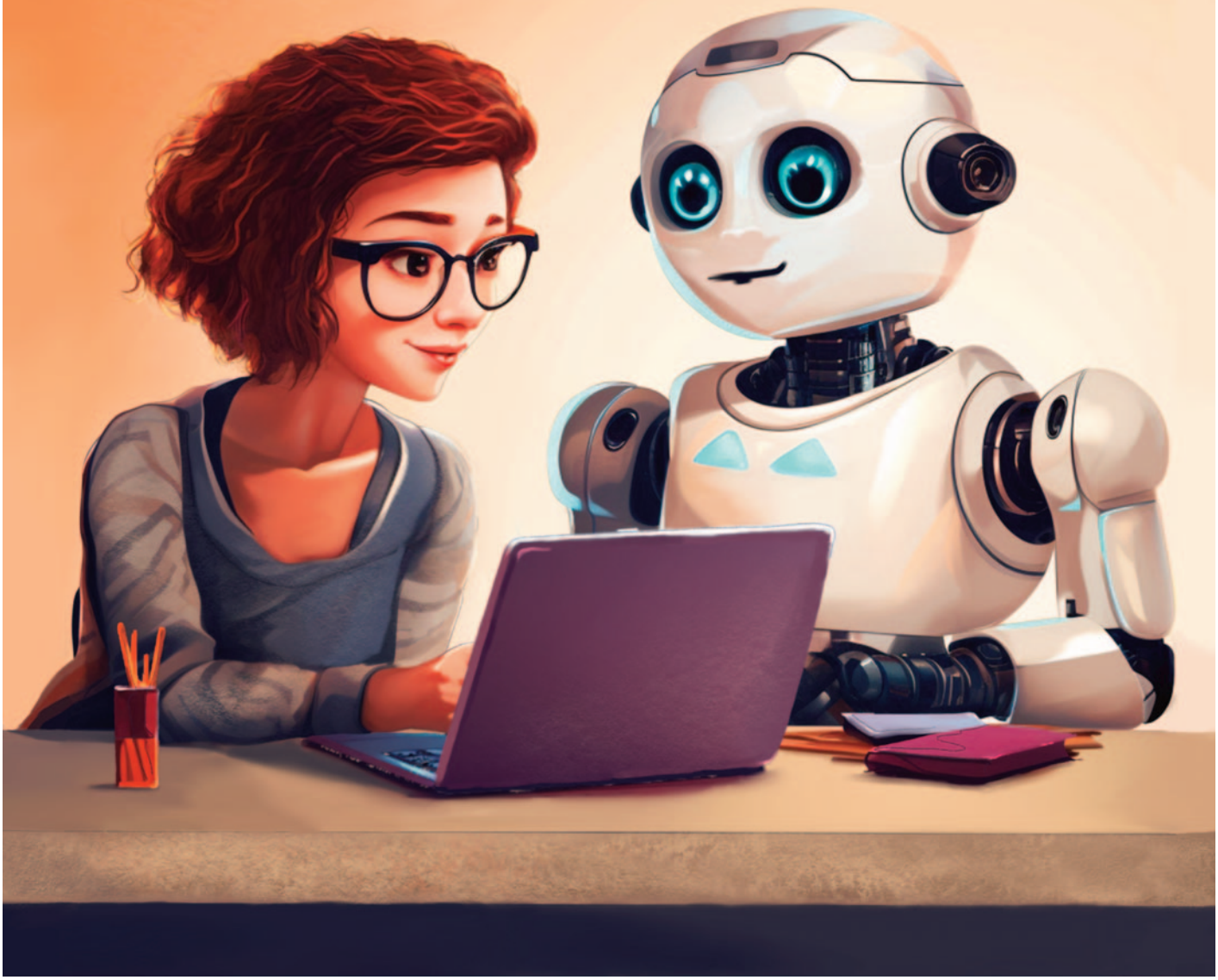
Medical Writing

Artificial Intelligence and Machine Learning



ALSO IN THIS ISSUE...

Volume 32 Number 3 | **September 2023**

EMWA EUROPEAN MEDICAL WRITERS ASSOCIATION

Medical Writing is the official journal of the European Medical Writers Association (EMWA). It is a quarterly journal that publishes articles on topics relevant to professional medical writers. Members of EMWA receive *Medical Writing* as part of their membership. For more information, contact mew@emwa.org.

Medical Writing

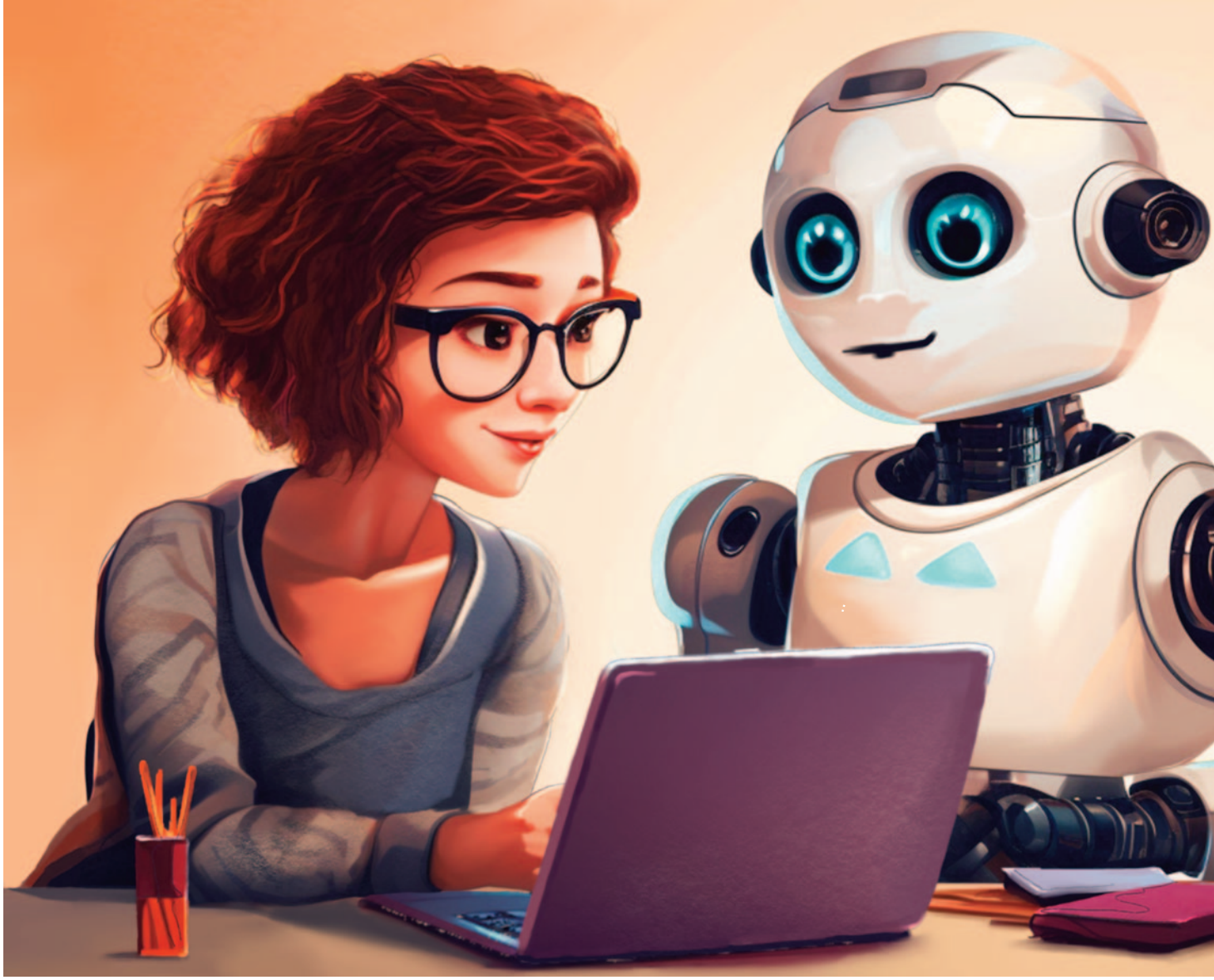
About the cover
Judit Mészáros, Scientific Manager at Ashfield Medcomms Gmbh and member of EMWA's Creative Team, created the cover image with the assistance of Midjourney, an AI art generator tool.

