TABLE OF CONTENTS

- Description p.1
- Audience p.2
- Impact Factor p.2
- Abstracting and Indexing p.2
- Editorial Board p.2
- Guide for Authors p.5

DESCRIPTION

*Clinical Therapeutics* provides peer-reviewed, rapid publication of recent developments in drug and other therapies as well as in diagnostics, pharmacoeconomics, health policy, treatment outcomes, and innovations in drug and biologics research. In addition, *Clinical Therapeutics* features updates on specific topics collated by expert Topic Editors. Clinical Therapeutics is read by a large international audience of scientists and clinicians in a variety of research, academic, and clinical practice settings. Articles are indexed by all major biomedical abstracting databases.

Published articles range from pivotal studies exploring new chemical entities in large, multicenter trials to those exploring repurposing of marketed agents. Additionally, pilot studies; reports that assess drug safety and tolerability in all phases of development; new routes of administration and new formulations; pharmacokinetic, bio-availability, and biosimilarity; and changes in practice guidelines and standards, are all of interest for publication. Clinical Therapeutics also understands the importance of strengthening the body of evidence surrounding particular agents through the publication of replication studies, negative trials, and failed trials.

Beyond the clinic, we seek reports that examine the real-world implications of therapeutics such as comparative effectiveness and pharmacoeconomics studies as well as work that has implications for health policy. Commentaries, which include perspectives and contemporary issues, are sought to offer a balance of viewpoints and scholarly opinion on a broad array of drug-related topics. Case reports, which remain a vital part of our mission, offer clinically valuable lessons. All manuscripts are peer reviewed by independent clinicians or scientists for clinical relevance, technical accuracy, methodological rigor, clarity, and objectivity using a blind review process.

In addition to feature articles published monthly, each issue of *Clinical Therapeutics* features a specific theme section dedicated to an annual update of a specific topic area. A special guest editor will compose each update with reviews, commentaries, and original research highlighting what's new or controversial in the topical specialty. Authors are invited to submit manuscripts for consideration in the topic updates, identifying submissions as such in their cover letters. Submissions not selected for the updates will be considered for general publication. Submit your manuscript at [https://www.editorialmanager.com/clinther](https://www.editorialmanager.com/clinther).
AUDIENCE

Research Clinicians in Academia and Industry, Practicing Physicians, Pharmacologists, and Specialists in Pharmacoeconomics, Outcomes Research and Health Policy.

IMPACT FACTOR

2019: 3.119 © Clarivate Analytics Journal Citation Reports 2020

ABSTRACTING AND INDEXING

Current Contents - Clinical Medicine
Chemical Abstracts
Current Opinion Series
Cancerlit
BIOSIS Citation Index
De Haen Drug Data
Embase
International Pharmaceutical Abstracts
Web of Science
Cambridge Scientific Abstracts
Martindale: The Extra Pharmacopeia (Martindale Online)
PubMed/Medline
Medical Documentation Service
Nursing and Allied Health
Smoking and Health
Research Alert
CINAHL
Current Awareness in Biological Sciences
PsycINFO
Iowa Drug Information Service (IDIS)
Derwent Drug File
Sociedad Iberoamericana de Informacion Cientifica (SIIC) Data Bases
Science Citation Index
PharmacoEconomics and Outcomes News
MUST
Scopus

EDITORIAL BOARD

Editors-in-Chief
Ravi Jhaveri, Northwestern University Feinberg School of Medicine, Chicago, Illinois, United States of America
Jill L. Maron, Tufts University School of Medicine, Boston, Massachusetts, United States of America

Topic Editors
Allergy, Asthma, and Immunology
Theoharis Theoharides, Tufts University School of Medicine, Boston, Massachusetts, United States of America

At Large
Philip Walson, University of Göttingen, Göttingen, Germany

Cardiology and Cardiovascular Diseases
Ferrah Choudhary, Nottingham City Hospital, Nottingham, United Kingdom
Anna Franzone, University of Naples Federico II, Napoli, Italy
Federica Ilardi, University of Naples Federico II, Napoli, Italy

Devices
Paul Slowey, Oasis Diagnostics, Vancouver, Washington, United States of America
Oncology and Hematology
Andrea Bullock, BETH ISRAEL DEACONESS MEDICAL CENTER, Boston, Massachusetts, United States of America

Pain Management and Treatment
Jason Hack, Brown University Warren Alpert Medical School, Providence, Rhode Island, United States of America

Pharmacoepidemiology
Gregory S. Calip, University of Illinois at Chicago, Chicago, IL, United States of America
Cynthia Willey, University of Rhode Island, Kingston, Rhode Island, United States of America

Placebo and Nocebo Research
Seetal Dodd, Deakin University, Victoria, Australia

Statistics
Janet Forrester, Tufts University School of Medicine, Boston, Massachusetts, United States of America

Editors-in-Chief Emeritus
Richard Shader, Tufts University School of Medicine, Boston, Massachusetts, United States of America
Philip Walson, University of Göttingen, Göttingen, Germany

Women’s Health
Megan L. Evans, Tufts University School of Medicine, Boston, Massachusetts, United States of America

International Consulting Editors
Romuald Bellman, Medical University of Innsbruck, Innsbruck, Austria
Marie Besson, University Hospitals Geneva, Geneve, Switzerland
Bernard Cheung, Queen Mary Hospital, Hong Kong Hong Kong
Emilio Clementi, University of Milan, Milan, Italy
Jozef Glasa, Slovak Medical University, Bratislava, Slovakia
Sinem Ezgi Gulmez, Koc University, Istanbul, Turkey
Maria Teresa Herdeiro, University of Aveiro, Aveiro, Portugal
Alexander Khokhlov, Yaroslavl State Medical University, Yaroslavl, Russian Federation
Adrian Llerena, University Hospital Complex Badajoz, Badajoz, Spain
Stefan Oswald, University of Greifswald, Greifswald, Germany
Donald Singer, Fellowship of Postgraduate Medicine, London, United Kingdom
INTRODUCTION

Clinical Therapeutics provides peer-reviewed, rapid publication of recent developments in drug and other therapies as well as in diagnostics, pharmacoeconomics, health policy, treatment outcomes, and innovations in drug and biologics research. In addition Clinical Therapeutics features updates on specific topics collated by expert Topic Editors. Clinical Therapeutics is read by a large international audience of scientists and clinicians in a variety of research, academic, and clinical practice settings. Articles are indexed by all major biomedical abstracting databases.

Published articles range from pivotal studies exploring new chemical entities in large, multicenter trials to those exploring repurposing of marketed agents. Additionally, pilot studies; reports that assess drug safety and tolerability in all phases of development; new routes of administration and new formulations; pharmacokinetic, bio-availability, and biosimilarity; and changes in practice guidelines and standards, are all of interest for publication. Clinical Therapeutics also understands the importance of strengthening the body of evidence surrounding particular agents through the publication of replication studies, negative trials, and failed trials.

Beyond the clinic, we seek reports that examine the real-world implications of therapeutics such as comparative effectiveness and pharmacoeconomics studies as well as work that has implications for health policy. Commentaries, which include perspectives and contemporary issues, are sought to offer a balance of viewpoints and scholarly opinion on a broad array of drug-related topics. Case reports, which remain a vital part of our mission, offer clinically valuable lessons. All manuscripts are peer reviewed by independent clinicians or scientists for clinical relevance, technical accuracy, methodological rigor, clarity, and objectivity using a blind review process.

In addition to feature articles published monthly, each issue of Clinical Therapeutics features a specific theme section dedicated to an annual update of a specific topic area. A special guest editor will comprise each update with reviews, commentaries, and original research highlighting what's new or controversial in the topical specialty. Authors are invited to submit manuscripts for consideration in the topic updates, clearly identifying submissions as such in their cover letters. Submissions not selected for the updates will be considered for general publication. Submit your manuscript at https://www.editorialmanager.com/clinther.

Pre-submission Inquiries

Clinical Therapeutics is delighted to respond to pre-submission inquiries. Please send a letter of inquiry together with your proposed manuscript title and abstract for consideration to the editorial office at clinther@elsevier.com; all queries will be dealt with promptly.

Page and Manuscript Fees

Clinical Therapeutics charges page fees to publish. Page fees are not optional unless the author is approved for a fee waiver (see waiver information below). Please note, page fees as described, are completely separate from the payment option to publish your paper as an Open Access article.

