The fifth revised edition of this highly successful book presents the most extensive enhancement since Using and Understanding Medical Statistics was first published 30 years ago. Without question, the single greatest change has been the inclusion of source code, together with selected output, for the award-winning, open-source, statistical package known as R. This innovation has enabled the authors to de-emphasize formulae and calculations, and let software do all of the ‘heavy lifting’.

This edition also introduces readers to several graphical statistical tools, such as Q-Q plots to check normality, residual plots for multiple regression models, funnel plots to detect publication bias in a meta-analysis and Bland-Altman plots for assessing agreement in clinical measurements. New examples that better serve the expository goals have been added to a half-dozen chapters. In addition, there are new sections describing exact confidence bands for the Kaplan-Meier estimator, as well as negative binomial and zero-inflated Poisson regression models for over-dispersed count data.

The end result is not only an excellent introduction to medical statistics, but also an invaluable reference for every discerning reader of medical research literature.

Contents
Preface to the Fifth Edition
Prefaces to the Previous Editions
• Basic Concepts
• Tests of Significance
• Fisher’s Test for 2 × 2 Contingency Tables
• Approximate Significance Tests for Contingency Tables
• Some Warnings concerning 2 × 2 Tables
• Kaplan-Meier or ‘Actuarial’ Survival Curves
• The Log-Rank or Mantel-Haenszel Test for Comparing Survival Curves
• An Introduction to the Normal Distribution
• Analyzing Normally Distributed Data
• Linear Regression Models for Medical Data
• Binary Logistic Regression
• Regression Models for Count Data
• Proportional Hazards Regression
• The Analysis of Longitudinal Data
• Analysis of Variance
• Data Analysis
  • The Question of Sample Size
  • The Design of Clinical Trials
  • Further Comments regarding Clinical Trials
  • Meta-Analysis
  • Epidemiological Applications
  • Diagnostic Tests
  • Agreement and Reliability

References
Subject Index
Chemotherapy

International Journal of Experimental and Clinical Chemotherapy

Founded 1959 as ‘Chemotherapia’ by H.P. Kuemmerle and P. Rentchnick

Editor-in-Chief
G. Minotti, Rome

Associate Editors
G. Delogu, Rome
G. Graziani, Rome

Editorial Board
A.M. Biroccio, Rome
C. Chiesa, Rome
S. Gemma, Siena
S. Horkovics-Kovats, Kundl
S. Kohno, Nagasaki
C. Landersdorfer, Parkville, Vic.
P. Linder, Geneva
K. Machka, Munich
P. Menna, Rome
E. Monti, Busto Arsizio
K.G. Naber, Straubing
R. Nau, Göttingen
P. Preziosi, Rome
E. Salvatorelli, Rome
M. Sanguinetti, Rome
G. Sava, Trieste
G.M. Shah, Quebec, Que.
F. Sörgel, Nuremberg-Heroldsberg
J.C. Stingl, Bonn
F. Van Bambeke, Brussels
M. Wilhelm, Nuremberg

The founder of chemotherapy

Paul Ehrlich
1854–1915

KARGER

Printed in Germany on acid-free and non-aging paper
(ISO 9706) by Stückle Druck, Ettenheim
Guidelines for Authors

Submission
Before submission, please read the Guidelines for Authors for specific requirements for manuscript preparation. Manuscripts written in English are considered and should be submitted online at www.karger.com/che (a link leads you to the Submission Website).

Submission of an article implies author agreement with the below Conditions. To be considered for publication, all manuscripts must be accompanied by a cover letter signed by all authors stating that the work has not been published, nor is it under consideration elsewhere, and that all authors approve the submission.

A Copyright Transfer Form, available on the Submission Website, with the corresponding author's original (hand-written) signature must be received by the editorial office. Please print and sign the form, and upload it during submission (or fax or scan and email) to make it legally binding.

Names, postal and e-mail addresses of 4 international experts in the appropriate area of research should accompany each manuscript. At the Editors' discretion, scientist(s) selected from this list may be invited to act as referee(s). Referees suggested should not be from the same institution as the author.

Presentation of manuscripts should follow the Uniform Requirements for Manuscripts Submitted to Biomedical Journals [see International Committee of Medical Journal Editors. Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication (April 2010 version). Available from: http://www.ICMJE.org].