THIS ISSUE **September 2023** | Volume 32 Number 3

Artificial Intelligence and Machine Learning

"If we view AI as a tool that can supplement our work, make us more efficient and accurate, and relieve us of some of the heavy lifting, then it can become a powerful resource, freeing us to focus on the more valuable work of critical thinking and crafting a strong narrative in our highly complex and vital work."

Jamie Norman and Lisa Chamberlain James, p. 67



Artificial Intelligence and Machine Learning

GUEST EDITORS

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doi: 10.56012/vrpa5453

We are in an era in which most people cannot imagine living without either computers or smartphones. We are well aware of how machine learning (ML) and artificial intelligence (AI) tools support our daily lives. And now, with their rapid development, medical writers can leverage these technologies to enhance productivity, quality, and innovation. The idea for a *Medical Writing* issue focusing on automation in medical writing arose about 2 years ago. This was quite a few months before ChatGPT became a household term, and the tool itself went swiftly into use with almost every copy-editing professional, every lawyer, and every person in any industry that uses text as their main tool of the trade. We were very interested in taking a snapshot of the landscape of tools that are currently available to medical writers and how they are being used.

Anjana Bose's article explores the transformative impact of AI/ML applications in drug development and medical devices, highlighting the potential benefits of these technologies in areas such as clinical trials, post-marketing surveillance, and regulatory writing. The article also underscores the challenges of transparency, validation, and data privacy, emphasising the need for careful integration and collaboration between AI and human expertise to ensure responsible innovation in healthcare.

Within the narrower context of medical writing, AI and automation tools can be classified into two general categories: those that generate natural language text from data or other sources, and those that curate pre-made content from approved sources.

In this issue, we explore how various platforms can support the writing of MedComms and, employing tools in one or both of these categories.

Azza Gramoun provides an overview of AI tools that support the review, summarisation, and evaluation of clinical information to assess medical, useful for writers of clinical evaluation reports. **Katja Martin** highlights the growing impact of generative AI driven by large language models in the realm of medical writing, catering to the familiarity with AI of various user groups. Emphasising the need for comprehensive understanding, the article offers a balanced perspective that counters exaggerated AI expectations while exploring its benefits.

The article delves into specific AI applications, showcasing the potential of generative AI to enhance efficiency and quality in medical communication.

Lucy Cobb and **Nicola Haycock** describe their experiences with automation software in writing patient narratives for clinical study reports that require more than 100 narratives. The current tools do not use ML capabilities. What they do use is pre-programmed natural language text, into which specific data items are imported from the data set generated from electronic data capture (EDC) systems used in clinical studies. As we know from our own experience, the amount of work needed for a medical writer to edit and revise such a machine-generated narrative into coherent text with a clear story is quite substantial. Significant programming efforts are required to tailor the program to a specific product, study, and study population. Many times, specifically for medically complex cases, such machine-generated narratives need to be supplemented with information coming from sources external to the electronic data captures systems, such as the Council for International Organizations of Medical Sciences reporting forms. The option of having AI integrate information from both natural language sources and coded, cleaned, and meticulously queried databases is very exciting. We believe that it will not only reduce a lot of the grunt work required of medical writers, but will also make these narratives much more useful to the reviewers and any stakeholders who would like to use them as sources to identify potential problems with any product.

Mati Kargren, John April, Gina Clark, Jonathan Mackinnon, Aliza Nathoo, and **Elizabeth Theron** share their experience with structured content authoring for regulatory documents, specifically protocols. The article focuses on bulk text that must be reiterated across various submission documents or across protocols that serve different trials within the development program of a single product. These usually include background text such as description of the regulatory landscape, the development history of the product itself, information about the indication, and more. These texts can be authored and agreed upon once and then imported automatically into the various documents from the pre-approved source. As writers are involved in large submission projects with a significant number of documents containing repetitive text, it would be very interesting to see what the future holds for such amazing tools, especially with respect to the dynamics of updates. Will we be able to revise the text once and have a computer program import the revised text or the relevant revisions across the entire set of documents containing the same text? Most importantly, such tools will provide consistency across documents while also benefitting the process of submission preparation tremendously. Specific subject matter experts will be responsible for authoring and updating specific text paragraphs, and the required updates will be implemented in real time in all relevant documents. This will save others the need (or temptation) to re-review and revise these sections upon encountering them again in documents reviewed

EUROPEAN MEDICAL WRITERS ASSOCIATION

Submissions:
For instructions to authors, go to the journal section of EMWA's website (www.journal.emwa.org).
All manuscripts should be submitted to mew@emwa.org.

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Paper from responsible sources
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later during the work, and would very effectively reduce the time and effort required to write these heavy submission documents.

As the use of AI authoring tools expands, **Natalie Bourré** has been exploring the topic of whether readers can correctly assess whether medical texts were written by humans or such AI tools. She reports on her experiment in which a range of respondents, including healthcare professionals, medical writers, and others, were presented with sample medical texts and asked to guess "who" wrote which prose. Our guest editors volunteered to be subjects in the research. You can read the intriguing research results in this issue.

AI and automation are not only changing the way medical writers work, but also the way they learn and grow. Medical writers need to keep up with the latest developments in these technologies and acquire new skills and competencies to use them effectively. Moreover, medical writers need to collaborate with other stakeholders, such as programmers, data managers, statisticians, reviewers, regulators, and patients, to ensure that the AI and automation tools serve the best interests of all parties involved. In the Digital Communication section, the article by **Sofie Bergstrand**, **Catherine Heddle**, **Montse Sabaté**, and **Marta Mas** discusses the integration of AI tools into medical writing processes, focusing on the potential benefits and challenges. Microsoft's AI tool, Microsoft 365 Copilot, is introduced, highlighting its potential to improve collaboration and productivity in medical writing.

Guest Editor **Daniela Kamir** interviewed **Uri Kartoun** about improving clinical risk assessment tools such as the MELD (Model for End-Stage Liver Disease) score. Assessing fairness by AI involves evaluating whether AI outcomes are unbiased across demographics, ensuring equitable decision-making and avoiding discrimination.

Valérie Lannoy looks at plagiarism's damaging impact on the biomedical academic publication domain. While AI offers hope in addressing this issue, a worrisome trend is emerging as new AI-based tools facilitate plagiarism. This article examines the historical context of plagiarism, particularly in the medical field, and explores the potential of AI to detect a unique form of plagiarism known as aigiarism. Additionally, the article emphasises the risks associated with AI-powered services that aid in paraphrasing copied content, and proposes potential solutions.