Corresponding authors of manuscripts accepted for publication will be charged the following rates:

- For Original Research papers: A fee of USD $600 per printed journal page is charged for accepted papers; for example, a 10 page paper will be invoiced at $6000
- For Review articles: A flat fee of USD $2500
- For Commentaries, Brief Reports, Pilot Studies, and Case Reports: A flat fee of USD $2000
- For Research Letters: A flat fee of USD $1000

Upon article acceptance and delivery of a composed article proof, payment instructions will be provided to corresponding author with a link to a payment portal ("Submission Start"). Author is expected to complete payment with 48 hours, and to do so, prior to returning article proofs. Please note: author’s article will not be published until such time payment has been satisfied.
Express track

Clinical Therapeutics offers Express Track peer review service for time-sensitive manuscripts, for a fee of $1000 USD per submitted manuscript for Original Research. This fee is nonrefundable and noncancellable. Payment instructions are provided at the time of submission. Express Track submission fee guarantees you:

- High-quality peer review, completed within 5-10 business days.
- A reject or revise decision provided to the author within 3 business days of receipt of reviewers' comments by the editorial office.
- A final decision on revised manuscripts within 15 business days of receipt (excluding requests for subsequent revisions).

A fee of $750 per printed journal page is charged for accepted Express Track papers. Upon article acceptance and delivery of a composed article proof, payment instructions will be provided to corresponding author with a link to a payment portal ("Submission Start"). Author is expected to complete payment with 48 hours, and to do so, prior to returning article proofs.

Accepted manuscripts are published online in advance of print within 20 days from acceptance (pending author approval of finished proof and payment of page charges), and are scheduled for publication in the next available issue.

If you would like to use Express Track peer review service, please request this in your cover letter.

Waiver Policy
If you have no funding for page charges, you MUST request a waiver at the time of submission, state the reason for requesting a waiver, and provide appropriate formal documentation which supports your request. Such information must be presented at the time of submission, and it must clearly indicate that your research/study/grant does not support funds for publication. Such documentation may include a copy of the grant proposal, or an official letter from your institution, dean, or sponsor which clearly states there is no money for publication fees.

Please complete the Waive Fee Request form and upload it with your manuscript and formal documentation at the time of submission. Waive Fee Requests that are not supported by formal documentation will not be considered. Please note: No fee waiver or reduction in fees will be granted after a manuscript is submitted.

The ability to pay the fee does not influence decisions regarding the acceptance of a paper, which is solely dependent on the peer-review process. Please note: Express Track manuscripts are not eligible for a reduced or waived fee.

Any paper that is granted a full fee waiver will be published ONLINE ONLY.

ARTICLE TYPES

Original Research
Submissions categorized as Original Research describe substantive, well-controlled clinical research projects including clinical trials, pharmacokinetic/pharmacodynamic studies, meta-analyses, observational studies, health economic evaluations, and epidemiologic studies. Manuscripts should be prepared as described (See PREPARATION AND formatting) and must provide enough detail about the study design, population, interventions, data collection and analysis methods, and outcomes to permit study replication. Data must be original and presented in accordance with journal policies (See EDITORIAL POLICIES) and EQUATOR Reporting Guidelines for the applicable study design (eg, CONSORT for randomized trials, STROBE for observational studies, CHEERS for economic evaluations, PRISMA for meta-analyses).

Abstract: ≤400 words, structured (See Abstract)

Keywords: 4-6 terms

Main Text: ≤6000 words, structured as follows: Introduction, Participants and Methods, Results, Discussion, Conclusions

Tables/Figures: ≤8

References: Required, unlimited
Supplemental Material: Allowed, unlimited length (See Supplemental Material)

Reviews
Comprehensive, evidence-based narrative and systematic reviews are welcome. Systematic reviews without meta-analyses are considered and published as Reviews, while systematic reviews with meta-analyses should be submitted as Original Research. For the Pharmacoeconomics, Outcomes, and Health Policy section, only systematic reviews will be considered. Authors should contact the editorial office to discuss the topic area to avoid duplication with previously submitted or accepted manuscripts.

Systematic reviews should critically assess available data on a specific topic relevant to clinical practice, disease prevention, diagnostics, therapeutics, or health policy. Systematic reviews should follow PRISMA guidelines (http://www.prisma-statement.org/index.htm) and include a PRISMA-style flow diagram (as a Figure or Supplemental Material) and checklist for review. The Methods section should identify the databases that were searched, search terms used, and inclusion/exclusion criteria for identified articles; an assessment of the validity of reviewed studies; and a summary that includes future directions for studies in this area. Each study mentioned in the review should include the study design, a description of the study population (age range, disease/severity), the dose and duration of each treatment administered, and the data and P values to accompany any valid comparisons. While not required, prospective registration of systematic review protocols is strongly encouraged. If available, the protocol registration number, registry name, and URL should be indicated in the Methods. Systematic reviews should be identified as such in the title or subtitle.

Abstract: ≤400 words, structured (See Abstract)

Keywords: 4-6 terms

Main Text: ≤6000 words, structured as follows: Introduction, Methods, Results. Discussion, Conclusions

Tables/Figures: ≤6

References: Required, unlimited

Supplemental Material: Allowed, unlimited length (See Supplemental Material)

Narrative reviews should provide up-to-date information relevant to clinical practice, public health, or clinical-stage development of therapeutics and/or diagnostics. Narrative reviews should not focus solely on the authors' own work. Narrative reviews should include an Introduction that describes the background, purpose, and perspective of the article; a Methods section that describes the approach and literature search criteria (if any). A separate Results section is not required. Each study mentioned in the review should include the study design, a description of the study population (age range, disease/severity), the dose and duration of each treatment administered, and the data and P values to accompany any valid comparisons. Discussion of pre-clinical data is permitted to complement discussion of therapeutic/diagnostic strategies and their development. Narrative reviews must be identified as such in the Abstract and Methods.

Abstract: ≤400 words, structured (See Abstract)

Keywords: 4-6 terms

Main Text: ≤6000 words, structured as follows: Introduction, Methods, Results (optional), Discussion, Conclusions

Tables/Figures: ≤6

References: Required, unlimited

Supplemental Material: Allowed, unlimited length (See Supplemental Material)

Commentaries
These papers should address an important and current issue in clinical practice, health policy, or therapeutics/diagnostics research from the author's perspective. All clinical recommendations should be supported by relevant published guidelines or peer-reviewed literature. Evidence-based statements must be clearly distinguished from author opinion. Discussion of pre-clinical data is permitted to complement discussion of therapeutic/diagnostic strategies and their development. The submission should include a descriptive title, a brief Abstract, an Introduction, pertinent information detailing the position of the paper, a Discussion, a Conclusion (which may be part of the discussion), and references.

Abstract: ≤300 words, unstructured (See Abstract)

Keywords: 4-6 terms

Main Text: 3000-3500 words, structured as follows: Introduction, Discussion, Conclusions

Tables/Figures: ≤5

References: ≤60, required

Supplemental Material: Not permitted
**Brief Reports**
These papers are reports of preliminary clinical investigations that are narrowly focused or provide limited findings. The submission should include a descriptive and succinct title, a structured Abstract, an Introduction that specifies the importance of the study, a Methods section, Results, a Discussion, a Conclusion, and references. Although these submissions are shorter in length, Brief Reports must adhere to the journal’s ethical requirements and data reporting policies (See EDITORIAL POLICIES).

Abstract: ≤250 words, structured (See Abstract)

Keywords: 4-6 terms

Main Text: 2000-3000 words, structured as follows: Introduction, Methods, Discussion, Conclusions

Tables/Figures: ≤3

References: ≤30, required

Supplemental Material: Allowed, unlimited (See Supplemental Material)

**Pilot Studies**
A pilot study is a preliminary, exploratory, preparatory, small-sample effort undertaken to decide whether a larger study is warranted. The sample size is too small to permit generalizability, but it should provide a window into what a larger trial would look like. The submission should include a descriptive and succinct title, a structured Abstract, an Introduction that specifies the importance of the study, a Methods section, Results, a Discussion, a Conclusion, and references. Pilot Studies must adhere to the journal’s ethical requirements and data reporting policies (See EDITORIAL POLICIES).

Abstract: ≤250 words, structured (See Abstract)

Keywords: 4-6 terms

Main Text: 2000-3000 words, structured as follows: Introduction, Methods, Discussion, Conclusions

Tables/Figures: ≤3

References: ≤30, required

Supplemental Material: Allowed, unlimited (See Supplemental Material)

**Research Letters**
These letters are focused on previously published studies from which new findings have been generated. Since methods and other informative material are contained in the original paper, they can be referenced rather than repeated. Alternatively, research letters can describe novel or hypothesis-generating research that may stimulate further investigation or alert readers to clinically relevant but preliminary findings. These submissions should include a descriptive and succinct title; an Introduction that specifies the rationale for the report, beginning with a statement similar to "This communication provides..."; a description of any new methods and results; a Discussion/Conclusion section; and selected references. Please note that Research Letters may be chosen, at the editor’s discretion, to be published online only. In such instances, authors will be informed of this decision at acceptance and are free to withdraw their submission. Online only articles are indexed and are available in full text or PDF formats identical to that of print articles.