In case of problems with submission, please contact: che@karger.com
S. Karger AG – Medical and Scientific Publishers
Editorial Office 'Chemotherapy'
Allschwilerstrasse 10
CH–4009 Basel (Switzerland)
Tel. +41 61 306 13 61
Fax +41 61 306 14 34

Conditions
All manuscripts are subject to editorial and peer review. Manuscripts are received with the explicit understanding that the work has not been published (wholly or in part), and is not under simultaneous consideration in any language elsewhere. Furthermore, all authors have made substantial contributions and confirm that they have seen and approved the manuscript submission. Submission of an article implies the transfer of the copyright from the author to Karger Publishers upon acceptance. Accepted papers become the permanent property of Chemotherapy and may not be reproduced by any means, in whole or in part, without the written consent of the publisher. It is the author's responsibility to obtain permission to reproduce illustrations, tables, etc. from other publications.

Conflict of Interest
Authors are required to disclose any sponsorship or funding arrangements related to the research presented in the manuscript and any possible conflicts of interest. A possible conflict of interest does not preclude consideration of a manuscript for publication, but the Editor might consider it appropriate to publish the disclosed information with the paper. All forms of support and financial involvement should be listed in the Acknowledgements section of the paper. The cover letter should certify that all forms of conflict of interest by all authors were clearly identified in the text.

Guidelines for Authors

Ethics
Research must comply with the guidelines for human studies and animal welfare regulations. Manuscripts reporting studies on human subjects should include evidence that the research was ethically conducted in accordance with the Declaration of Helsinki (World Medical Association; http://www.wma.net/en/30publications/10policies/b3/index.html). In particular, authors should state in the Materials and Methods section that subjects have given their informed written consent and that the study protocol was approved by an appropriate ethics committee. All patients should be identified by numbers or aliases, not by their real names. Authors should also state that animal experimentation was approved by an independent ethics committee. Copies of these guidelines and policy statements must be available for review by the editors if necessary.

Plagiarism Policy
Whether intentional or not, plagiarism is a serious violation. Karger Publishers defines plagiarism as reproduction of another work with at least 25% similarity and without citation. If evidence of plagiarism is found before/after acceptance or after publication of the paper, the author will be offered a chance for rebuttal. If the arguments are not found to be satisfactory, the manuscript will be retracted and the author sanctioned from publishing papers for a period to be determined by the responsible Editor(s).

Sections
Authors should indicate in the cover letter which manuscript type is being submitted for publication:

- Original Papers: Fully documented reports of original research that must describe full sets of significant, original experiments in current anti-infective and antitumor chemotherapy research. Abstract, Introduction, Materials and Methods, Results, and Discussion sections are required. Consideration for publication is based on originality, novelty, scientific soundness, and appropriate analysis (maximum 3,000 words, 80 references, plus tables/figures).

- Reviews: Comprehensive, state-of-the-art papers covering a timely topic by experts in the field (maximum 4,000 words, plus tables/figures, references). Reviews are usually invited by the Editor but may be unsolicited. Authors are asked to contact the Editor-in-Chief before submission in order to avoid clashes with other pending reviews. All reviews are subject to peer review. An unstructured abstract of no more than 200 words is required.

- Novel Insights from Clinical Practice: The journal only considers case reports that provide significant new insights into a clinical problem or an extremely unusual clinical case course. Submissions can be based around a case or a number of similar cases. The most important aspect of the presentation is that it provides a new perspective on a recognized clinical scenario or may represent an entirely new clinical condition. The novel aspects of the case(s) may be in the phenotype, the presentation, the investigation and/or the management. The manuscript should contain an unstructured abstract (maximum 150 words), introduction, case report and discussion section (maximum 2,000 words, maximum 2 tables or figures). Boxes containing bullet points on Established Facts (what is already known) and Novel Insights (new information gained) are required on the first page of the report. These should highlight the novelty of the clinical observation.

- Short Communications: Short reports, brief laboratory observations, and preliminary communications can be submitted for accelerated publication under Short Communications. They must present new findings of sufficient importance to justify their accelerated acceptance. Such communications should represent complete, original studies and should be arranged in the same way as full length manuscripts (maximum 1,600 words).