> "The more that you read, the more things you will know. The more that you learn, the more places you'll go."
>
> DR SEUSS

Veerle Persy examines the present applications, advantages, and limitations of AI in medical writing, and highlights the dynamic interplay between technological innovation and human expertise.

A collaborative article by **Viviana Moroso**, **Mats O. Magnusson**, and **E. Niclas Jonsson** presents their software-based solution to address the challenges of reporting complex pharmacometric analyses. By integrating various software tools, they are able to enhance efficiency, accuracy, and reliability in summarising and describing input and output data for drug development and regulatory assessment.

Jamie Norman and **Lisa Chamberlain James** discuss the current role of AI in medical writing and ask the question: AI for medical writers – friend or foe?

AI tools have their advantages and disadvantages. On one hand, AI and automation tools can reduce the amount of grunt work that medical writers face, such as writing repetitive text, formatting documents, checking references, and ensuring consistency. On the other hand, AI and automation tools can also introduce new challenges, such as ensuring the quality, accuracy, and reliability of machine-generated text, maintaining the human touch and creativity of the medical writing style, and dealing with ethical and legal issues related to health information privacy and intellectual property, among others. AI and automation are not threats to medical writing; they are opportunities for medical writing to evolve and improve. Medical writers who embrace these technologies with curiosity, creativity, and critical thinking will be able to harness their potential and create value for themselves and their clients.

Last, but not least, we are happy to introduce you to the members of the EMWA AI working group, **Sarah Tilly**, **Slavka Baronikova**, **Martin Delahunty**, **Namrata Singh**, and **Claire Harmer**, each of whom answers some questions about the working group itself and AI specifically.

We hope that you will enjoy reading the current issue on automation in medical writing as much as we enjoyed putting it together. Finally, be on the lookout for a dedicated AI/automation section in *Medical Writing* from December 2023 onward!

About the guest editors

Daniela Kamir, PhD, has been a medical writer with the Bioforum Group, a global, data-focused, technology-driven clinical research organisation, since 2020. Daniela has an extensive international research background, with an emphasis on molecular biology and new technologies in the sciences and medicine. She is experienced in writing pre-approval regulatory documents and scientific writing.

Shiri Diskin, PhD, has been working as a medical writer since 2009. She founded the Medical Writing Department at Bioforum in 2018 and has been leading it ever since. Shiri manages large-scale writing projects in the pharmaceutical industry and is also a medical writing instructor.

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When you volunteer to assist EMWA in any capacity, you are furthering the development of our association.

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- Webinar contributions
- Webinar team

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- Increase your visibility and communication opportunities within the medical writing community
- Add some prestige to your CV
- Improve your knowledge of medical writing and related topics

TO FIND OUT MORE

If you are a member of EMWA and eager to support ongoing initiatives, please contact info@emwa.org.

From the Editor

The D's of robotics: Are we ready to delegate?

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0000-0003-1975-8762

doi: 10.56012/bzfs2718

When Shiri Diskin and Daniela Kamir suggested in 2021 to have a *Medical Writing* issue on automation in medical writing, little did I imagine how imperative this topic would be in 2023. I sincerely thank them for their avant-garde mindset and for producing this AI-some issue.

The dirty, the dangerous, and the dull

Robots were supposedly created to perform the **3D** tasks – the **d**irty (e.g., **d**eclogging sewage systems), the **d**angerous (e.g., **d**efusing bombs), and the **d**ull (e.g., **d**rudgery of repetitive assembly work). At least that's how it was for many years. More recently, robotics has been coupled with artificial intelligence (AI), and taking alliteration even further, more D's have been added to their tasks, including the **d**ear (i.e., expensive) and the **d**ifficult.[1] These last two are **d**istressing to many – will we soon be **d**emoted, and eventually **d**isplaced? Then there's an even **d**arker side of AI featured in many a **d**ystopic film, a **d**igital **d**emon we can't see that **d**eceives, **d**isrupts, and **d**estroys.

It's not all **d**ebacles and **d**oomsday. Present day robots have proven to be useful in other D's – think about **d**omestic bots, **d**rones used in **d**isaster management, **d**elivering relief goods to remote places. **D**evices help overcome **d**isabilities and expedite **d**iagnoses. **D**eep machine learning supposedly gives medicine ("Deep Medicine") a more human touch.[2]

> I still can't see an artificial system fully understanding the principles of Good Clinical Practice anytime soon.

What about medical writing? Are we ready to **d**elegate our **d**eliverable **d**ocuments to a **d**igital **d**o-it-all?

Without actually realising it, I have been using **d**igital tools over the years, with or without AI.

The dreary and the detection of errors

Early in my career, I manually created in-text tables and drafted hundreds of patient narratives. Let's face it, such tasks are **d**ull and **d**epressing. Nowadays, there are computer programmes that do these for us.

Manual data entry is not only **d**ull and **d**reary, it is also prone to error. Quality control of our documents – from data checks to readability metrics – is crucial. **D**etection of errors and mistakes is a very useful AI capability we should take advantage of.

These are just a few examples. Many articles in this issue tell us more about the uses of AI in medical writing, from systematic literature reviews to detecting plagiarism, to pharmacometrics and structured content authoring.

The dear and the difficult

So back to the question – if AI can do all that is **d**ull, **d**ear, and **d**ifficult, where does that leave us? Will robots finally overcome the triple constraints[3] of "Cheap, Fast, and Good – Pick Any Two" and companies can have all three?

In medical writing, it should never be a pick of any two. "Good" has always been, and will always be, the standard; there is no trade-off on quality. But leveraging AI, we can pair quality with speed. Think about it – we can develop good regulatory documents quicker and get treatments to patients faster. The first COVID-19 vaccines that got approved in record time surely had a little AI help. And they weren't cheap.

Delegation and direction

Clinical research requires skill sets that AI can never fully provide. In the standard project RACI (Responsible, Accountable, Consulted, Informed) matrix,[4] the "responsibility" and "accountability" remain in our hands. Because AI, like human intelligence, has limitations. We have heard about AI hallucinations, ethical considerations, and the lack of context and creativity. I still can't see an artificial system fully understanding the principles of Good Clinical Practice anytime soon.

Let's look beyond the document and focus on the goal. I never thought I'd be ready for a self-driving car, but there seems to be no stopping it. In the same way, we cannot do without AI in medical writing. We can **d**elegate the **d**riving, the autopiloting, but we **d**etermine the **d**irection and the **d**estination.

In fact, we are finding ways to co-exist with this new generation of AI-driven virtual robots. The articles in this edition attest to this. And, by the way, congratulations to the newly formed EMWA AI Working Group (p. 70).

Disclosure

No alliteration generator was used in writing this piece.

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So back to the question – if AI can do all that is dull, dear, and difficult, where does that leave us?

