

John G. Brock-Utne

# Clinical Research

Case Studies  
of Successes  
and Failures



Springer

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ISBN 978-1-4939-2515-5                      ISBN 978-1-4939-2516-2 (eBook)  
DOI 10.1007/978-1-4939-2516-2

Library of Congress Control Number: 2015938594

Springer New York Heidelberg Dordrecht London  
© Springer Science+Business Media New York 2015

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Printed on acid-free paper

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*For the next generation:*

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*Tobias J. Brock-Utne*

*Anders C. Brock-Utne*

*Jasper L. Brock-Utne*

*Stefan S. Brock-Utne*

*Charlotte E. Brock-Utne*



# Preface

The intention of this book is to highlight the many pitfalls that can occur when contemplating doing clinical research. This is based on my over 45 years of involvement in clinical research in four continents. Even though some of my mishaps have occurred over 40 years ago, I can assure you that these mistakes occur even to this day with monotonous regularity. Hence the book.

After each case history a question is posed. These are questions you may be faced with as a clinical researcher. The solutions suggested may be controversial and as such may form the basis for discussions on how best to proceed in your special circumstance.

The object of these many stories is to alert the clinical researcher and especially the El Toro researcher that there are many potential disasters waiting to happen when you embark on clinical research. But most of all the reader will hopefully understand that meticulous planning is essential for being successful in this field.

Always remember that the object is to achieve one's research goals quickly with a minimal risk of wasting time and resources.

To quote Marks (1) and to paraphrase Hippocrates of Kos (2):

- (1. "The success of research project depends on how well thought out a project is and how potential problems have been identified and resolved before data collection begins" (Marks RG. Designing a research project. The basics of biomedical research methodology. Belmont: Lifetime Learning Publications: A division of Wadsworth 1982).
2. The Art is long  
Life is short  
Experiments perilous  
Decisions difficult.)

Stanford, CA, USA

John G. Brock-Utne



# Acknowledgment

To the following, who started me on my clinical research venture. They are presented in the order in which I met them:

- 1971, Dr. Jon Gjessing, Professor of Anesthesia, Rikshospitalet, University of Oslo, Norway
- 1973, Dr. John W. Downing, Professor of Anesthesia, University of Natal, Durban, South Africa
- 1977, Dr. Jay B. Brodsky, Professor of Anesthesia, Anesthesiology, Perioperative and Pain Medicine, Director of the Operating Room at Stanford University School of Medicine, Stanford, CA 94305, USA

A person who must not go unmentioned is my friend Dr. Steve Shafer, Professor of Anesthesiology, Perioperative and Pain Medicine, Stanford University School of Medicine Stanford, CA 94305, USA, and Editor in Chief of *Anesthesia & Analgesia*. His many excellent Editorials and comments about clinical research have been invaluable to me. This is especially true about plagiarism and fraud in clinical research.

To my wife, Sue (48 years married), for her constant encouragement and help with proofreading.

To Shelley Reinhardt (Springer) and Joanna Perey (Springer) for all their help and support

I am also indebted to my research colleagues around the world with whom I have published. I thank them for their hard work, camaraderie, and commitment in our quest to find answers to the questions posed or the clinical observations made. The list is shown below. It may be that I have unintentionally left a few out for which I sincerely apologize.

Barry Adam, Miriam Adhikari, Scott Ahlbrand, Neetu Ahluwalia, John Atchison, Craig T. Albanese, DM Alexander, Karim Ali, Russell Allen, Eric Amador, Gabriel Amir, Nick Anast, Wayne Anderson, Andrew Andrews, Trevor Andrews, Tim Angelotti, Martin Angst, John Archer, Kayvan Ariani, Christopher Arkind, Dave Armstrong, Dan Azar, Nasima Badsha, Brian Baker, Andy J. Barclay, John