Abstract: None

Keywords: 4-6

Main Text: 1000-2000 words, structured as follows: Introduction, Methods, Discussion, Conclusions

Tables/Figures: ≤2

References: ≤30, required

Supplemental Material: Not permitted

**Case Reports**
Case reports are retrospective analyses of one, two, or three clinical cases. Case reports are an important part of post-marketing surveillance. They serve an alerting function by informing about new, unusual, or unexpected events. These events may be adverse drug reactions, drug-drug interactions, or drug-disease interactions. Before submitting a case report, the author(s) must conduct a thorough literature search as well as a review of product labeling when a drug is involved. This will reduce the reporting of what may already be well known.

Reports of suspected adverse drug reactions should provide a description of the event, details regarding the implicated medication (e.g., purpose, when initiated), effects of discontinuation or re-challenge, treatment for the reaction, and duration of patient follow-up, if any. Evidence for causality must be strong. In the case of adverse drug events, use of the Naranjo Adverse Drug Reaction probability scale to determine the likelihood that the events were drug-related (Naranjo

Importantly, authors should clearly indicate in the cover letter whether the case was part of a larger study or meta-analysis, and whether the case was reported in aggregate elsewhere.

The report should include a descriptive, succinct title; an introduction; a well-documented case description; discussion; conclusions; and references. The Introduction should announce the subject and purpose of the report, including statements of why the case is important and how the literature search was performed. The Case Description should include a narrative account of the case with brief, pertinent clinical, laboratory, and medication information. The Discussion should comment on evidence that the case is new or unusual and consider possible alternative explanations for case features. The Conclusions should provide a summary of the adverse drug reaction-medications relationship, how to treat it, and how to avoid it. (For more information about what constitutes a good case report, see Vandenbroucke JP. In defense of case reports and case series. Ann Intern Med. 2001;134:330-334 and DeBakey L, DeBakey S. The case report. I. Guidelines for preparation. Int J Cardiol. 1983;4:357-364.)

To be considered, authors must provide documentation of patient informed consent to publish, which can be attached to the cover letter. All identifying information must be masked per HIPAA guidelines prior to submission. (See Ethical Considerations for Case Reports).

Please note that Case Reports may be selected, at the editor's discretion, to be published online only. Additionally, authors may be asked to reduce the length of the report substantially if similar cases were reported previously. In such cases, authors will be informed of the decision to forgo print at acceptance. Online only articles will be indexed and available as full text or PDF, identical to that of print articles.

Abstract: None
Keywords: 4-6
Main Text: 1500-3500 words, structured as follows: Introduction, Case Description, Discussion, Conclusions
Tables/Figures: ≤2
References: ≤15, required
Supplemental Material: Not permitted

Letters to the Editor
These are objective, constructive, or educational critiques of papers published in Clinical Therapeutics. Accepted letters will be sent to the author of the original paper for a response. Each letter and response is published together. Alternatively, letters may focus on topical issues that are of interest to readers of
Abstract: None
Keywords: None
Main Text: ≤1000 words, unstructured
Tables/Figures: ≤1
References: Required, ≤5
Supplemental Material: Not permitted

Video Articles
Clinical Therapeutics encourages authors who have presented a talk at a meeting to convert their talk into a video production for online publication. Interested authors are encouraged to view the following example: Untangling tau imaging. Alzheimers Dement (Amst). 2016;4:39-42. A pre-submission inquiry is required for this type of submission. See Video Article Guidelines for preparation instructions.

PREPARATION AND FORMATTING
The basic elements of all submissions are as follows, and details on each item are provided below. Manuscripts, tables, figures, and supplemental material must be submitted in their original file formats; do not submit PDFs.1 Document Requirement Cover Letter Required ICMJE Form(s) Required for each author Declaration of Interest Required Title Page Required Highlights Required for Original Research Graphical Abstract Optional Manuscript File (without author details) Required for new and revised submissions Tables Optional Figures Optional Supplemental Material Optional
Double-blind review
This journal uses double-blind review, which means the identities of the authors are concealed from the reviewers, and vice versa. More information is available on our website. To facilitate this, please include the following separately:

Title page (with author details): This should include the title, authors' names, affiliations, and a complete address for the corresponding author including an e-mail address. Authors may provide their individual contribution statement on the title page if they are not using the CRediT roles.

Blinded manuscript (no author details): The main body of the paper (including the legends, references, and any acknowledgments) should not include any identifying information, such as the authors' names or affiliations.

Cover Letter
A cover letter is required for all article types. To facilitate double-blind peer review, the cover letter must be uploaded as a separate file in Word of PDF format; it will not be made available to reviewers. The cover letter should include:

- Title, authors, number of pages, and numbers of tables and figures
- Indication that the paper has been read and approved by all authors
- Name of the Special Section in which the paper is to be included, if applicable
- Information about any previous presentation of the data (e.g., abstract, poster or presentation at a meeting or published on a preprint service [provide DOI])
- Information about the existence of any closely related manuscripts that have been submitted for simultaneous consideration to the same or another journal
- A copy of the permission granted to reproduce or adapt any copyrighted material from another source or a notice that permissions are pending

ICMJE Form(s)
Each author must complete the ICMJE form for disclosure of Potential Conflicts of Interest available here. Download the form to your computer. Open the form in Adobe Acrobat Reader, fill it out and then save it to your computer. The corresponding author is responsible for collecting the completed forms from each author and submitting them direct as part of the manuscript upload.

Declaration of Interest
All authors must disclose any financial and personal relationships with other people or organizations that could inappropriately influence (bias) their work. Examples of potential competing interests include employment, consultancies, stock ownership, honoraria, paid expert testimony, patent applications/registrations, and grants or other funding. Authors must disclose any interests in two places: 1. A summary declaration of interest statement in the title page file (if double-blind) or the manuscript file (if single-blind). If there are no interests to declare then please state this: 'Declarations of interest: none'. This summary statement will be ultimately published if the article is accepted. 2. Detailed disclosures as part of a separate Declaration of Interest form, which forms part of the journal's official records. It is important for potential interests to be declared in both places and that the information matches. More information.

Authors should declare the role of study sponsors, if any, in the study design; in the collection, analysis and interpretation of data; in the writing of the manuscript; and in the decision to submit the manuscript for publication.

Title Page
To facilitate double-blind peer review, the title page must be uploaded as a separate file in the original file format; it will not be made available to reviewers.

Essential title page information
- Title. Concise and informative. Titles are often used in information-retrieval systems. Avoid abbreviations and formulae where possible. See Title.
- Author names and affiliations. Please clearly indicate the given name(s) and family name(s) of each author and check that all names are accurately spelled. You can add your name between parentheses in your own script behind the English transliteration. Following each author name, indicate the highest academic degree(s) obtained. Present the authors' affiliation addresses (where the actual work was done) below the names. Indicate all affiliations with a lower-case superscript...
letter immediately after the author's name and in front of the appropriate address. Provide the full postal address of each affiliation, including the country name and, if available, the e-mail address of each author.

- **Corresponding author.** Clearly indicate who will handle correspondence at all stages of refereeing and publication, also post-publication. This responsibility includes answering any future queries about Methodology and Materials. **Ensure that the e-mail address is given and that contact details are kept up to date by the corresponding author.**
- **Present/permanent address.** If an author has moved since the work described in the article was done, or was visiting at the time, a 'Present address' (or 'Permanent address') may be indicated as a footnote to that author's name. The address at which the author actually did the work must be retained as the main, affiliation address. Superscript Arabic numerals are used for such footnotes.
- **Author declaration of individual contribution.** All authors must have materially participated in the research and/or article preparation, so individual roles for all authors must be described. (See Author Contributions). Add this information here if not using the CRedit roles.

**Highlights**

Highlights are mandatory for Original Research as they help increase the discoverability of your article via search engines. They consist of a short collection of bullet points that capture the novel results of your research as well as new methods that were used during the study (if any). Please have a look at the examples here: example Highlights.

Highlights should be submitted in a separate editable file in the online submission system. Please use 'Highlights' in the file name and include 3 to 5 bullet points (maximum 85 characters, including spaces, per bullet point).

**Graphical Abstract**

Although a graphical abstract is optional, its use is encouraged as it draws more attention to the online article. The graphical abstract should summarize the contents of the article in a concise, pictorial form designed to capture the attention of a wide readership. Graphical abstracts should be submitted as a separate file in the online submission system. Image size: Please provide an image with a minimum of 531 × 1328 pixels (h × w) or proportionally more. The image should be readable at a size of 5 × 13 cm using a regular screen resolution of 96 dpi. Preferred file types: TIFF, EPS, PDF or MS Office files. You can view Example Graphical Abstracts on our information site.

Authors can make use of Elsevier's Illustration Services to ensure the best presentation of their images and in accordance with all technical requirements.