Resources on AI regulations for health products

Regulatory resources:

- EMA. Reflection paper on the use of artificial intelligence in the lifecycle of medicines. July 2023. Available from: https://www.ema.europa.eu/en/documents/scientific-guideline/draft-reflection-paper-use-artificial-intelligence-ai-medicinal-product-lifecycle_en.pdf
- US FDA Draft Guidance for Industry and Staff. Marketing submission recommendations for a predetermined change control plan for artificial intelligence/machine learning (AI/ML)-enabled device software functions. April 2023.
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- Hines PA, Herold R, Pinheiro L, et al. Artificial intelligence in European medicines regulation. Nat Rev Drug Discov. 2023;22(2):81–2. doi:10.1038/d41573-022-00190-3
- Fraser AG, Biasin E, Bijnens B, et al. Artificial intelligence in medical device software and high-risk medical devices - a review of definitions, expert recommendations and regulatory initiatives. Expert Rev Med Devices. 2023;20(6):467–91. doi:10.1080/17434440.2023.2184685

Resources on guidelines for use of AI in writing manuscripts

Flanagin A, Kendall-Taylor J, Bibbins-Domingo K. Guidance for authors, peer reviewers, and editors on use of AI, language models, and chatbots. JAMA. July 2023. doi:10.1001/jama.2023.12500

Marušić A. JoGH policy on the use of artificial intelligence in scholarly manuscripts. J Glob Health 2023;13:01002. doi: 10.7189/jogh.13.01002

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NEJM Editorial Policies: Use of AI-Assisted Technologies. Available from: https://www.nejm.org/about-nejm/editorial-policiespolicies. https://www.nejm.org/about-nejm/editorial-policies

Thanks to Martin Delahunty for helping compile this list.

President's Message

A look forward – and back! - at AI in *Medical Writing*

Maria Kołtowska-Häggström
EMWA President 2023-24
president@emwa.org

doi: 10.56012/djds3468

Hello Everyone,

This issue of *Medical Writing* is devoted to automation and artificial intelligence (AI), the hot topic that interests all of us and that is likely to change our lives dramatically, at least our professional lives.

While thinking what to write in my message, I've asked myself;

"When did EMWA for the first time present anything about automation?" Guess what I found! In 1993, in the Newsletter from the European Medical Writers Association, a report from the Management Forum Seminar on computer-assisted marketing applications for new drugs 1992 was published. By the way, in 1993 EMWA was a chapter of AMWA, that's why the newsletter was published as "American Medical Writers Association Journal Europe" (See it here at: https://journal.emwa.org/documents/journal/TWS/ The%20Write%20Stuff%201993%20Vol%2001%20issue%201.pdf)

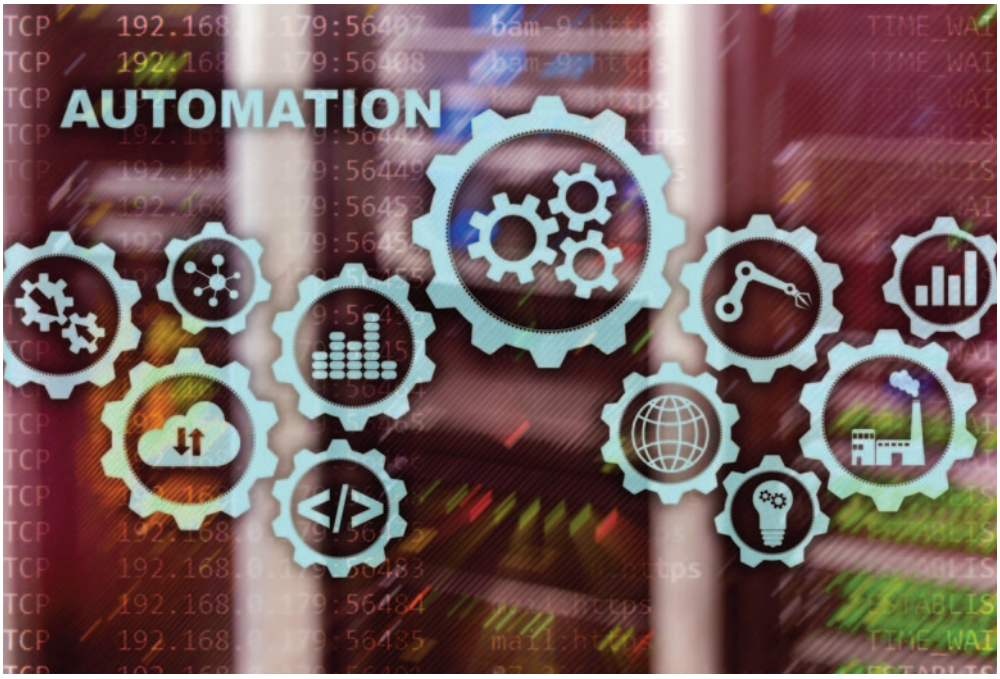
In the seminar, representatives from governments and industry from Europe and USA discussed developments of CANDA (computer-assisted marketing applications for new drugs). Several advantages of this new application method were mentioned, such as an improvement of in-house documentation systems, an enhancement of communication between companies and authorities, and reduction of paper burden. These advantages are still valid.

> AI is likely to change our lives dramatically, at least our professional lives.

Then, in 2014 a *Medical Writing* issue, Software for Medical Writers (https://journal.emwa.org/software-for-medical-writers) was published. Secrets of Microsoft Word, PowerPoint, different templates, Datavision, and a few others were revealed. My favorite articles were: a critical review of translation tools written by Laura C. Collada Ali and Laurence Auffret, and tips on medical writers's must-have software provided by Shirin Ghodke.

EMWA and *Medical Writing* keep a close eye on the progress in the IT world so in 2019 an issue on AI and digital health was published (https://journal.emwa.org/artificial-intelligence-and-digital-health/). Evguenia Alechine, a guest editor of that issue, wrote in her editorial:

> *"Artificial intelligence (AI) and digital health are changing the way we live and work. They are already and increasingly present in medicine and are slowly permeating the medical writing industry. For many medical writers, this raises the question whether these new technologies will be friends or foes, whether they will make our work easier, or whether 'we will be replaced by robots' ".*



Time flies! It's now more than 30 years after EMWA's first mention of "computer assistance" in medical writing and the question from Evguenia's editorial is more valid than ever.

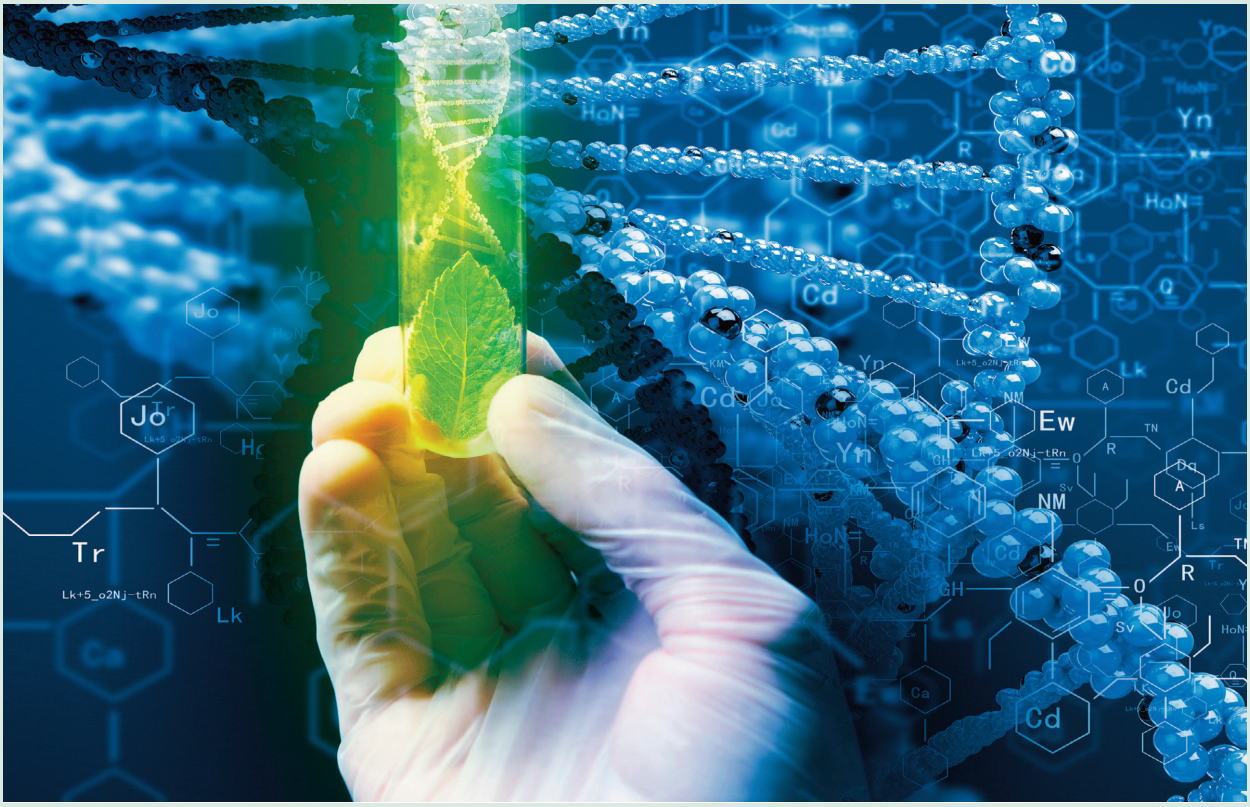
Leaving *Medical Writing* a bit aside, I am very pleased to inform you that EMWA has initiated a group (the AI Working Group) looking into AI and how it will impact medical writers (that is us, EMWA members). This group, chaired by Sarah Tilly, our President-Elect, is distinct from the Special Interest Groups, yet closely cooperates with all of them to enable EMWA to remain current, have a voice in these activities, and to be able to educate our members. For more details on how the AI Working Group operates and how you can engage, read the Q&A article published in this issue on p. 70.