Letters to the Editor:
Letters to the Editor are encouraged if they directly concern articles recently published in this journal. If accepted, the Editor reserves the right to submit such letters to the authors of the articles concerned prior to publication in order to allow them to respond in the same issue of the journal. In exceptional cases, Letters to the Editor may also address data published in another journal or general subjects related to matters discussed in the journal. No abstract is required (maximum 1,200 words).

Arrangement
The preferred word processing program is MS-Word. The cover letter, the manuscript, the tables and the figures must be submitted in separate files. The manuscript file must contain all the text elements in the following order: title page, abstract and key words, main text, acknowledgments, references, table and figure legends. Tables and figures should be submitted as separate files according to the instructions below. Automatic line numbering should be used consecutively from the title page through to the final page. All pages should be numbered, starting from the title page, including tables, figure legends and figures.

Title page: The first page should contain the concise title of the article along with a short title for use as a running head, the full names of the authors and their affiliations (department, institute, hospital, university etc. where the work was conducted). The full postal address, telephone and fax numbers, as well as the e-mail address of the author to whom correspondence should be sent must be given at the bottom of the title page.

Key words: Please supply 3–10 key words that reflect the content of the paper.

Abstract: Each original paper needs an abstract of up to 250 words structured with subheadings as follows: Background/Aims, Methods, Results, Conclusions. Structured abstracts are not needed for Reviews and Novel Insights from Clinical Practice.

Footnotes: Footnotes should be avoided. When essential, they should be numbered consecutively and appear at the foot of the appropriate page.

Acknowledgements: Include all sources of funding for the research presented in the manuscript and substantive contributions of individuals regarding the research or manuscript. All possible conflicts of interest should also be given here.

Abbreviations: Abbreviations (with the exception of those clearly well-established in the field) should be explained when they are first used.

Units of measurement: Measurements should be expressed in SI units wherever possible.

Drug names: Use generic names of drugs (first letter: lowercase) whenever possible. Registered trade names (first letter: uppercase) should be marked with the superscript registration symbol ® or ™ when they are first mentioned.

Tables and illustrations: Tables and figures must be numbered (e.g. Figure 1, Figure 2) and submitted as separate files. Tables require a heading and figures a legend, which must provide sufficient information for either to stand alone. Each figure and table must be cited in the text numerically. Tables should be in Word format. b/w half-tone and color figures must have a final resolution of 300 dpi after scaling to final size, line drawings 1200 dpi. Color figures must be in RGB format. All figures should be in a common format such as PSD, TIF, PNG, EPS or WMF. Vector graphics should be in PPT, AI or EPS format.
Color Illustrations

Online edition: Color figures are reproduced free of charge. In the print version, the figures are reproduced in black and white. Referring to colors in the text and figure legends should be avoided.

Print edition: Up to 6 color figures per page can be integrated within the text at CHF 960.00 per page.

References

Identity references in the text using Arabic numerals (in square brackets). Do not alphabetize; number references sequentially in the order cited in the text. Material submitted for publication but not yet accepted should be referred to as [unpublished data] and should not be included in the reference list. The reference list should include only those publications which are cited in the text. Authors' surnames should be followed by their initials with no punctuation other than a comma to separate individual authors. Preferably cite all authors (if not possible include at least 3 authors followed by et al). Abbreviate journal names according to the list of journals indexed for MEDLINE on the NLM website. Also see International Committee of Medical Journal Editors: Uniform Requirements for Manuscripts Submitted to Biomedical Journals (http://www.ICMJE.org).

Examples


Reference Management Software: The use of EndNote is recommended to facilitate formatting of citations and reference lists. The journal output style can be downloaded from http://endnote.com/downloads/styles.

Supplementary Material and Multimedia Files

Multimedia files and other supplementary files, directly relevant but not essential to the conclusions of a paper, enhance the online version of a publication and increase its visibility on the web. These files will undergo editorial review. The Editors reserve the right to limit the scope and length of the supplementary material. Multimedia and supplementary material should meet production quality standards for publication without the need for any modification or editing. Files should not exceed 10 MB in size. Figures and tables need to have titles and legends, and all files should be supplied separately and labeled clearly. All supplementary material should be referred to in the main text. A DOI number will be assigned to supplementary material and it will be hosted online at https://karger.figshare.com under a CC BY license. Authors will be charged a processing fee of CHF 250.00 for supplementary material.