**Manuscript File**

The manuscript file should contain the following items: title, abstract, clinical trial registration (if applicable), keywords, main text, acknowledgments, figure/table legends, references. These items are described in detail below. All author names and identifying information must be removed from the manuscript file to facilitate double-blind peer review. The manuscript file should be structured according to article type, be double-spaced, include page numbers, and follow AMA style except as indicated below (See Style).

**Title**

The title should be concise, informative, and focused on the study objective. Statements about the conclusion(s) of the work should be avoided. Randomized controlled trials, meta-analyses, and systematic reviews should be identified as such in the title. Subtitles can be used to provide supplementary information (eg, study design); however, titles should be able to stand alone. Use nonproprietary drug names (See Names of Drugs and Devices); avoid abbreviations and formulae where possible.

**Abstract**

Abstracts should be structured or unstructured according to article type and word limits as detailed below. Abstracts are often presented separately from the article; therefore, must be able to stand alone. References should be avoided (if essential, the complete reference per AMA style must be given within the lines of text). Non-standard or uncommon abbreviations should be avoided (when necessary, they must be defined at their first use in the abstract).

**Structured abstracts** are required for Original Research (≤400 words), Reviews (≤400 words), Brief Reports (≤250 words), and Pilot Studies (≤250 words). Structured abstracts should contain sufficient detail as directed by the extension to the **CONSORT statement for abstracts**, and should be formatted as follows:
**Purpose:** Briefly provides the frame of reference for the reader and identifies the knowledge gap that the article seeks to address; clearly states the purpose of the research; and identifies the scientific hypotheses and questions being asked.

**Methods:** Succinctly describes study methodology, including study design, study dates, setting/data sources, inclusion and exclusion criteria, interventions, outcomes, statistical approaches, and adverse event assessment methodology.

**Findings:** Provides demographics of the study population, including sex, age range, and numbers of participants in each group; reports principle data and outcomes in a quantitative fashion, including effect sizes and confidence intervals or P values; includes adverse events.

**Implications:** Covers any limitations or problems in interpretation or generalization from the study findings as well as implication and future directions; must be strictly limited to what can be supported directly by the Findings, and what was identified in the Purpose section.

For manuscripts that require **clinical trial registration** (See Reporting and Registration of Clinical Trials), the name of the trial registry, trial registration number, and URL of the registry should be included immediately following the Implications section of the abstract.

**Unstructured abstracts** are required for Commentaries (?300 words). Unstructured abstracts should briefly describe the importance and clinical relevance of the topic, the objective, approach, and a summary of key points. Abstracts are not required for Research Letters, Case Reports, and Letters to the Editor.

**Keywords**
Immediately after the abstract, provide 4-6 keywords, using American spelling and avoiding general and plural terms and multiple concepts (avoid, for example, ‘and’, ‘of’). Be sparing with abbreviations: only abbreviations firmly established in the field may be eligible. These keywords will be used for indexing purposes.

**Body of Manuscript**
The main text should adhere to word limits and structure according to article type as detailed above. All submissions should adhere to journal policies (See EDITORIAL POLICIES) and EQUATOR Reporting Guidelines for the applicable study design (eg, CONSORT for randomized trials, STROBE for observational studies, CHEERS for economic evaluations, PRISMA for systematic reviews and meta-analyses).

**Introduction:** State the objectives/hypotheses of the work and provide an adequate background; avoid a detailed literature survey or a summary of the results. Required for all article types except Letters to the Editor.

**Methods:** Provide sufficient detail to allow the work to be replicated by others. Methods already published should be indicated by a reference: only relevant modifications should be described. For work involving human subjects, describe the (1) study design and randomization procedures; (2) study dates and setting; (3) institutional review board (RB) approval or waiver, including name of the IRB/ethics committee; (4) details of patient consent or assent of youth and children; (5) participants and conditions/factors studied, including full inclusion and exclusion criteria; (6) interventions, if any, with full description of placebo, sham, or control conditions [See Placebos in Clinical Trials]; (7) primary and secondary outcome measures, including whether secondary analyses were pre-specified; (8) detailed statistical analyses, with a priori significance thresholds, methods for handling missing data or outliers if applicable, and any relevant citations. Rationale for inclusion of only one sex or age group should be provided and scientifically justified [See Inclusion of Sex and Gender]. Systematic reviews and meta-analyses should follow PRISMA guidelines. Subheadings (up to two additional levels) are encouraged. A **Participants and Methods** section is required for Original Research, Brief Reports, Pilot Studies, and Research Letters. A **Methods** section is required for Reviews.

**Results:** The Results should be clear, concise, and relevant to the stated objectives/hypotheses. Describe the study population first, including sex, age, and other relevant demographic characteristics of subjects. All numeric data should be reported with descriptive and/or inferential statistical test results (including exact p-values, if available). For each outcome, report results for each group, the effect size, and its precision (ie, 95% confidence interval). Do not discuss implications or limitations.
in this section. Tables, figures, and subheadings (up to two additional levels) are encouraged. Results are required for Original Research (including meta-analyses), systematic Reviews, Brief Reports, and Pilot Studies; optional for narrative Reviews.

**Discussion:** The Discussion should explore the importance and relevance of the results of the work, not repeat them. Authors should critically examine the work, describe unexpected and/or contradictory findings, and address any limitations of the study design or statistically indeterminate results here. All inferences must be supported by evidence presented in the Results section. Authors should also discuss generalizability and clinical implications of findings, as well as any future studies needed. Avoid extensive citations and discussion of published literature. Subheadings (up to one additional level) are permitted. A Discussion is required for all article types except Letters to the Editor; a combined Results and Discussion section is often appropriate for narrative reviews.

**Conclusions:** The main conclusions of the study should be present.

**Acknowledgments**
Collate acknowledgments in a separate section at the end of the article before the references and do not, therefore, include them on the title page, as a footnote to the title or otherwise. List here those individuals who provided materials or assistance during the research (e.g., language help, writing assistance, or proofreading the article, etc). Do NOT list the names of authors or funder(s) in this paragraph.

**Disclosure of Funding Support**
All financial support for the submitted work must be reported in a separate section below the Acknowledgements. Authors should declare the role of study sponsors, if any, in the study design; in the collection, analysis and interpretation of data; in the writing of the manuscript; and in the decision to submit the manuscript for publication.

List funding sources in this standard way to facilitate compliance to funder's requirements:

Funding: This work was supported by the National Institutes of Health [grant numbers xxxx, yyyy]; the Bill & Melinda Gates Foundation, Seattle, WA [grant number zzzz]; and the United States Institutes of Peace [grant number aaaa].

It is not necessary to include detailed descriptions on the program or type of grants and awards. When funding is from a block grant or other resources available to a university, college, or other research institution, submit the name of the institute or organization that provided the funding.

If no funding has been provided for the research, please include the following sentence:

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

**Figure Captions**
Ensure that each illustration has a caption. Supply captions separately, not attached to the figure. A caption should comprise a brief title (not on the figure itself) and a description of the illustration. Keep text in the illustrations themselves to a minimum but explain all symbols and abbreviations used. If figures are not original, it is the author's responsibility to obtain permission from the original publisher; the source and a statement that permission has been obtained must be included in the caption.

**References**
Permissible Sources
References should include only published works or articles in press. Citation of a reference as 'in press' implies that the item has been accepted for publication and a DOI number must be included. Abstracts, unpublished data, and personal communications are not permitted in the reference list. Unpublished results and data published in abstract form may be mentioned in the text only if the methodological details and data are made available in supplemental digital content. Research datasets that have been assigned a global persistent identifier number are permitted.
Citation in Text
In-text citations should be indicated sequentially by superscript number(s) or in brackets. The authors can be referred to, but the reference number(s) must always be given. Please ensure that every reference cited in the text is also present in the reference list (and vice versa).

Reference List Format
There are no strict requirements for formatting the reference list at submission. References can be in any style or format as long as the style is consistent. Where applicable, author(s) name(s), journal title/book title, chapter title/article title, year of publication, volume number/book chapter and the pagination must be present. Use of DOI is highly encouraged. The reference style used by the journal will be applied to the accepted article by Elsevier at the proof stage. Note that missing data will be highlighted at proof stage for the author to correct. Journal names should be abbreviated according to the list of title word abbreviations: http://www.issn.org/2-22661-LTWA-online.php.

Data references
This journal encourages you to cite underlying or relevant datasets in your manuscript by citing them in your text and including a data reference in your Reference List. Data references should include the following elements: author name(s), dataset title, data repository, version (where available), year, and global persistent identifier. Add [dataset] immediately before the reference so we can properly identify it as a data reference. The [dataset] identifier will not appear in your published article.