Now, just to conclude – we are looking very much forward to the news on the revolutionary AI development presented in this issue of *Medical Writing*.

Happy reading.
Maria

Don't miss!

The December 2023 edition



Biotechnology

Biotechnology uses biological systems and living organisms in R&D and production processes. Biotechnologies include biologic and biosimilar pharmaceuticals like monoclonal antibodies, vaccines, and advanced therapy medicinal products, for example, gene and cell therapies and tissue engineered products. In addition, biotechnologies support the product lifecycle, for instance, in non-clinical work using in silico, in vitro, and animal testing methods. Also, support services personnel like those in biobanks and supply chains require an understanding of biotechnology. This issue focuses on the crucial role of writing and communications in biotechnology and product development.

Guest editor: Jennifer Bell

EMWA News

SECTION EDITOR

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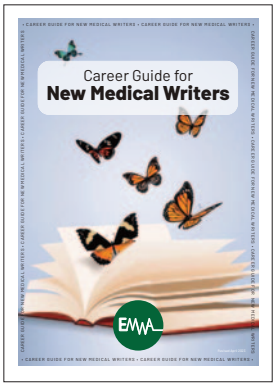
info@sombasu.com



Career guide for new medical writers

The Getting into Medical Writing (GIMW) group is delighted to announce the recent publication of the updated **Career Guide for New Medical Writers**, which you can access here: https://www.emwa.org/about-us/getting-into-medical-writing/career-guide-for-new-medical-writers/

If you are new to medical writing, this guide is a useful resource that will help you take your first steps on this rewarding career path.

If you have comments or suggestions, we would love to hear from you. You can email us at gettingintoMW@emwa.org.

Creating a national network in Italy

The first meeting of Italian Medical Writers was held at the Mario Negri Institute on March 6, 2023. The meeting was organised by **Andrea Rossi** (EMWA Ambassador and Past President), **Johanna Chester** (EMWA EPDC member), and **Laura Collada Ali** (EMWA Co-Education Officer) to facilitate the exchange of experience among local professionals and create a national network.

The event hosted over 50 attendees. Most were Italian native speakers, and over 75% had a scientific degree. Over a third were self-employed, and a third were employed in a business environment. A small percentage were business owners, translators, or newcomers interested in starting a career in medical writing.

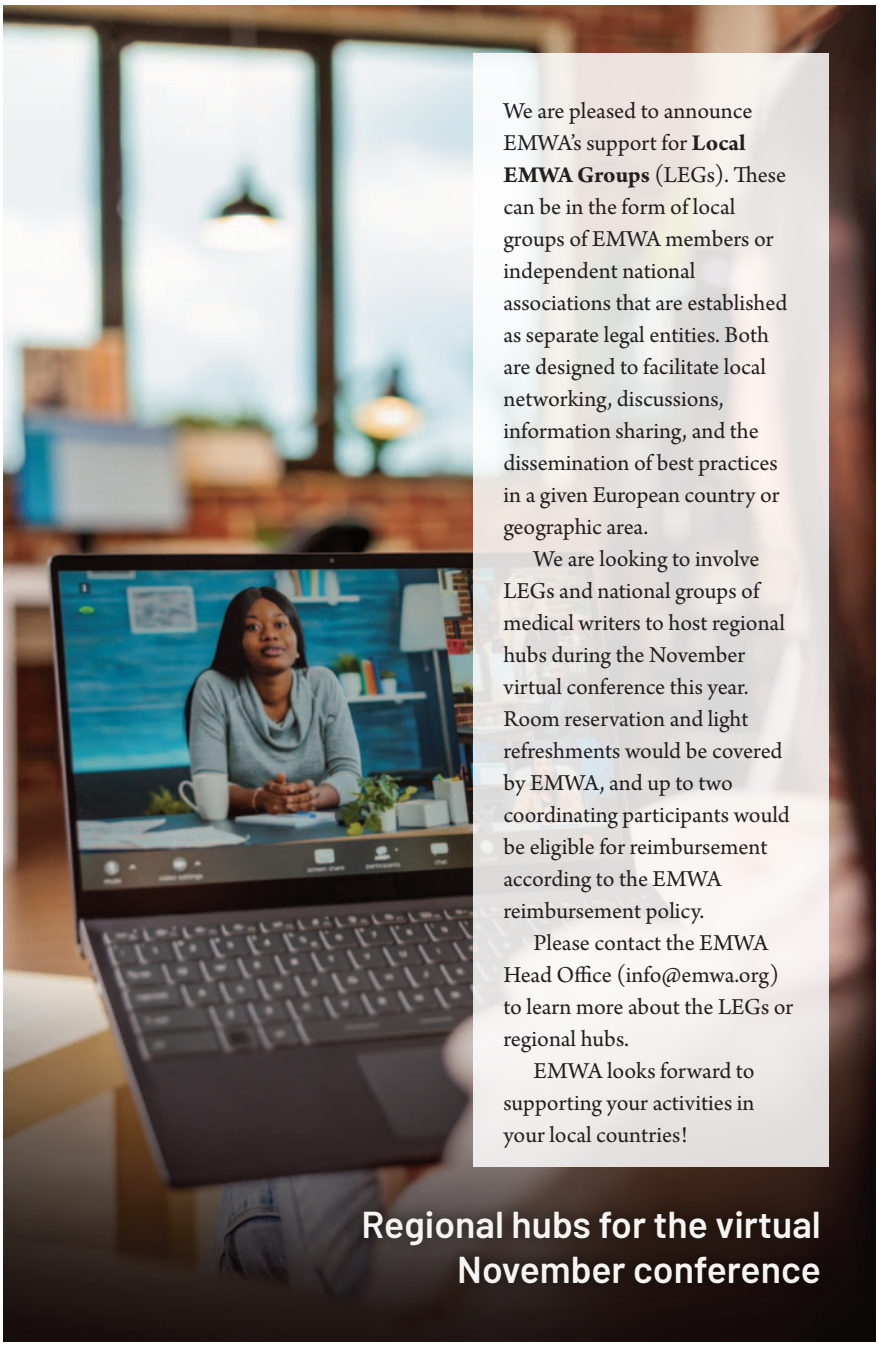
Johanna and Andrea prepared presentations for the morning session. They included: an introduction to medical writing; the benefits of joining EMWA; professional use of social media; and future challenges for medical writers.

