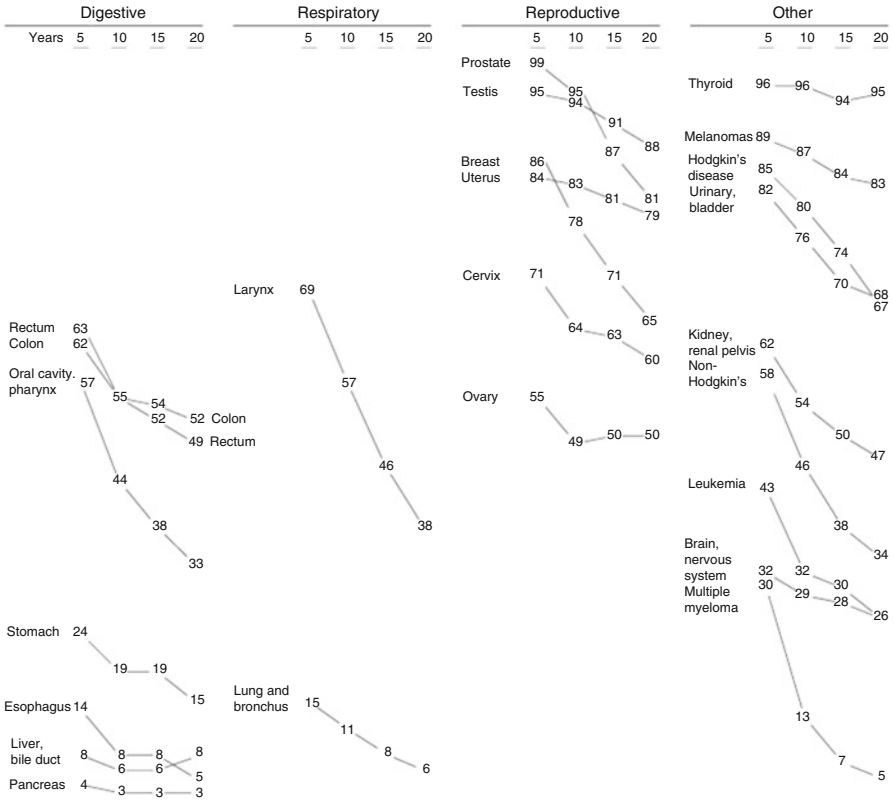

Fig. 4 Cancer survival rates by cancer site and time as semi-graphic, stratified by locus

Nash (2006) in a Web discussion of the Tufte graphs suggested further modifications, suggesting that grouping on cancer types allows for intersecting lines without substantial loss of legibility due to the lower number of intersecting lines (Fig. 4).

Nash collaborated with Tufte on the choice of line weights and text alignments and—most importantly—the placing of the names of the cancer types that are repeated on the right-hand side for better visualization.

These examples show that graphs can be art—creative, informative, and beautiful to the eye. They also demonstrate clearly the importance of extracting, distilling, and presenting efficiently the information contained in the data.

Even though no one disputes the importance of good graphics for efficient data analysis, they are still not as widely used as they could be. Part of the reason might be that graphs can often be improved once the data are seen and understood. However, the life sciences industry works under time pressure, and analysis programs producing tables, listings, and figures are often on the critical path in the development of new treatment therapies. Thus, the graphs are programmed before seeing the data; for example, before database lock and release of the treatment code

("unblinding"). Once the data are available, the results must be available quickly. The graphs are created and delivered without a close looking at the data in the interest of time. That conflict between time pressure and thorough analysis can be critical in that information is missed. But of course, it will probably not even get noticed.

Help is on its way: as data volumes explode in all industries, investment and research in analysis, visualization, business intelligence, and data discovery software is ever-increasing. In the life sciences, the most popular software systems for graphical exploration include R and S-PLUS™, Spotfire™, and SAS™. Microsoft Excel™ seems to still be the most widely used graphical analysis software.

While modern software is necessary in enabling graphical analysis it is not sufficient; and sound graphics principles are required for optimal discovery and communication of information in data. Some of the aforementioned software applications enable sound principles to be followed and others make this difficult!