Data Reference

Reference management software
Most Elsevier journals have their reference template available in many of the most popular reference management software products. These include all products that support Citation Style Language styles, such as Mendeley. Using citation plug-ins from these products, authors only need to select the appropriate journal template when preparing their article, after which citations and bibliographies will be automatically formatted in the journal's style. If no template is yet available for this journal, please follow the format of the sample references and citations as shown in this Guide. If you use reference management software, please ensure that you remove all field codes before submitting the electronic manuscript. More information on how to remove field codes from different reference management software.

Tables
Number tables consecutively in accordance with their appearance in the text. Each table should have a concise and descriptive caption. Place footnotes to tables below the table body and indicate them with superscript lowercase letters. Avoid vertical rules. Be sparing in the use of tables and ensure that the data presented in tables do not duplicate results described elsewhere in the article. Submit each table as a separate file in its original file format.

Figures
Figures should be numbered consecutively in accordance with their appearance in the text and uploaded as individual high-resolution files. Brief Figure Captions are required and should be supplied separately above the References section in the manuscript file (See Figure Captions). Authors are urged to consult the detailed guide on electronic artwork and adhere to the following:

Electronic Artwork
General points
• Make sure you use uniform lettering and sizing of your original artwork.
• Embed the used fonts if the application provides that option.
• Aim to use the following fonts in your illustrations: Arial, Courier, Times New Roman, Symbol, or use fonts that look similar.
• Number the illustrations according to their sequence in the text.
• Use a logical naming convention for your artwork files.
• Provide captions to illustrations separately.
• Size the illustrations close to the desired dimensions of the published version.
• Submit each illustration as a separate file.
• Ensure that color images are accessible to all, including those with impaired color vision.

Formats
If your electronic artwork is created in a Microsoft Office application (Word, PowerPoint, Excel) then please supply 'as is' in the native document format. Regardless of the application used other than Microsoft Office, when your electronic artwork is finalized, please 'Save as' or convert the images to one of the following formats (note the resolution requirements for line drawings, halftones, and line/halftone combinations given below):

- EPS (or PDF): Vector drawings, embed all used fonts.
- TIFF (or JPEG): Color or grayscale photographs (halftones), keep to a minimum of 300 dpi.
- TIFF (or JPEG): Bitmapped (pure black & white pixels) line drawings, keep to a minimum of 1000 dpi.
- TIFF (or JPEG): Combinations bitmapped line/half-tone (color or grayscale), keep to a minimum of 500 dpi.

Please do not:
- Supply files that are optimized for screen use (e.g., GIF, BMP, PICT, WPG); these typically have a low number of pixels and limited set of colors;
- Supply files that are too low in resolution;
- Submit graphics that are disproportionately large for the content.

**Color Artwork**

Please make sure that artwork files are in an acceptable format (TIFF [or JPEG], EPS [or PDF], or MS Office files) and with the correct resolution. For further information on the preparation of electronic artwork, please see [https://www.elsevier.com/artworkinstructions](https://www.elsevier.com/artworkinstructions).

Please note: Because of technical complications which can arise by converting color figures to 'gray scale' (for the printed version should you not opt for color in print) please submit in addition usable black and white versions of all the color illustrations.

**Supplemental Material**

Supplementary material such as applications, images, and sound clips, can be made available online via links published with your article. Supplementary material relevant to the work, but not critical to support the primary findings, is allowed for Original Research, Reviews, Brief Reports, and Pilot Studies. All supplemental materials, including tables and figures, must be mentioned in the main text and must be numbered consecutively in accordance with their appearance in the text (e.g., Table S1, S2, Figure S1). Submitted supplementary items are published online exactly as they are received (Excel or PowerPoint files will appear as such online). Please submit your material together with the article and supply a concise, descriptive caption for each supplementary file. Authors are encouraged to submit a single, consolidated file containing a table of contents followed by all supplemental material in order of appearance in the text. If you wish to make changes to supplemental material during any stage of the process, please make sure to provide an updated file. **Do not annotate any corrections** on a previous version. Please switch off the 'Track Changes' option in Microsoft Office files as these will appear in the published version.

**STYLE**

Manuscripts submitted to *Clinical Therapeutics* should be prepared in accordance with AMA Style unless otherwise noted. See *American Medical Association Manual of Style: A Guide for Authors and Editors, 10th Edition*.

**Abbreviations**

Define abbreviations that are not standard in this field in a footnote to be placed on the first page of the article. Such abbreviations that are unavoidable in the abstract must be defined at their first mention there, as well as in the footnote. Ensure consistency of abbreviations throughout the article.

**Names of Drugs and Devices**

Drugs should be referred to by their universally accepted generic names, not by proprietary names, unless the specific trade name is essential to the methods or discussion. In such cases, use the proprietary name once and the generic or descriptive name thereafter. US adopted names (USANs) are acceptable. If unnamed compounds are referred to, as much information as possible (e.g., class of compound) should be included and published references to the compound should be provided. If this is not possible because of intellectual property reasons, then this should be stated.

For drug-device combinations, capitalize the first letter of each term. At first mention in the abstract and in the main text, include the active ingredient and dose in parentheses following the product name.
Where proprietary names of drugs and drug-device combinations are used as permitted above, capitalize only the initial letter of the trademarked word (unless the trademarked name is an abbreviation) and do not include trademark symbols.

**Units of Measure**

Follow internationally accepted rules and conventions: use the international system of units (SI). If other units are mentioned, please give their equivalent in SI.

**Currency Values**

*Clinical Therapeutics* endeavors to make all manuscripts readily understandable by using universally accepted chemical names, structures, spelling, abbreviations, and formatting. For Pharmacoeconomics submissions, results are sometimes reported in the currency of the author(s)’s country. The relative value of currencies from some countries may not be obvious to some readers. Therefore, we now require that equivalencies in US dollars (USD) and European Union euros (EUR) be added in parentheses after other currencies. For example, 68 Indian rupees or INRs would be followed by ($1.00 USD/0.85 EUR). We recognize that currency values fluctuate. Therefore, equivalencies should reflect values at the time of submission.

**Language (usage and editing services)**

Please write your text in standard, grammatically correct English. If English is not your first language, authors are encouraged to consult with a colleague or professional whose native language is English to improve grammar and syntax prior to submission. Alternatively, authors may wish to visit Elsevier's language editing and copyediting services which are available both pre- and post-submission at: https://webshop.elsevier.com/language-editing-services/language-editing/ or our customer support site at https://service.elsevier.com for more information. Articles that are not cogent and clearly written will be returned to the author.

**Use of Inclusive Language**

Inclusive language acknowledges diversity, conveys respect to all people, is sensitive to differences, and promotes equal opportunities. Articles should make no assumptions about the beliefs or commitments of any reader, should contain nothing which might imply that one individual is superior to another on the grounds of race, sex, culture or any other characteristic, and should use inclusive language throughout. Authors should ensure that writing is free from bias, for instance by using 'he or she', 'his/her' instead of 'he' or 'his', and by making use of job titles that are free of stereotyping (e.g. 'chairperson' instead of 'chairman' and 'flight attendant' instead of 'stewardess').

**Usage of Sex vs Gender**

The term sex should be used when describing biological factors and the term gender should be used when referring to sociocultural factors.

**Footnotes**

Footnotes should be used sparingly. Number them consecutively throughout the article. Many word processors can build footnotes into the text, and this feature may be used. Otherwise, please indicate the position of footnotes in the text and list the footnotes themselves separately at the end of the article. Do not include footnotes in the Reference list.

**EDITORIAL POLICIES**

**Ethics in Publishing**

For information on Ethics in publishing and Ethical guidelines for journal publication see https://www.elsevier.com/publishingethics and https://www.elsevier.com/journal-authors/ethics.

Prospective authors are encouraged to read the Authors’ Submission Toolkit: A practical guide to getting your research published (available at http://informahealthcare.com/doi/pdfplus/10.1185/03007995.2010.499344). The Author Toolkit summarizes tips and “best practices” to increase awareness of editorial requirements, journal selection, submission processes, publication ethics, peer review, and effective communication with editors.

**Authorship**

All authors should have made substantial contributions to all of the following: (1) the conception and design of the study, or acquisition of data, or analysis and interpretation of data, (2) drafting the article or revising it critically for important intellectual content, (3) final approval of the version to be submitted.
Changes to Authorship
This policy concerns the addition, deletion, or rearrangement of author names in the authorship of accepted manuscripts:

Before the accepted manuscript is published in an online issue: Requests to add or remove an author, or to rearrange the author names, must be sent to the editorial office from the corresponding author of the accepted manuscript and must include: (a) the reason the name should be added or removed, or the author names rearranged and (b) written confirmation (e-mail, fax, letter) from all authors that they agree with the addition, removal or rearrangement. In the case of addition or removal of authors, this includes confirmation from the author being added or removed. Note that publication of the accepted manuscript in an online issue is suspended until authorship has been agreed.