The afternoon offered a change of pace. Laura managed interactive discussions around critical issues of national and international interest for medical writers, encouraging brainstorming and contributions based on personal perspectives and experiences. The exchanges were dynamic and animated.

The group concurred that a consensus of the medical writing profession in Italy is essential for the definition of a national framework. They created a private LinkedIn group, "Professionisti della Comunicazione Scientifica e Medical Writers Italiani", and are also looking forward to working with EMWA on developing an Italian Local EMWA Group (LEG). They are actively preparing a second meeting to be held in conjunction with the virtual opening of the Autumn EMWA Conference in November.

If you are living or working in Italy, or are an Italian living abroad, and are interested in joining this group, please contact them at medicalwritersitaly@gmail.com.

Johanna Chester, Antonella Ruscioni, Alessia Spina, Giulia Radighieri, and Cristina Vinci



Regional hubs for the virtual November conference

We are pleased to announce EMWA's support for **Local EMWA Groups** (LEGs). These can be in the form of local groups of EMWA members or independent national associations that are established as separate legal entities. Both are designed to facilitate local networking, discussions, information sharing, and the dissemination of best practices in a given European country or geographic area.

We are looking to involve LEGs and national groups of medical writers to host regional hubs during the November virtual conference this year. Room reservation and light refreshments would be covered by EMWA, and up to two coordinating participants would be eligible for reimbursement according to the EMWA reimbursement policy.

Please contact the EMWA Head Office (info@emwa.org) to learn more about the LEGs or regional hubs.

EMWA looks forward to supporting your activities in your local countries!

EMWA Ambassador Programme news

The EMWA Ambassador Programme is continuing its efforts to reach out to new audiences to promote medical writing and EMWA and has supported the following events:

On May 10, at the EMWA Spring Conference in Prague, the Ambassadors held a lunchtime meeting to discuss the current status and plans. The meeting was attended by Andrea Rossi, Evguenia Alechine, Ricardo Milho, Arunon Sivananthan, Nadia Grewal, and Maria Kołtowska-Häggström. The group is currently in the process of organising a standing committee to coordinate future events.

On June 22–23**, Andrea Rossi** presented on careers in medical writing at the University of Florence. He then followed up with a presentation at the university career day on July 4–5.

If you are an experienced medical writer and EMWA volunteer and are interested in becoming an EMWA Ambassador or know of any upcoming career events in your locality, please contact Abe Shevack (aspscientist@gmail.com).

EMWA Professional Development Committee update

The EMWA Professional Development Committee (EPDC) has two new members: **Sergey Sulima** and **Johanna Chester**, who will take the place of outgoing members **Sarah Tilly** (President-elect) and **Raquel Billiones** (Journal Editor-in-Chief). We warmly welcome our new EPDC members and thank our outgoing members for their work.

To learn more about the EPDC activities, please check EMWA's education page: https://www.emwa.org/education/the-epdp-programme/

Erratum:

Abstracts from the EMWA Spring Conference Poster Session

In the June 2023 issue of *Medical Writing*, the author list for one of the conference posters was incorrect. The online version has been corrected. The correct authors for the poster "A case study of whether ChatGPT can produce abstracts that meet CONSORT for Abstracts requirements" (Poster 10) are:

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Regulatory initiatives for artificial intelligence applications: Regulatory writing implications

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Abstract

Applications of artificial intelligence (AI)/machine learning (ML) components in drug development are growing exponentially. The trend is expected to continue. The growth has resulted in increased engagements on the part of regulatory agencies to ensure safe and effective use. This article explores the utilisation and opportunities in three areas: medical devices (built-in software applications); post-marketing surveillance (processing of large volumes of reported adverse reactions); and clinical development (pharmacokinetic profile, dose selection, clinical trial design, and regulatory writing). AI/ML-based applications are not perfect. Potential risks are enormous. Continued public/private engagement, vigilance, and oversight for all parties is essential for successful utilisation of these tools.

Introduction

Technological innovations have revolutionised computing architecture, opening new horizons in drug development. The processing power, the ability to scan through a variety of data sources and synthesise information using established rules have enabled researchers to explore areas that were previously beyond reach.

As per International Medical Device Regulatory Forum,[1] "Artificial Intelligence" (AI) is a branch of computer science, statistics, and engineering that uses algorithms or models to perform tasks and exhibit behaviours such as learning, making decisions, and making predictions. The subset of AI known as machine learning (ML) allows ML models to be developed by ML training algorithms through analysis of data, without models being explicitly programmed."

The number of regulatory submissions with AI/ML components is growing, with ~10-fold increase in 2021 compared to 2020.[2] This trend is expected to continue. Common types of analysis included outcome prediction, covariate selection, image analyses, modelling, dose selection/adjustment, endpoint/biomarker assessment, and post-marketing surveillance.

The diverse applications of AI/ML in drug development have led to increased focus on part of regulatory agencies in developing guidelines and discussion papers to ensure the safe and effective development of new treatments, including devices. In a broader effort to communicate with various stakeholders, the FDA issued a discussion paper in May 2023, requesting feedback on the use of AI and ML in the development of drugs and biologics.[3] This discussion paper focuses on the landscape of current and potential uses of AI/ML and considerations for the use of AI/ML along with next steps for stakeholder engagement.

This paper reviews recent AI/ML-based applications in drug development, associated challenges, relevant regulatory guidelines, and implications for regulatory writing.

AI/ML applications in medical devices

AI-based systems are typically implemented as software in medical devices or as Software as a Medical Device (SaMD). The first AI-based medical device approved by the FDA in April 2018[4] (IDx-DR) is a software program that used an AI algorithm to analyse images of the eye taken with a retinal camera to detect diabetic retinopathy in adults with diabetes.

Since then, the use of AI/ML-based devices in healthcare settings and daily life has grown exponentially. AI/ML-based technologies are being used by medical device manufacturers for product innovation, patient care, and improving quality of life. The built-in algorithms in the devices are programmed to learn from real-world experiences and adapt accordingly, e.g., sensors, stimulators, glucose monitors, enhanced imaging systems, wearable devices, etc. The number of approvals is steadily increasing, with 41 approvals in 2022 and 15 approvals as of April 30, 2023.[5] Examples of recent approvals include the Prospera™ spinal cord stimulation system, an implanted spinal cord stimulation system intended to treat long-term (chronic) pain, and the MiniMed™ 780G system intended to continuously measure glucose levels to manage type 1 diabetes mellitus in adults and children.[5]

In recent years, there has been increased collaboration between the FDA and other regulatory agencies. The goal is to mitigate potential adverse consequences of algorithm changes on patients' safety and wellbeing and support favourable benefit/risk balance. The complexities involved are enormous, given the continuous auto modifications of rules as part of ML.

The FDA, Health Canada, and MHRA jointly identified 10 guiding principles for medical device development to promote safe, effective, and high-quality medical devices that use AI and ML.[6] Although these principles were developed for medical device development, many of these (e.g., multidisciplinary collaboration; data quality assurance, software engineering and good security practices; representativeness of study participants, and data sets) are also applicable to drug development.