J. Barry, John Bean, Peter Bean, David Benaron, Melissa Berhow, Orr Bernstein, Tess Bhatia, Kevin Blaine, Gordon Blake, Paul Blignaut, Patrick Bolton, Gail Boltz, Jerry Bortz, Adrian Bosenberg, Erin Botha, Gregory Botz, Robin Boulle, Jonathan Bradley, Ioana Brisc, Arne J. Brock-Utne, Jay B. Brodsky, Helen M. Bronte-Stewart, Michael Brook, Christopher Brouckaert, Colin Brown, Douglas Brown, Davie Browne, Susan Browne, Carlos Brun, John Bryer, Robert Buley, Ross Bullock, Erin Bushell, Sharon Bux, Jorge Caballero, Pat Callander, Walter Cannon, Alice Cantwell, Brian Cantwell, Carol Canup, Barbara Carr, Brendan Carvalho, Jane Ceranski, Anant Chandel, Peter Chang, Steven D. Chang, Paul Chard, Michael Charles, Robert Cheetham, Marianne Chen, Samuel Chen, Alan Cheng, Rena Chhokra, Alexander Chiu, John Chow, Anne Chowet, Larry F. Chu, Sam Chun, Christopher Church, Rebecca Claire, Michael Coady, Michael Cochran, Sheila Cohen, Anthony Coleman, Jeremy S. Collins, Joe Conradie, Russell Cooper, Jerry Coovadia, Eric Cornidez, John Cosnett, Doug Crockett, Chris Cuerden, John Cummings, Miram Curet, Charles Debattista, Carol A. Diachun, Friederike Dietz, Michael Dillingham, George Dimopoulos, Tom Dow, Laura Downey, John W. Downing, David Drover, Johan DuPreez, Barry Dyck, Paul Eckinger, Henry Edwards, Joshua Edwards, Talmage Egan, Mark Eggen, Christoph Egger-Halbeis, Arne Martin Eide, Inga Elson, Matthew Eng, Herbert Engelbrecht, Michael Ennis, Roy Esaki, Paul Fairbrother, Gary Fanton, Marie Farstad, Bill Feaster, Larry Feld, Vladimir Firago, Steve Fischer, Jason Fleming, Linda Foppiano, Seth Friedland, Maika Fujiki, Louise Furukawa, David M. Gaba, Ray Gaeta, Stephen L. Gaffin, Kingsuk Ganguly, Premjith Gathiram, Monica Gerstner, Rona Giffard, Jon Gjessing, Mark Gjolaj, Christopher Good, Steven Goodman, Stuart Goodman, Neal Goodwin, Dennis Grahm, Lorentz Gran, Mike Greenberg, Ronald Green-Thompson, Mike Gregory, Steve Griffin, Cosmin Guta, Ali Habibi, Alvin Hackel, Gordon Haddow, Ariff Ahmed Haffejee, Jennifer Hah, Christopher Hamilton, David Hamilton, William A. Hampton, Frank L. Hanley, Leland Hanowell, Edmund John Harris, Kyle Harrison, Natalya Hasan, James Healzer, Craig Heller, Jaimie Henderson, Cathy Heninger, Erin K. Hennessey, Erin Hepworth, Jerome Hester, John Hicks, Jesse Hill, Lauren Hill, Gillian Hilton, Lerner B. Hinshaw, Asher Hirshberg, Shawn Hodge, Robert Holbrook, Allan Hold, Jeffrey P. Holden, Allison Holloway, Jung Hong, Susan Hoopes, Peter Houlton, Steve Howard, William Huizinga, David Humphrey, Paul Husby, Jerry Ingrande, Richard A. Jaffe, Mike James, Mark Jamieson, David Jarvis, Stephanie Jeffrey, Chrystina Jette, Derek G. Jordaan, John Jordaan, Bassam Kadry, Ahmed (Mahmood) Kadwa, Hassan Kadwa, Soromini Kallichurum, Sunder Roopsun Kambaran, Komal Kamra, Norman Kaplan, Jadwiga Katolik, Ralph Katzwinkel, Robert Kaye, Michael Keating, Steve Kelleher, Mary Khaing, Muhammad Fazl-Ur Rahman Khan, Andrew Kim, Tae-Wu Edward Kim, Harry Kingston, Yvonne Koen, Marie Koller, Jiang-T Kong, Ted Kreitzman, R Kremer, Vivek Kulkarni, Joseph Kumm, Erin Lachman, Cathy Lammers, Gary Lau, Kenneth Lau, Nigel Lavies, George Lederhaas, Eugene S. Lee, Jennifer Lee, Phoebe Leith, Harry Lemmens, Jody Leng, Theodore Leng, David C. Levi, Robert Levitan, Geoffrey Lighthall, Per Gustav Lilleaasen, Yuan-Chi Lin, Steven Lipman,