After the accepted manuscript is published in an online issue: Any requests to add, delete, or rearrange author names in an article published in an online issue will follow the same policies as noted above and result in an erratum.

Author contributions
For transparency, each author is required to declare his or her individual contribution to the article: all authors must have materially participated in the research and/or article preparation, so roles for all authors should be described. The statement that all authors have approved the final article should be true and included in the cover letter. Please add the information regarding each author's individual contribution to the manuscript on the title page after the corresponding author's address.

Alternatively, authors may choose to submit an author statement file outlining their individual contributions to the paper using the relevant CRediT roles: Conceptualization; Data curation; Formal analysis; Funding acquisition; Investigation; Methodology; Project administration; Resources; Software; Supervision; Validation; Visualization; Roles/Writing - original draft; Writing - review & editing. Authorship statements should be formatted with the names of authors first and CRediT role(s) following. If authors choose the CRediT roles they should use the "CRediT Author Statement" file type for anonymity. More details and an example

Declaration of Interest
All authors must disclose any financial and personal relationships with other people or organizations that could inappropriately influence (bias) their work. Examples of potential competing interests include employment, consultancies, stock ownership, honoraria, paid expert testimony, patent applications/registrations, and grants or other funding. Authors must disclose any interests in two places: 1. A summary declaration of interest statement in the title page file (if double-blind) or the manuscript file (if single-blind). If there are no interests to declare then please state this: 'Declarations of interest: none'. This summary statement will be ultimately published if the article is accepted. 2. Detailed disclosures as part of a separate Declaration of Interest form, which forms part of the journal's official records. It is important for potential interests to be declared in both places and that the information matches. More information.

Authors should declare the role of study sponsors, if any, in the study design; in the collection, analysis and interpretation of data; in the writing of the manuscript; and in the decision to submit the manuscript for publication.

Submission Declaration and Verification
Submission of an article implies that the work described has not been published previously (except in the form of an abstract, a published lecture or academic thesis, see 'Multiple, redundant or concurrent publication' for more information), that it is not under consideration for publication elsewhere, that its publication is approved by all authors and tacitly or explicitly by the responsible authorities where the work was carried out, and that, if accepted, it will not be published elsewhere in the same form, in English or in any other language, including electronically without the written consent of the copyright-holder. To verify originality, your article may be checked by the originality detection service Crossref Similarity Check.

Human and Animal Subjects Research
The work described in your article must have been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/; EC Directive 86/609/EEC for animal experiments.
http://ec.europa.eu/environment/chemicals/lab_animals/legislation_en.htm; Uniform Requirements for manuscripts submitted to Biomedical journals http://www.icmje.org. This must be stated at an appropriate point in the article.

**Ethics Review of Studies Involving Human Subjects**
Pre- or post-marketing studies must undergo review by an institutional review board (IRB) or ethics committee. Patients must give written informed consent unless a waiver of consent is allowed by the IRB. Patients must be informed of any real or potential conflicts of interest, including compensation of the investigator and potential costs to the patient that may result from their participation in the study. The amount of the remuneration of the investigators for their participation in pre- or post-marketing studies must be approved by the IRB/ethics committee. If the design of a prospective pre- or post-marketing study calls for a treatment intervention such as a switch or withdrawal, then criteria must be established a priori for patient selection, the implementation of the intervention, and assessment of success/failure of such intervention. Such criteria must be scientifically justified, documented, uniformly applied and enforced, and clearly reported in the study report. Additionally, the patient or his/her insurance provider will not be required to pay for costs related to prospective interventions, such as those that may result from a drug switch or withdrawal.

All other studies that involve identifiable human subjects, including retrospective studies, chart reviews, post-marketing surveillance studies, or government mandated phase IV trials require IRB or ethics committee approval or waiver. In each case, detailed IRB or ethics committee information should be clearly stated in the Methods section.

Studies that only utilize pre-existing, de-identified (according to HIPAA standards) patient data are not required to seek IRB approval.

**Informed Consent and Patient Details**
Studies on patients or volunteers require ethics committee approval and informed consent, which should be documented in the paper. Appropriate consents, permissions and releases must be obtained where an author wishes to include case details or other personal information or images of patients and any other individuals in an Elsevier publication. Written consents must be retained by the author but copies should not be provided to the journal. Only if specifically requested by the journal in exceptional circumstances (for example if a legal issue arises) the author must provide copies of the consents or evidence that such consents have been obtained. For more information, please review the Elsevier Policy on the Use of Images or Personal Information of Patients or other Individuals. Unless you have written permission from the patient (or, where applicable, the next of kin), the personal details of any patient included in any part of the article and in any supplementary materials (including all illustrations and videos) must be removed before submission.

**Reporting and registration of clinical trials**
All randomized controlled trials submitted for publication should include a completed Consolidated Standards of Reporting Trials (CONSORT) flow diagram (as a Figure or Supplemental Material) and a completed CONSORT checklist for review. Please refer to the CONSORT statement website at http://www.consort-statement.org for more information.

This journal has adopted the proposal from the International Committee of Medical Journal Editors (ICMJE) which require, as a condition of consideration for publication of clinical trials, registration in a public trials registry such as https://clinicaltrials.gov, which can be used by all countries. In addition to a listing in https://www.clinicaltrials.gov, submitting authors should also include the identification number received from trials listed in http://www.controlled-trials.com, another registry recognized by the World Health Organization and the International Committee of Medical Journal Editors. The controlled-trials site provides listings to trials at various stages -- complete, in process, proposed. Please note that requirements for registration may change so authors should always check that they are consulting an up-to-date site. Trials must register at or before the onset of patient enrollment. The clinical trial registration number should be included at the end of the abstract of the article. For this purpose, a clinical trial is defined as any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects of health outcomes. Health-related interventions include any intervention used to modify a biomedical or health-related outcome (for example drugs, surgical procedures, devices, behavioral treatments, dietary interventions including vitamin or herbal supplements, and process-of-care changes). Health outcomes include any biomedical or health-related measures obtained in patients or participants,
including pharmacokinetic measures and adverse events. Purely observational studies (those in which the assignment of the medical intervention is not at the discretion of the investigator) will not require registration. Further information can be found at http://www.icmje.org.

Studies that were initiated without registration can be registered retrospectively and will be considered for publication on a subjective basis.

**Placebos in Clinical Trials**
A full description of any placebo (PBO) or matched control used in a clinical trial must be given in the Methods section. It will no longer be sufficient to simply indicate that a PBO was used. This means that color; type (capsule or pill or liquid); contents (e.g., lactose) including dyes; taste (if there is any); and packaging (e.g., double-dummy) must be noted. For solid PBOs, shape must also be described, as well as whether the PBO is active or inactive. In addition, any efforts to study the success of matching should be included. For example, could subjects/patients or evaluating/rating clinicians guess assignments? Sham procedures must also be described in detail. We are instituting this change as part of our ongoing effort to facilitate replication of findings from trials. All too often this valuable information is omitted from published trial results. When appropriate these descriptions may be designated as Supplemental Digital Content. For more information, see Shader RI. Placebos, Active Placebos, and Clinical Trials. Clin Ther. 2017;39(3):451-454.

**Safety and Tolerability**
For submissions to Clinical Therapeutics, a statement about safety should explicitly include the time period and only when there is a clear absence of harm as determined by relevant questioning, observation, and testing. It is possible that a drug or biologic may be considered tolerable at the same time that tests show it to be unsafe (e.g., a lengthened QTc interval). Conversely, a drug may be considered safe by all objective assessments, and yet produce side effects that can contribute to high degrees of dose interruption or discontinuation. Furthermore, a drug may also be considered prima facie unsafe when pharmacogenomic information suggests it will yield unwanted metabolites in certain individuals or be highly prone to clinically significant drug interactions with frequently used additional agents or foods. Safety assessments may need to be different for different age groups (e.g., effects on growth and development in children and youth, increased propensity to falls in the elderly, effects on life style for active adults). It is also important to remember that safety concerns may stem from excipients added during the manufacturing process rather than from the drug or biologic per se.) For more information, see Shader RI. Safety Versus Tolerability. Clin Ther. 2018;40(5):672-673.

**Pharmacology, Pharmacokinetics, and Pharmacodynamics**
For submissions to the Pharmacology, Pharmacokinetics, and Pharmacodynamics section of Clinical Therapeutics, all manuscripts must include a complete description of the bioanalytic assay(s) and methodology utilized in the generation of the data presented. It is not acceptable to simply state that a validated method was used. Although the complete information included in a pure “Methods” paper is not necessary here, required items at minimum should include: type of instrumentation used, method of extraction, HPLC column and mobile phase, internal standard, type of detection used (e.g. ultraviolet), mass spectrometer settings, m/z monitored, and basic quality control information such as within- and between-day variability, and lower limits of sensitivity. Finally, if the assay(s) have been previously published, or are based upon a published method, appropriate citations must be provided.