In April 2023, the FDA issued a new draft guidance ''Marketing Submission Recommendations for a Predetermined Change Control Plan for Artificial Intelligence/Machine Learning (AI/ML)-Enabled Device

Software Functions".[7] In this guidance, the FDA recognises that the development of ML-enabled device software functions (ML-DSFs) is an iterative process. The guidance describes an approach that would "support the ability to modify an ML-DSF while continuing to provide a reasonable assurance of safety and effectiveness across relevant patient populations". The guidance also provides helpful tools for medical writers in preparing quality documents for submission. It elaborates on the goals and contents of the device modification protocols. It also describes the required documentation regarding the assessment of the benefits and risks of implementing a Predetermined Change Control Plan for an ML-DSF, as well as the mitigations of those risks. The plan can be submitted as part of the marketing submission to ensure the continued safety and effectiveness of the device.

AI/ML applications in post-marketing safety surveillance

Another AI/ML-based application is in post-marketing surveillance. In the US, FDA's MedWatch, a medical product safety reporting program, is used for reporting adverse drug reactions (ADRs) by healthcare professionals and consumers. The FDA Adverse Events Reporting System is a database containing ADRs, medication error reports, and product quality complaints that have been submitted to the FDA.

The volume of data is large, and the sources consist of a mixture of structured and unstructured data, and substantial processing is required to make these data usable. AI/ML-based systems are used by sponsors, independent pharmacovigilance providers, and regulatory bodies for case processing, case evaluations (assessing the likelihood of a causal relationship between the drug and the adverse event (AE)), and case submissions (aggregate reports in a time-sensitive manner).

The FDA uses the Sentinel system for the safety surveillance of medicinal products.[8] It was initially launched in May 2008. Its capabilities have expanded significantly and continue to grow since the initial launch. It uses natural language processing and other ML approaches to extract and process relevant information from submitted AE reports. The future of the system is outlined in Sentinel System Five-Year Strategy: 2019-2023.[9] The goal is to incorporate emerging data sciences and electronic health records data for safety surveillance.

In the EU, EMA's Pharmacovigilance Risk Assessment Committee is responsible for assessing and monitoring the safety of human medicines. The reported ADRs are collected in the Eudra Vigilance database, which is used to detect emerging safety signals.[10]

Additionally, AI/ML-based applications are useful for data tabulation and summary reports for authoring periodic safety reports and other documents based on post-marketing surveillance data.

AI/ML applications in clinical development

AI/ML-based applications in healthcare have gained considerable momentum in recent years and are continuously growing.[11] The most common applications are in oncology and neurology and are used in the design and conduct of clinical trials, the selection of stratification variables for randomisation, the implementation of enrichment strategies, site selection, clinical outcome measures, and the assessment of endpoints. These tools are also used in modelling and simulation to predict pharmacokinetic profiles, exposure-response relationship to help dose selection, and optimisation.

Additionally, the COVID-19 pandemic led to an uptake in the use of digital health technologies

(DHTs), including telehealth, remote monitoring, and patient portals. The FDA issued a new guidance in Dec 2021 regarding the use of DHTs for remote data acquisition.[12] The guidance provided directions and recommendations for selection of DHTs suitable for clinical investigation, validation of DHTs, and use of DHTs in collecting data. It also elaborated on the identification and management of risks associated with the use of DHTs in clinical trials.

Familiarity with new guidance documents regarding decentralised trials and DHTs is essential for medical writers involved with protocol preparation. It helps to adequately describe the study endpoints, efficacy, and safety measures assessed using a DHT, and the assessment schedule.

The ML based tools are also frequently being used in authoring regulatory documents, particularly for the "reuse" of information from previously approved documents (e.g., trial protocols, statistical analysis plans, data tables, and/or sections of final clinical study reports) in new study reports or summary documents. There is considerable efficiency when these tools are used appropriately.

However, it requires vigilance on the part of the medical writer and others in the development team to ensure the accuracy and validity of all source materials utilised, including data collection tools, curation, and review. It is encouraged to list the details involved in every step and include them in the electronic Common Technical Document to enable verification during the review process. Overall, the AI/ML tools when used judiciously are helpful and can expedite the submission process.

AI/ML applications have opened pathways for disease areas where conventional placebo-controlled randomised trials are not feasible. In these cases, AI/ML-based applications have enabled the use of real-world data (RWD) and real-world evidence (RWE), which refer to data collected outside of trials in routine healthcare settings (such as claims data, electronic health records, registries, etc.). New guidance documents from the FDA and EMA in recent years have provided much needed guidance on the use of these alternative resources and have encouraged discussions with Sponsors to address concerns throughout the development cycle.

One particular application is data curation for data collected from numerous diverse sources outside the clinical trial, each with a different purpose for data collection leading to missing data, incomplete data dictionaries, uncoded data, etc. ML-based tools have helped to make the data fit for use in clinical trials and in sophisticated algorithms for accurate diagnostic assessments.[13]

Other AI/ML-based applications include the ability to interact with patients remotely, reducing the need for in-person visits and enabling access to a diverse population. This has the potential for improved retention and compliance. The opportunities and challenges are further elaborated in the FDA guidance on decentralised trials, that is, trials where the activities occur outside of clinical sites (patient's home or other healthcare settings).[14] The guidance provided is helpful for medical writers to address issues related to protocol deviations, baseline comparability, and remote assessments.

Other regulatory initiatives

Ethics guidelines for trustworthy AI were issued in April 2019 by the EMA High-Level Expert Group on AI.[15] This included seven key requirements: human oversight; technical robustness and safety; privacy and data governance; transparency; diversity, non-discrimination and fairness; societal and environmental wellbeing; and accountability. The goal was to minimise unintentional harm, foster diversity, and ensure adequate data governance mechanisms. Following a piloting process, the prototype was revised and the final list was published in 2020.[16]

The International Coalition of Medicine Regulatory Authorities Informal Network for Innovation working group led by EMA provided the following recommendations to regulators to address challenges posed by AI.[17] The report called for regulatory guidelines related to AI for "data provenance, reliability, transparency and understandability, pharmacovigilance, and real-world monitoring of patient functioning", and recommended that regulators "may need to apply a risk-based approach" when assessing and regulating AI. Additional recommendation for sponsors and developers includes setting up "strong governance structures to oversee algorithms and AI deployments that are closely linked to the benefit/risk of a medicinal product".

These new directives enforce ethical use, reliability, and transparency of the sources and applications, which are vital in authoring high-quality documents.

Discussion and conclusions

The AI/ML applications are wide ranging. The ability to scan through myriad unstructured data sources, synthesise using established rules, and predict new targets and potential solutions have changed the landscape and offer new hope. It has the potential to identify the "bad factor" and further replacements to create a new treatment paradigm.

AI/ML-based applications, like any other tool, are not perfect. The potential risks are not transparent, ML outcomes are not foreseeable, and the consequences could be serious. To be used effectively, all AI-based applications (software and devices) must undergo a stringent validation process before being implemented in clinical practice.