The landmark books by Tufte (1990, 1997, 2001, 2006) and Few (2004, 2009) establish general principles for good visualizations. Cleveland (1993, 1994) establishes the techniques from a statistical point of view, including the groundbreaking conditional multivariate Trellis display (Becker et al., 1996), codified now in R through the lattice package (Sarkar, 2008). Tufte can be viewed as somewhat of a minimalist and artist, while Cleveland's methods brought strength to the scientific community in the quest to discover and distill information from multivariate data.

Color was researched by Brewer et al. (2002), resulting in the groundbreaking ColorBrewer and corresponding R package on CRAN.

CTSpedia (CTSpedia, 2012) is a knowledge base for clinical and translational research. Among the topics covered are statistical graphics. The Web page gives general advice and tries to organize the types of graphics by the question and the data at hand. It guides through a variety of graphical tools and suggests standards for good graphics.

Visualization and data discovery has been the topic of several TED lectures (TED, 2012), with prime example being Hans Rosling's presentation of interactive graphics analyzing the world's poverty data (Rosling, 2006). The accompanying software, GapMinder (Rosling, 2009), is now available for free download (Gapminder, 2012). It is based on Google's Motion Chart (Google Chart Tools), another free software tool. Similarly, IBM offers the creation and discussion of data sets and analyses online with its Many Eyes initiative (IBM Many Eyes, 2012).

There are several other recent graphics references that are relevant to graphical analysis in the life sciences. Robbins (2004) introduces general principles by showing hands-on examples; Unwin et al (2006) focus on visualization of large data sets. Leckart (2010) provides an interesting update on medication package inserts in the popular magazine Wired. The Jung + Wenig (2010) art design company is the creator of one of the redesigned package inserts. One of their designs is shown in Fig. 5, illustrating that "boring" laboratory results that mostly contain only a large amount of text can be made so much more visually interesting and informative.

The aim of our book is to provide a standard reference for life science graphics, leveraging the pioneering concepts described by Tufte, Cleveland, Few, and others; in a modern framework and with life science context.