English Language Editing

For authors whose native language is not English, use of a professional language editing service prior to submission can help to avoid delays with the review process.

Digital Object Identifier (DOI)

A DOI number will be available as a unique identifier on the title page of each article. DOIs are useful for identifying and citing articles published online without volume or issue information (for more information, see www.doi.org).

Self-Archiving/Green Open Access

Karger permits authors to archive their pre-prints (i.e. pre-peer review) or post-prints (i.e. accepted manuscript after peer review but before production) on their personal or their institution's internal website. In addition, authors may post their accepted manuscripts in public Open Access repositories and scientific networks (e.g. ResearchGate or Mendeley) no earlier than 12 months following publication of the final version of their article. For all self-archiving, the posted manuscripts must:

- Be used for noncommercial purposes only
- Be linked to the final version on www.karger.com

Include the following statement:

‘This is the peer-reviewed but unedited manuscript version of the following article: [insert full citation, e.g. Cytogenet Genome Res 2014;142:227–238 [DOI: 10.1159/000361001]]. The final, published version is available at http://www.karger.com/doi-[insert DOI number].’

It is the author’s responsibility to fulfill these requirements.

For papers published online first with a DOI number only, full citation details must be added as soon as the paper is published in its final version. This is important to ensure that citations can be credited to the article.

Manuscripts to be archived in PubMed Central due to funding requirements will be submitted by Karger on the author’s behalf (see Funding Organizations (NIH etc.)).

For self-archiving Author’s Choice™ (Gold Open Access) articles, see Author’s Choice™.

Author’s Choice™

Karger’s Author’s Choice™ service broadens the reach of your article and gives all users worldwide free and full access for reading, downloading and printing at www.karger.com. The option is available for a one-time fee of CHF 3,000.00, which is a permissible cost in grant allocation. More information can be found at www.karger.com/author_choice.

The final, published version of the article may be posted at any time and in any repository or on other websites, in accordance with the relevant Creative Commons license. Reposted Open Access articles must:

- Follow the terms of the relevant Creative Commons license
- Be linked to the final version on www.karger.com
- Include the following statement:

‘The final, published version of this article is available at http://www.karger.com/doi-[insert DOI number]. It is the author’s responsibility to fulfill these requirements.’

For papers published online first with a DOI number only, full citation details must be added as soon as the paper is published in its final version. This is important to ensure that citations can be credited to the article.

Funding Organizations (NIH etc.)

The U.S. National Institutes of Health (NIH) Public Access Policy mandates that accepted, peer-reviewed manuscripts are archived in its digital database, PubMed Central (PMC), within 12 months of the official publication date. Authors are to submit NIH-funded articles to PMC on behalf of the authors immediately upon publication. The NIH assigns a PMCID within approximately 1 month and the manuscript will appear in PMC after a 12-month embargo. For authors making their paper Open Access through Author’s Choice™, the embargo will be overridden, thereby accelerating the accessibility of the article. Karger also complies with other funders’ requirements (including Wellcome Trust and RCUK) for submission to PMC. Authors should include information on their grants in the Acknowledgements section of their papers.

Copy Editing

Manuscripts accepted for publication by Karger Publishers are subject to copy editing.

Proofs

An email containing a link to download the proofs will be sent to the corresponding author. Proofs should be returned within 48 hours. Alterations made in proofs, other than the correction of printer’s (introduced) errors, are charged to the author and may require editorial approval.

Page Charges

There is no page charge for papers of 3 or fewer printed pages (including tables, illustrations and references). Authors are charged CHF 325.00 for each additional complete or partial printed page.

Reprints

An order form with a price list can be requested when returning the corrected proofs. Orders submitted after the issue is printed are subject to considerably higher prices.
General Information

Subscription Rates: Subscriptions run for a full calendar year. Prices are given per year.