Sanford Littwin, N Lopes, Jaime R. Lopez, Andrew Love, Tom Lund, Joe Luther, Alex Macario, Robin MacGillvray, Bruce MacIver, Rob MacKenzie, Sean Mackey, TA MacPherson, Rajend Maharaj, Nisha Malhotra, Ann Marie Mallat, Kevin Mallott, Emmanuel (“Mannie”) Mankowitz, Steve Manos, Steve Mantin, Ed Mariano, Masizane Marivate, Jim B.D. Mark, James Mark, Maurice Mars, Aileen Marszalek, William Mathers, Amitabh Mathur, Parag Mathur, Nasim Mayat, Robin McAravey, Larry McFadden, Ashley Micks, Fred Mihm, Samuel A. Mireles, Jon Miser, Lyle L. Moldawer, Vanessa Moll, Jack Moodley, Linesh Moodley, David Morrell, John Morton, Mike Moshal, Ali Mossa, Ryan Mountjoy, Robert Moynihan, Khobi Msimang, Radha Muthukumarasamy, Rai Naidu, Clint Naiker, Sim Naicker, Robert Negrin, Andy Neice, Vladimir Nekhendzy, Camran Nezhat, John Nguyen, Birgit Niestroj, James Nixon, Andy Norbury, Robert Norman Steve O’Keefe, Eli Ohayon, Christopher Olcott, Matthew Oldroyd, Megan Olejniczak, Brent Oskarssen, Einar Ottestad, Ilian Parachikov, David Parris, Andrew Patterson, David Patterson, Nirupa Paulraj, Tim Pavy, Ronald Pearl, Bridget Phillip, Cindy Pillay, Fausto Pinto, John Pollard, Diane Pond, John Propst, Dennis Pudifin, Alex Quick, Deshandra Raidoo, Chandra Ramamoorthy, RJ Ramamurthi, George Ramjee, SA Ramzi, Emily Ratner, Andrew Rauch, Mahmood Razavi, Vadiyala M. Reddy, Catherine Reid, Ed Riley, Sherman Ripley, Archie Ritchie, Peter Ritchie, Frain Rivera, John Robbs, Joe Roberson, George Roberts, Joseph Robertson, Berklee Robins, RM Robins-Browne, Marnie Robinson, Beaver Robles, Tony Roche, Ed Ronningen, JL Rosen, Jeanne L. Rosner, Chris Rout, Joe Rubin, Cathy Russo, Tom Ruttman, John Ryu, Lawrence Saidman, Robert Salisbury, Stanley Samuels, Robert Sanborn, Frank H. Sarnquist, Sunita Sastry, Amit Saxena, Carolyn Schiffner, Cliff Schmiesing, Ingela Schnittger, HS Schoeman, David Schurman, Robert Schuster, Inga Schwegmann, Soraya Seedat, Lars Segadal, David Seidman, Lori Sheehan, Paul Shuttleworth, Lawrence Siegel, Ruwan Amila Silva, Larry Silver, Vanila Singh, Mark Singleton, Jan Sliwa, David Smith, Roy Soetikno, Ezra Sohar, Hugh Brent Solvason, Ted Sommerville, Shaina Sonobe, Eldar Soreide, David Spain, Jean Marie Spitaels, Gary Steinberg, David Stemple, David Stevenson, Robin Stiebel, Marie Strassburg, Paul Strube, Naiyi Sun, David Sze, John Talavera, James Tan, Chris Tataru, Vivianne Tawfik, Renae Tays, Natacha Telusca, Stephen Ternlund, P Tew, J Thai, Kyu Thin, Shaun Mark Thompson, Sandie R. Thomson, Peter John Tomlin, Rodney Torralva, HS Townsend, James R. Trudell, Kendall Truelsen, Brian Tunink, Scott Tweten, Ankeet D. Udani, James Van Dellen, Johan Van den Ende, Pieter Van der Starre, Jason Varner, William Vaughan, G. Hoosen M. Vawda, Mark Vierra, Terry Vitez, Tracey Vogel, Lindsey Vokach-Brodsky, BJ Vorster, Hendrik J. Vreman, David Walker, Brant Walton, Michael Wang, Rachel Wang, David Waterpough, Michelle Wells, Steve Welman, Nigel Welsh, Brian Wessels, Mike Wiggins, Frank Wilkins, Deborah Williams, Ron Williamson, Gail Wilmot, Tim Winning, Russell Kong-Yen, Bernhard Wranne, Troy Wu, Imad Yamout, Steve Yu, Amadeo Zanotti, Karl Zheng, Gail Zisook, Andy Zumaran, Gary Zupfer, and Stephan Zweig.