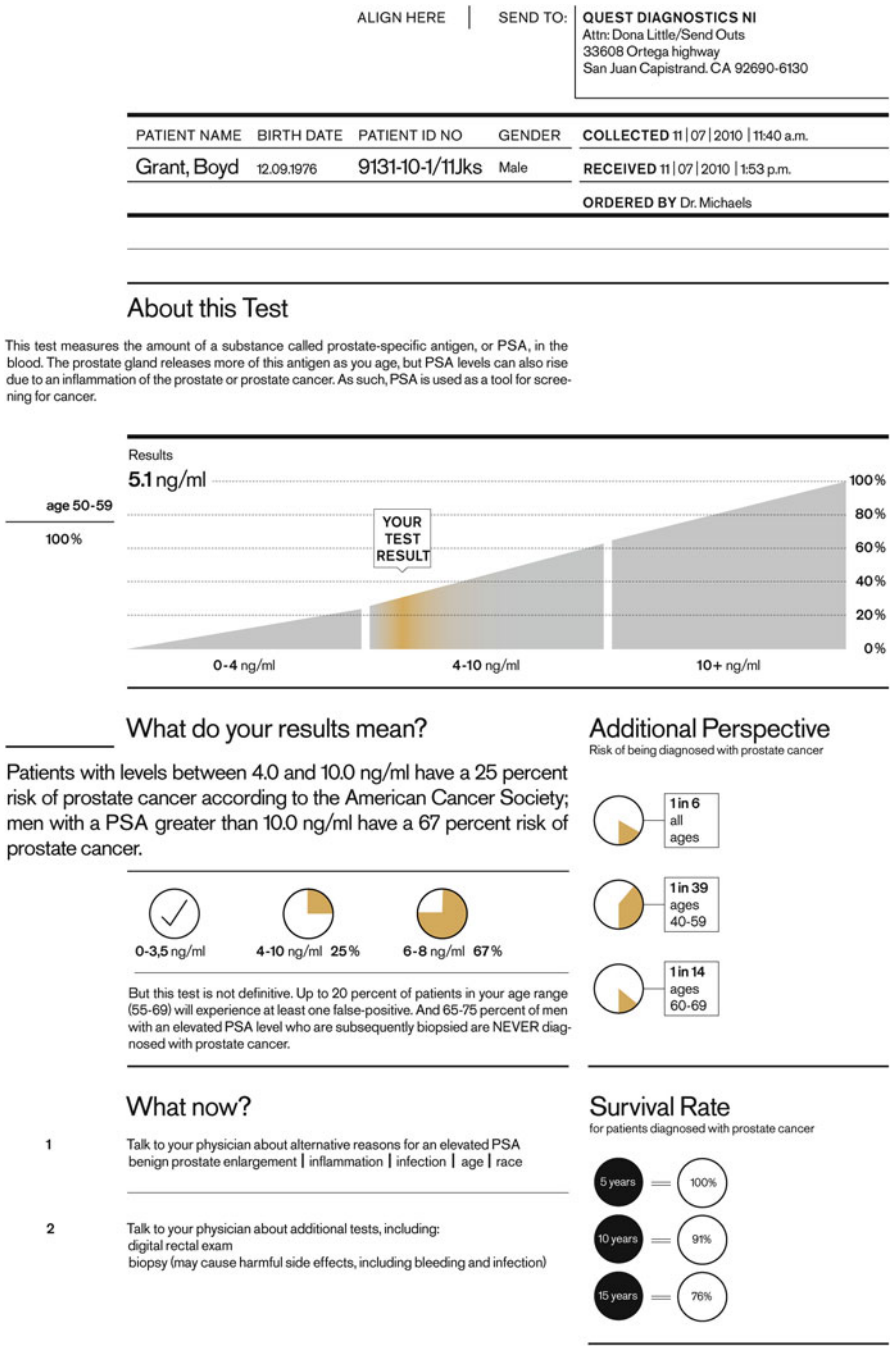

Fig. 5 Blood work results redesigned

We hope that the book serves as a source of inspiration—not only to the creators of scientific graphics, e.g., statisticians and programmers, but in particular to consumers of graphics and key decision makers, physicians, and managers in the life sciences industry.

We will have achieved our mission if business users and decision makers ask statisticians and information technology functional areas for more and better graphs of all their data. As better graphics are used throughout the industry, everyone in the life science ecosystem benefits, including the general population receiving better information and medications through better decision making.

Book Structure

The book is divided into parts. The part "General Principles and Reviews of Graphics" motivates the topic, reviews and establishes general principles, and suggests structured and innovative uses of graphics and also tables.

The part "Preclinical and Early Clinical Development" contains chapters that illustrate a variety of applications for PK/PD, biomarker, and genetic data.

The largest part, "Clinical Trial Graphics," contains chapters on efficacy and safety in therapeutic areas such as oncology and respiratory disease, safety reviews for cardiac and general safety, meta-analysis, and dose–response visualization. The principles are generally applicable to a large variety of applications.

The part on "Operations, Marketing, and Post-Approval Graphics" shows illustrative case studies in clinical trials data management, exploratory visualization of medical safety in observational studies, and post-approval visualizations.

Book Web Site

Being able to use computer programs right away will help getting up to speed quickly. For this purpose, this book has a companion Web site:

http://www.elmo.ch/doc/life-science-graphics/

The Web site contains computer programs for download and further information about the book.

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Acknowledgments

Over the past 10 years, we have been involved in many sessions and tutorials on life sciences graphics in a wide variety of public forums including the Joint Statistical Meetings (JSM), the American Conference on Pharmacometrics (ACOP), the Drug Information Association (DIA) Annual Meeting, the BASS Conference, the Deming Conference, the Graybill Conference, the Midwest Biopharmaceutical Workshop and the Association of American Pharmaceutical Scientists (AAPS) Annual Meeting. The AAPS Sunrise School workshop (at 7 am!) was organized by Stacey Tannenbaum. It was Stacey who suggested the title "A picture is worth a thousand tables." So thank you, Stacey, for the inspiration!

All of these sessions have included our collaborators and colleagues, many of whom are featured in this book. A big hats-off to all the contributors to this book. The community that all of us have created has grown dramatically over this period and spawned other initiatives that have progressed the use of graphics across the life science industry.

Finally, we gratefully acknowledge the highly professional and efficient collaboration with Springer-Verlag throughout the entire process. Our special thanks go to Carolyn Honour, Renata Hutter, and John Kimmel in this regard; and to Springer for the terrific job they do with publications in the life sciences.

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