<table>
<thead>
<tr>
<th></th>
<th>Print or Online</th>
<th>Print+Online combined</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Personal</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CHF</td>
<td>CHF 1232.00</td>
<td>CHF 1280.00</td>
</tr>
<tr>
<td>EUR</td>
<td>EUR 1027.00</td>
<td>EUR 1066.00</td>
</tr>
<tr>
<td>USD</td>
<td>USD 1257.00</td>
<td>USD 1305.00</td>
</tr>
<tr>
<td><strong>postage and handling</strong></td>
<td>(added to print and print-online)</td>
<td>(added to print and print-online)</td>
</tr>
<tr>
<td>CHF</td>
<td>CHF 45.60 Europe, CHF 67.20 Overseas</td>
<td></td>
</tr>
<tr>
<td>EUR</td>
<td>EUR 40.80</td>
<td></td>
</tr>
<tr>
<td>USD</td>
<td>USD 62.40</td>
<td></td>
</tr>
</tbody>
</table>

**Institutional subscription:**

<table>
<thead>
<tr>
<th></th>
<th>Print or Online</th>
<th>Print+Online combined</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHF</td>
<td>CHF 2464.00</td>
<td>CHF 2834.00</td>
</tr>
<tr>
<td>EUR</td>
<td>EUR 2053.00</td>
<td>EUR 2361.00</td>
</tr>
<tr>
<td>USD</td>
<td>USD 2514.00</td>
<td>USD 2891.00</td>
</tr>
<tr>
<td><strong>postage and handling</strong></td>
<td>(added to print and print-online)</td>
<td>(added to print and print-online)</td>
</tr>
<tr>
<td>CHF</td>
<td>CHF 57.00 Europe, CHF 84.00 Overseas</td>
<td></td>
</tr>
<tr>
<td>EUR</td>
<td>EUR 51.00</td>
<td></td>
</tr>
<tr>
<td>USD</td>
<td>USD 78.00</td>
<td></td>
</tr>
</tbody>
</table>

Back Volumes and Single Issues: Information on availability and prices of single print issues and print or electronic back volumes can be obtained from Customer Service at service@karger.com.

Bibliographic Indices: This journal is regularly listed in bibliographic services, including Current Contents® and PubMed/MEDLINE.

Photocopying: This journal has been registered with the Copyright Clearance Center (CCC), as indicated by the code appearing on the first page of each article. For readers in the US, this code signals consent for copying of articles for personal or internal use, or for the personal or internal use of specific clients, provided that the stated fee is paid per copy directly to Copyright Clearance Center Inc., 222 Rosewood Drive Danvers, MA 01923 (USA).

A copy of the first page of the article must accompany payment. Consent does not extend to copying for general distribution, for promotion, for creating new works, or for resale. In these cases, specific written permission must be obtained from the copyright owner, S. Karger AG, P.O. Box CH–4009 Basel (Switzerland).

Change of Address:
Both old and new address should be sent to the subscription source.

Photo of Paul Ehrlich on inner title page
Courtesy of the Paul-Ehrlich-Institute, Langen, Germany
PTS50 - The Prokaryotic Phosphoenolpyruvate: Sugar Phosphotransferase System
50 Years After Its Discovery

Editor
Milton H. Saier

In 1964 Saul Roseman first described the phosphotransferase system (PTS) – a novel sugar-phosphorylating system in Escherichia coli. This compendium results from an international meeting held in Göttingen, Germany, during the summer of 2014 to commemorate the 50th anniversary of his discovery. A number of active researchers with a focus on the PTS reported their most recent findings concerning the structures, functions, mechanisms of action and physiological consequences of this complex system. The numerous aspects of the PTS, including a discussion regarding its impact on bacterial physiology, pathogenesis and ecology, are presented in this up-to-date compendium, which will provide a valuable source of information for many years to come.

Researchers, students and teachers of the physiology of archaean and bacteria will find this compendium an essential source of reference. Additionally, biochemists and geneticists interested in the functions and mechanisms of complex enzymes, transport or regulatory systems in microbes will present in this up-to-date compendium, which will provide a valuable source of information for many years to come.

The easiest way to order: www.karger.com

Karger – Medical and Scientific Publishers
CH-4009 Basel, Switzerland
orders@karger.com, t +41 61 306 12 34
www.karger.com
Where do we come from? Is our destiny determined by the genes we inherit? In this book Gottfried Schatz, the world-renowned biochemist and co-discoverer of mitochondrial DNA, gives lucid – albeit often surprising – answers to universal questions and takes the reader on a fascinating journey of discovery across the boundaries of scientific disciplines. With passion and a keen sense of wonder he draws on philosophy, cultural history and art to formulate his reflections on the mysteries of life. These essays on key issues in the natural sciences will appeal not only to scientists but to all inquisitive minds, regardless of educational and professional background.