Clinical Therapeutics does not accept articles dealing with bioequivalence between innovator and generic small molecules. Clinical Therapeutics will consider studies comparing innovator biologics to follow-on biologics, dose-escalation studies, studies that examine different formulations and/or routes of administration of the same drug, and studies that assess the influence of genetic variation on the ADME (absorption, distribution, metabolism, and excretion) processes. For more information, see Shader RI. Phase I Trials. Clin Ther. 2014;36(4):459 and Shader RI. More Thoughts on Phase I Trials. Clin Ther. 2014;36(8):1127-1128.

**Health Economic Evaluations**
To optimize the quality, consistency, and transparency of health economic and outcomes research reporting and dissemination, Clinical Therapeutics endorses the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement. Authors submitting economic evaluations of pharmacotherapies and other treatment interventions for publication should consult with the CHEERS statement and follow its 24-item checklist of recommendations. Please refer to the statement published in Clinical Therapeutics (http://dx.doi.org/10.1016/j.clinthera.2013.03.003; Husereau D, Drummond M, Petrou S, Carswell C, Moher D, Greenberg D, Augustovski F, Briggs
AH, Mauskopf J, Loder E, CHEERS Task Force. Consolidated Health Economic Evaluation Reporting Standards (CHEERS) Statement. 2013;35:356-363) or the CHEERS statement website for more information. For this purpose, health economic evaluation is defined as the comparative analysis of alternative pharmaceutical and health interventions in terms of their costs and their consequences. All health economic evaluations assess costs, but approaches to measuring consequences of health interventions may differ and can be valued in terms of monetary units; natural units, such as life years gained or disability days avoided; and preference-based health measures, such as quality-adjusted life years or disability-adjusted life years.

**Ethical Considerations for Case Reports**

Because case reports place patient-specific information into the public domain, *Clinical Therapeutics requires that authors obtain written consent to publish case details*. Cases involving patients under 18 require assent by children and/or youth as well as written consent from a parent or guardian. In the United States, case reports must comply with the Health Insurance Portability and Accountability Act of 1996 (HIPPA) regulations. While some institutions exempt case reports that de-identify the patient completely, *Clinical Therapeutics requires consent to publish even if the case details have been de-identified. Authors must:*

Provide de-identified documentation of patient or parental informed consent to publish, which can be attached to the cover letter. Indicate in the manuscript text that written consent has been obtained.

*Clinical Therapeutics* requires that the patient's age and sex be correctly reported. *Clinical Therapeutics* does not allow inclusion of other information such as the patient's name, initials, case number, or any other identifying material that could allow the patient to be recognized. Some institutions require potential case report authors to use consent forms developed by the institution.

Case reports cover past experiences and as such most institutions do not require review or approval by ethics committees or institutional review boards (IRBs). However, some institutions do require IRB approval when four or more cases are involved and their data are aggregated and analyzed. *Clinical Therapeutics* concurs with this requirement because when four or more patients are involved and analyzed such findings are best reported as a Brief Report or Pilot Study.

**Inclusion of Sex and Gender**

*Clinical Therapeutics* encourages authors to consider sex and gender as variables in biomedical research. Studies involving human subjects should include both males and females. If only one sex is included in the study design or results, the reason for exclusion of the other sex should be scientifically justified and explained in the Methods, except for investigations of conditions that affect only one sex. To facilitate future studies and meta-analyses, authors are encouraged to make sex-disaggregated data available in the article or supplemental material. Further statistical analysis of disaggregated data is not required and should be conducted only when sample size is sufficient.

**MULTIMEDIA AND ARTICLE ENRICHMENTS**

**Video Article Guidelines**

*Clinical Therapeutics* encourages authors who have presented a talk at a meeting to convert their talk into a video production for online publication. The video article may be submitted in one of two ways:

1. Slide set and scripted narration.
2. A full video presentation of the author discussing his/her manuscript.

**Slide Set Requirements:**
The slide set presentation will consist of:

- PowerPoint slides without audible narration.
- A separate manuscript consisting of the written narrative.

Both the slides and the script will be submitted for peer review. When finalized, each slide will have its own narrative.

At the time of revision, the author will make any required changes to the slides and accompanying written narrative. Once the revised slides and narrative have been found acceptable, the author will provide us with audible narration to accompany the presentation.

**Video Requirements:**
The formats for video will be accepted:

- MP4 (.mp4); QuickTime (.mov); MPEG-1 or MPEG-2 (.mpg).
- Each video must start with a slide listing the authors’ conflicts of interest.
• Maximum length of videos is 4.5 minutes.
• Video file may not exceed 100 MB.
• Please ZIP the file and upload the zipped file to hasten the upload time.

Video Abstract Guidelines
Clinical Therapeutics offers authors a chance to submit a video abstract to accompany the online version of their article.

The following YouTube links explain
Why Create a Video Abstract
How to Create a Video Abstract

There are different approaches to presenting the information in your paper, and it is readily possible to impart to viewers the main take home message, the conceptual interest of the findings, and some supporting details in fewer than five minutes.

It is generally effective to use schematics, minimizing the amount of raw data/figure panels, to communicate your findings clearly, especially within the size of the flash player windows in which your video will appear. It is especially important not to have small text that won't be legible in the flash player (see below for more details on font size). While it may be tempting to primarily film slides presenting the figures in your paper with your voice explaining the data, the video is likely to be more engaging if you can mix up the presentation with both. Please see below for more specific information about video and file preparation.

Because all video abstracts will be included in our YouTube Channel, please supply the highest quality video possible in a YouTube-supported format with the maximum suggested resolution and bitrate.

Minimum specifications are as follows:
File size: <150 MB Frame rate: 30 frames per second 4:3, deinterlaced (16:9 is also acceptable) One of the following formats: .mov, .mpg, .avi, or .mp4 (.mp4 preferred) Frame size: 320 x 240 pixels or greater Video codec: H.264 (WRAW codec is strongly discouraged) Video bitrate: 2 Mbps Audio codec: AAC (SWOT Little Endian PCM Audio is strongly discouraged) Audio bitrate: 128 kbps

Any text within the video should be legible within the video at a frame size of 320 x 240 pixels. To determine whether the font will be legible in the final online product, view the video at a size of 320 x 240 in Quicktime by going to Window > Show Movie Inspector, and dragging the bottom-right corner of the movie screen inward so that the size of the screen is decreased to 320 pixels in width.

Please be aware that if you show any images from previously published papers you must obtain the appropriate permissions from the publisher. Other copyrighted images and sounds/music should not be used. Additionally, distribution rights to the video will be under nonexclusive copyright terms. You and your institution would be free to use the video in any way that you like. Clinical Therapeutics and Elsevier Inc. seeks non-exclusive rights to publish the video both in association with your article and as an independent item in electronic media; to grant permissions for reproductions; and to authorize document delivery and abstracting services. The video would be included with the article wherever the article appears in electronic format. Please do not include a copyright insignia from your institution in the video that you send us to be associated with your article.

Research Data
This journal encourages and enables you to share data that supports your research publication where appropriate, and enables you to interlink the data with your published articles. Research data refers to the results of observations or experimentation that validate research findings. To facilitate reproducibility and data reuse, this journal also encourages you to share your software, code, models, algorithms, protocols, methods and other useful materials related to the project.

Below are a number of ways in which you can associate data with your article or make a statement about the availability of your data when submitting your manuscript. If you are sharing data in one of these ways, you are encouraged to cite the data in your manuscript and reference list. Please refer to the "References" section for more information about data citation. For more information on depositing, sharing and using research data and other relevant research materials, visit the research data page.
Data Linking
If you have made your research data available in a data repository, you can link your article directly to the dataset. Elsevier collaborates with a number of repositories to link articles on ScienceDirect with relevant repositories, giving readers access to underlying data that gives them a better understanding of the research described.

There are different ways to link your datasets to your article. When available, you can directly link your dataset to your article by providing the relevant information in the submission system. For more information, visit the database linking page.

For supported data repositories a repository banner will automatically appear next to your published article on ScienceDirect.

In addition, you can link to relevant data or entities through identifiers within the text of your manuscript, using the following format: Database: xxxx (e.g., TAIR: AT1G01020; CCDC: 734053; PDB: 1XFN).

Mendeley Data
This journal supports Mendeley Data, enabling you to deposit any research data (including raw and processed data, video, code, software, algorithms, protocols, and methods) associated with your manuscript in a free-to-use, open access repository. During the submission process, after uploading your manuscript, you will have the opportunity to upload your relevant datasets directly to Mendeley Data. The datasets will be listed and directly accessible to readers next to your published article online.