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# Basic Premise

## A. Why Is Clinical Research Necessary?

Everything we do as physicians carries a potential hazard. It could be the technique and equipment which we use, or it could be the medication which we give. We use these techniques, etc., to treat our patients, hoping that the benefits will outweigh the potential harm. Our clinical decisions are based on what we are mostly taught by our peers, tradition, and some human and many animal studies. Our experience is limited, so where do we get the knowledge to help us make the best decisions to help each patient? The answer is a properly conducted clinical research.

From the early days of medicine, doctors knew that certain treatments were dangerous. Hippocrates of Kos (born 460 BC and died 370 BC) stated: “Primum non nocere” (First, do no harm) and he also said “Desperate diseases require desperate remedies.” I remember as a little boy that my father, a doctor, said: “Vondt skal vondt fordrive,” which in Norwegian means: “Pain will get rid of pain.” He told me this as he lanced an abscess from my finger, without using local anesthesia. (He did not have any.)

Before 1950, there were no government regulations regarding how clinical research should be performed. Most techniques or treatments were brought to the marketplace with minimal or no clinical studies to prove that they were beneficial or, more importantly, safe.

In September/October 1937, a congressional inquiry led to the beginning of the Food and Drug Administration (FDA) after the 73 deaths in the USA from a drug called “Elixir of Sulfanilamide.” This Elixir contained a solvent, diethylene glycol, which is toxic.

In France, an organic preparation called Stalinon (1956–1957) contained diethyltin diiodide (15 mg) and linoleic acid (100 mg) per capsule. The adult dose was six capsules a day which was a toxic dose. Two hundred and seventeen persons were severely poisoned by Stalinon, and of those, over 100 died.

Even though each country had an FDA of some sort, it was highly ineffective in controlling what was sold to the public. But all this changed with the Thalidomide

(Contergan) tragedy in 1961. The drug, when used by pregnant patients suffering from heartburn, led to the birth of deformed babies. The public all over the world was outraged. Governments decided that the pharmaceutical industry needed to be tightly regulated. As a result, governments decided that they would in the future:

1. Make sure that adequate clinical pharmacological studies would be done on new drugs prior to their release for general use. These studies should include safety testing (in both animals and humans) and clinical trials.
2. Recognize and publish any adverse effects that may arise after the release of a new drug [1].

Hence, clinical research is necessary to answer the questions:

1. How *good* are our medicines, techniques, and equipment?
2. How *bad* are our medicines, techniques, and equipment?

## B. Why Do Physicians Do Clinical Research?

Physicians start doing clinical research for various reasons. Many do it because they have passion for a certain technique, drug treatment, and/or a device. They want to show that their idea is better than everyone else's. These researchers often get "bitten by the bug" and make clinical research their life's work.

Others do research purely to get promoted in the university system. The well-known phrase "Publish or Die" is alive and well in academia. An academician's quality and quantity of research output is an easy way to measure his/her academic achievements.

Some people do research to get acknowledged by their peers and to see their name in "golden lights."

Some people do clinical research because of their clinical expertise. Outside agencies recognize this and pay the researcher to conduct research in their field. This financial support can be large and may even pay for part or whole of their annual salary. In addition to the salary, the outside supporters pay the university for using its facilities (usually 35 % of the grand total). In addition, they also pay for research assistants, laboratory fees, etc. In the USA, the financial support to do a 20-patient study can amount to about \$300,000.

The individual reasons for doing clinical research vary tremendously and can be one or a combination of any of the above factors. But most importantly, clinical research can be fascinating, rewarding, and fun.

So has the interest in clinical research increased, decreased, or stayed constant in the last 70 years? Take anesthesia, for example. Feneck et al. [2] have indicated that there appears to be a decline in published anesthetic articles. However, Green and Kumar [3] point out that Feneck et al. only reviewed seven journals. It is interesting to note that the first anesthetic journal, *Anesthesia & Analgesia*, came out in 1921.