Monographs in Virology
Compact and thorough reference volumes for virologists and non-virologists alike

A skilful selection of topics of exceptional importance and a panel of acknowledged experts as authors have ensured an outstanding reputation for this series. Each monograph, centered on an active area of virologic research, provides a critical evaluation of recent progress and a useful commentary on the direction of future research. Characterized by a consistently high standard of scholarship and clear presentation of content, volumes in this series have proved their enduring value as convenient reference tools for both virologists working in the field and scientists working in allied areas.
Contents

See the journal website for contents
Respiration brings together the results of both clinical and experimental investigations on all aspects of the respiratory system in health and disease. Clinical improvements in the diagnosis and treatment of chest and lung diseases are covered, as are the latest findings in physiology, biochemistry, pathology, immunology and pharmacology. The journal includes classic features such as editorials that accompany original articles in clinical and basic science research, reviews and letters to the editor. Further sections are: The Eye Catcher, What's Your Diagnosis?, New Insights from Clinical Practice, Selected contributions (Tokyo), Selected contributions (Tel Aviv), Selected contributions (Porto), Selected contributions (Melbourne, Vic.), and Selected contributions (Kakamigahara). A complete guide to progress in thoracic medicine.

Respiration

Founded: 1944
Category: Clinical Research
Field of Interest: Respiratory System

Listed in bibliographic services, including Journal Citation Reports, PubMed/MEDLINE, Embase, Ameded

2016: Volumes 91, 92
6 issues per volume
Language: English
ISSN 0025–7931
e-ISSN 1423–0356

Impact Factor: 2.593

More information at www.karger.com/res
Antimicrobial Section

249 Potential of Casiopeínas® Copper Complexes and Antituberculosis Drug Combination against Mycobacterium tuberculosis
Barbosa, A.R.; Caleffi-Ferracioli, K.R. (Maringá); Leite, C.Q.F. (São Paulo); García-Ramos, J.C.; Toledano-Magaña, Y.; Ruiz-Azuara, L. (Mexico D.F.); Siqueira, V.L.D. (Maringá); Pavan, F.R. (São Paulo); Cardoso, R.F. (Maringá)

275 Antibiotic Resistance Patterns and a Survey of Metallo-β-Lactamase Genes Including bla-IMP and bla-VIM Types in Acinetobacter baumannii Isolated from Hospital Patients in Tehran
Aghamiri, S. (Lahijan); Amirmozafari, N. (Tehran); Fallah Mehrabadi, J. (Qom); Fouladtan, B. (Lahijan); Hanafi Abdar, M. (Tehran)

Novel Insights from Clinical Practice

236 Gemcitabine-Induced Subacute Cutaneous Lupus Erythematosus: A Case Report
Ben Zvi, M.; Vaknine, H.; Menczer, J.; Peled, O.; Ben Shem, E.; Schreiber, L.; Levy, T. (Holon/Tel Aviv)

Anticancer Section

Review

223 Drug Resistance to EGFR Inhibitors in Lung Cancer
Tetsu, O.; Hangauer, M.J.; Phuchareon, J.; Eisele, D.W.; McCormick, F. (San Francisco, Calif.)

Original Papers

240 Second-Line Intraperitoneal Chemotherapy for Recurrent Epithelial Ovarian, Tubal and Peritoneal Cancer: A Propensity Score-Matching Study
Lu, C.-H.; Chang, Y.-H.; Lee, W.-H.; Chang, Y.; Peng, C.-W. (Taichung/Taipei); Chuang, C.-M. (Taipei); Task Force on Intraperitoneal Chemotherapy of Ovarian Cancer

256 Weight Loss Associated with Platinum-Based Chemotherapy in Patients with Advanced Lung Cancer

262 Efficacy and Safety Assessment of Paclitaxel in Patients with Docetaxel-Resistant Esophageal Squamous Cell Carcinoma

269 Clinical Impact of Bevacizumab in Patients with Relapsed Glioblastoma: Focus on a Real-Life Monocentric Survey (SVI Study)