For more information, visit the Mendeley Data for journals page.

Data Statement
To foster transparency, we encourage you to state the availability of your data in your submission. This may be a requirement of your funding body or institution. If your data is unavailable to access or unsuitable to post, you will have the opportunity to indicate why during the submission process, for example by stating that the research data is confidential. The statement will appear with your published article on ScienceDirect. For more information, visit the Data Statement page.

INITIAL SUBMISSION
Our online submission system guides you stepwise through the process of entering your article details and uploading your files. The system converts your article files to a single PDF file used in the peer-review process. Editable files (e.g., Word, LaTeX) are required to typeset your article for final publication. All correspondence, including notification of the Editor's decision and requests for revision, is sent by e-mail.

Submit your article
Please submit your article via https://www.editorialmanager.com/clinther/.

Submission Checklist
Ensure that all necessary files have been uploaded: Cover letter ICMJE forms for each author Declaration of Interest The role of the sponsor or funder has been provided in detail Title page, with e-mail and full postal address of designated corresponding author Highlights Manuscript file:
• Author information removed
• Abstract, structured or unstructured in accordance with article type
• Trial registration number (if applicable)
• Keywords
• Ethics statement
• Figure/table legends
• Acknowledgments
• References
All figures, each uploaded separately in original file format All tables, each uploaded separately in original file format All supplemental files (if applicable)

Further considerations Manuscript has been 'spell checked' and 'grammar checked' All figures, tables, and supplemental material are cited in the text Indicate clearly if color should be used for any figures in print All references mentioned in the Reference List are cited in the text, and vice versa, and references have been numbered Permission has been obtained for use of copyrighted material from other sources (including the Internet) A Declaration of Interest statement is provided, even if
the authors have no competing interests to declare. Each author's contribution to the manuscript has been declared. Journal policies detailed in this guide have been reviewed. Referee suggestions and contact details provided, based on journal requirements.

**REVISED SUBMISSION**

**Response to Review Document**

When submitting a revised manuscript, authors must upload a detailed response to reviewers as a separate file. This file will be made available to reviewers and therefore, should not contain identifying information or letterhead. The Response to Review Document should include a point-by-point response to each comment, including a description of any changes made to the manuscript as well as the corresponding line and page numbers.

**Manuscript Files**

Authors must upload two versions of the revised article: (1) a "clean" or "unmarked" version without tracked changes, and (2) a "marked" version with tracked changes or highlighting to indicate revisions. Do not include the original manuscript file; ensure author information is removed from the manuscript files, tables, figures, and any supplemental material.

**Promotion of Your Article**

At the time you submit the revised version of your article, please compose a question for which your paper's subject, topic or title is an answer. We will take your question, attach your paper's web address, and use it for social media promotion on Twitter. See example, below: Author composed question: How common are adverse events after corticosteroid treatment?


The final product, the question and the shortened web address, is the message we will promote on Twitter, to boost awareness and drive traffic to the published content.

**AFTER ACCEPTANCE**

**Proofs**

One set of page proofs (as PDF files) will be sent by e-mail to the corresponding author (if we do not have an e-mail address then paper proofs will be sent by post) or, a link will be provided in the e-mail so that authors can download the files themselves. Elsevier now provides authors with PDF proofs which can be annotated; for this you will need to download the free Adobe Reader, version 9 (or higher). Instructions on how to annotate PDF files will accompany the proofs (also given online). The exact system requirements are given at the Adobe site.

If you do not wish to use the PDF annotations function, you may list the corrections (including replies to the Query Form) and return them to Elsevier in an e-mail. Please list your corrections quoting line number. If, for any reason, this is not possible, then mark the corrections and any other comments (including replies to the Query Form) on a printout of your proof and scan the pages and return via e-mail. Please use this proof only for checking the typesetting, editing, completeness and correctness of the text, tables and figures. Significant changes to the article as accepted for publication will only be considered at this stage with permission from the Editor. We will do everything possible to get your article published quickly and accurately. It is important to ensure that all corrections are sent back to us in one communication: please check carefully before replying, as inclusion of any subsequent corrections cannot be guaranteed. Proofreading is solely your responsibility.

**Publication Options and Licenses**

**Funding body agreements and policies**

Elsevier has established a number of agreements with funding bodies which allow authors to comply with their funder's open access policies. Some funding bodies will reimburse the author for the gold open access publication fee. Details of existing agreements are available online. After acceptance, open access papers will be published under a noncommercial license. For authors requiring a commercial CC BY license, you can apply after your manuscript is accepted for publication.
Open Access (optional and subject to an additional fee)

Clinical Therapeutics charges page fees to publish. Please note, page fees as described are completely separate from the payment option to publish your paper as an Open Access article. The journal will apply the same peer review criteria and acceptance standards to all submissions.

To publish with Open Access, a gold open access publication fee will be charged.
• A gold open access publication fee is payable by authors or on their behalf, e.g. by their research funder or institution.

The gold open access publication fee for this journal is **USD 3250**, excluding taxes. Learn more about Elsevier's pricing policy: https://www.elsevier.com/openaccesspricing.

• Open access articles are freely available to both subscribers and the wider public with permitted reuse.

For gold open access articles, permitted third party (re)use is defined by the following Creative Commons user licenses:

**Creative Commons Attribution-NonCommercial-NoDerivs (CC BY-NC-ND)**
For non-commercial purposes, lets others distribute and copy the article, and to include in a collective work (such as an anthology), as long as they credit the author(s) and provided they do not alter or modify the article.

**Green open access**
Authors can share their research in a variety of different ways and Elsevier has a number of green open access options available. We recommend authors see our open access page for further information. Authors can also self-archive their manuscripts immediately and enable public access from their institution's repository after an embargo period. This is the version that has been accepted for publication and which typically includes author-incorporated changes suggested during submission, peer review and in editor-author communications. Embargo period: For subscription articles, an appropriate amount of time is needed for journals to deliver value to subscribing customers before an article becomes freely available to the public. This is the embargo period and it begins from the date the article is formally published online in its final and fully citable form. Find out more. The published journal article cannot be shared publicly, for example on ResearchGate or Academia.edu, to ensure the sustainability of peer-reviewed research in journal publications.

This journal has an embargo period of 12 months.

**Copyright**
Upon acceptance of an article, authors will be asked to complete a 'Journal Publishing Agreement' (see more information on this). An e-mail will be sent to the corresponding author confirming receipt of the manuscript together with a 'Journal Publishing Agreement' form or a link to the online version of this agreement.

Subscribers may reproduce tables of contents or prepare lists of articles including abstracts for internal circulation within their institutions. Permission of the Publisher is required for resale or distribution outside the institution and for all other derivative works, including compilations and translations. If excerpts from other copyrighted works are included, the author(s) must obtain written permission from the copyright owners and credit the source(s) in the article. Elsevier has preprinted forms for use by authors in these cases.

For gold open access articles: Upon acceptance of an article, authors will be asked to complete an 'Exclusive License Agreement' (more information). Permitted third party reuse of gold open access articles is determined by the author's choice of user license.

**Author rights**
As an author you (or your employer or institution) have certain rights to reuse your work. More information.

Elsevier supports responsible sharing
Find out how you can share your research published in Elsevier journals.
RESOURCES

Author Inquiries
For inquiries relating to the submission of articles (including electronic submission) please visit this journal's homepage or contact the editorial office (clinther@elsevier.com). For detailed instructions on the preparation of electronic artwork, please visit https://www.elsevier.com/artworkinstructions. Contact details for questions arising after acceptance of an article, especially those relating to proofs, will be provided by the publisher. You can track accepted articles at https://www.elsevier.com/trackarticle. You can also check our Author FAQs at https://www.elsevier.com/authorFAQ and/or contact Customer Support via https://service.elsevier.com.

Elsevier Researcher Academy
Researcher Academy is a free e-learning platform designed to support early and mid-career researchers throughout their research journey. The "Learn" environment at Researcher Academy offers several interactive modules, webinars, downloadable guides and resources to guide you through the process of writing for research and going through peer review. Feel free to use these free resources to improve your submission and navigate the publication process with ease.

Guide for Authors: Chinese version
Download Chinese Guide for Authors in PDF

Offprints
The corresponding author will, at no cost, receive a customized Share Link providing 50 days free access to the final published version of the article on ScienceDirect. The Share Link can be used for sharing the article via any communication channel, including email and social media. For an extra charge, paper offprints can be ordered via the offprint order form which is sent once the article is accepted for publication. Both corresponding and co-authors may order offprints at any time via Elsevier's Author Services. Corresponding authors who have published their article gold open access do not receive a Share Link as their final published version of the article is available open access on ScienceDirect and can be shared through the article DOI link.

© Copyright 2018 Elsevier | https://www.elsevier.com