The growing awareness of the potential safety risks has prompted discussions in both public and private settings to seek solutions. The effective use of documents authored using AI/ML applications require parallel review by specialists; one is not a replacement for the other. "AI and human intelligence offer synergy for responsible innovation and veritable prospects for improving healthcare from prevention to diagnosis to therapeutics while unintended consequences of automation emergent from AI and algorithms should be borne in mind on scientific cultures, work force, and society at large".[18]

One other major concern is data privacy. The search and decision-making algorithms built in ML-based applications may lead to unanticipated inferences and predictions. "As artificial intelligence evolves, it magnifies the ability to use personal information in ways that can intrude on privacy interests by raising analysis of personal information to new levels of power and speed".[19] There is also a potential for leaking and misusing patients' data. Adequate steps must be taken to safeguard privacy.[20]

In summary, AI/ML-based applications, when used effectively, hold a lot of promise. These tools have potential applications in all stages of drug development, including designing new molecules, identifying disease targets, increasing the efficiency of clinical trials, and post-marketing safety surveillance.

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The opinions expressed in this article are the author's own and not necessarily shared by her employer or EMWA.

Disclosures and conflicts of interest

The author declares no conflicts of interest.

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Digital tools for the clinical evaluation of medical devices:
A guide to empower regulatory writers

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Abstract

The implementation of the European Medical Device Regulation (EUMDR) has driven innovation in the digitalisation and the development of artificial intelligence (AI)-powered automations for regulatory writing. This article explores a selection of tools designed for device-related regulatory activities, highlighting their functionalities and use cases. The goals of the article are to demystify the role of AI in medical and regulatory writing, explain the process of developing AI-based automations, illustrate how these tools benefit medical writers, and most importantly enhance the readers' skills in assessing such tools. The article discusses five automation tools: avasis, DistillerSR, Fern.ai, MedBoard, and Nested Knowledge, providing an overview of their features and benefits. The article concludes by emphasising that these automations address certain pain points faced during medical writing, yet they prioritise different features. By doing so, they empower users to improve data quality and streamline tasks in regulatory writing. Since there is no one-size-fits-all tool, the decision-making process is ultimately that of the user, not only on the type of tool to select but also on how best to leverage the software to optimise their technical documentation.

Introduction

The implementation of the European Medical Device Regulation (EUMDR) has played a pivotal role in driving innovation in the development of digitalisation and automations powered by artificial intelligence (AI) for regulatory writing. The role of the EUMDR becomes evident when comparing the timelines of its implementation in May 2021 in parallel with the the number of newly developed tools tailored for medical writing during the same time period (Figure 1).

The surge in software innovation in the medical technology sector was primarily driven by the substantial burden of managing and updating clinical evidence and navigating stringent conformity assessment processes. That resulted in medical device manufacturers encountering unprecedented challenges, both in terms of costs and time, with limited coping strategies at their disposal.[1] These challenges have provided the medical device domain with the long-needed incentive to embrace out-of-the-box technological solutions, ushering the digitalisation industry into a more sophisticated digitalisation era.

However, the emergence of generative AI and its use in the field of medical writing has sparked controversy and raised concerns that could potentially impede the industry's progress and momentum in adopting automated solutions.[2] As a medical writer who worked in the field of software development, I perceive the widespread concern and scepticism surrounding AI-based automations as a threat to the progress achieved as well as an opportunity that has presented itself, to engage medical writers, leveraging their keen inquisitive interest in the matter.

This article is a quest to explore a selection of tools designed for device-related regulatory activities. While they primarily focus on addressing different stages of clinical evaluation and post-marketing surveillance (PMS) processes, these tools can also compile systematic literature reviews of other types. These tools were chosen to illustrate a broad range of capabilities and highlight some unique features intended to streamline the daily tasks of medical writers.

The following are the goals of the article:

- Demystify the role of AI in medical and regulatory writing.
- Explain the process of developing AI-based automations.
- Explore the various functionalities and use cases of automated platforms.
- Illustrate how these functionalities can benefit medical writers.

- Enhance the readers' skills in assessing and evaluating such tools.
- Encourage readers to approach new technologies with scientific curiosity while maintaining a healthy dose of scepticism.
- Foster engagement between all stakeholders, to build a trust-based dialogue that drives technological advancements.

Ultimately, this article should assist you in making informed decisions based on reliable information and in selecting the most suitable tool for your needs. As a disclaimer, I would like to clarify that this article is neither a promotional piece nor a systematic comparison of the showcased tools. The opinions expressed in this article are solely those of the author and are based on research, webinars, and interviews conducted with representatives of these companies.

Behind the scenes of an AI automation in the making

To provide you with a better understanding of the automation development process, I will be using my knowledge of certain aspects of my previous role as a lead medical writer involved in the development process to ascertain some facts. A key aspect of the role of the medical writing team was to actively participate in AI "sanity" verification, conceptualisation of decision-making trees, and validation of their logic. More importantly, as well-trained scientists and clinicians, we gathered high-quality clinical data pertaining to safety and performance of medical devices to ensure the "human-in-the-loop" approach. These datasets were subsequently utilised by machine learning engineers for AI training purposes. Once the models were operational on the platform, the medical writing team created literature review projects to assess and validate their accuracy and sensitivity, two important parameters used in measuring the performance of an AI model.

By underlining the role of medical writers in the process of AI training, some of the prevailing misconceptions surrounding AI automations should be discredited. One such misconception involves the origin and quality of the datasets used for AI training, with many question marks raised regarding the type of checks and quality control processes undertaken to guarantee the robustness of their performance. Given the stringent nature of the regulatory domain, such software solutions go through repeated assessment and validation processes to align with regulatory and legal expectations. The development process involves collaborative efforts between regulatory and medical writing professionals, as well as software and machine learning engineers, who come together to build

optimal products suitable for professionals operating within the intricate regulatory field.

In the following sections, I present five automations to highlight some of the most interesting functionalities currently available to medical writers. The solutions are listed in alphabetical order.

I present five automations to highlight some of the most interesting functionalities currently available to medical writers.

avasis

As a leader in process digitalisation, avasis offers a comprehensive suite of digital solutions that optimise tasks and facilitate the transformation of information from documents into digital datasets for enhanced reusability, traceability of information, and automated completeness checks, ensuring compliance and enhancing efficiency.[3] These solutions revolve around the core functionalities of Siemen's ALM Polarion software, which ensures the digitalisation of various processes within the medical device life cycle. avasis provides solutions that are particularly relevant to medical writers, enabling efficient management and documentation of content created as part of clinical evaluation, post-market clinical follow-up (PMCF), and PMS activities.

Customers of avasis can select one or more solutions from its portfolio to meet their specific requirements. These solutions can be further adapted to align with the company's specific product portfolio. For example, avaREGULATORY assists in managing regulatory documents and requirements, while avaCLINICAL streamlines reviewing the process of clinical evaluation and literature review, integrating it with risk management and product development. avaPMCF handles the management and documentation of PMCF activities, linking them to clinical evaluation and risk management. The latest addition to their offerings is avaADVERSE/ avaPMS, a tool specifically designed for PMS. Through an integration between these solutions, they allow semi-automated content creation, maintaining consistency, traceability, and improving overall efficiency.

The integration of avaADVERSE with national authorities' databases enables searches and direct access to vigilance data. Subsequently, the relevance and quality of the data can be directly assessed, before sending the information to avaRISK for further analysis. The solution seamlessly integrates with the clinical safety reporting components in avaCLINICAL. The solution provides four readily available templates for creation of safety database review files, safety database search plans, safety database search protocols, and safety database review reports.

Additionally, the avaIMDRF add-on centrally manages International Medical Device Regulators Forum (IMDRF) adverse event (AE) codes digitally, eliminating the need for Excel files. The integration of IMDRF AE terminology library grants users access codes, and the application of these the codes for information in

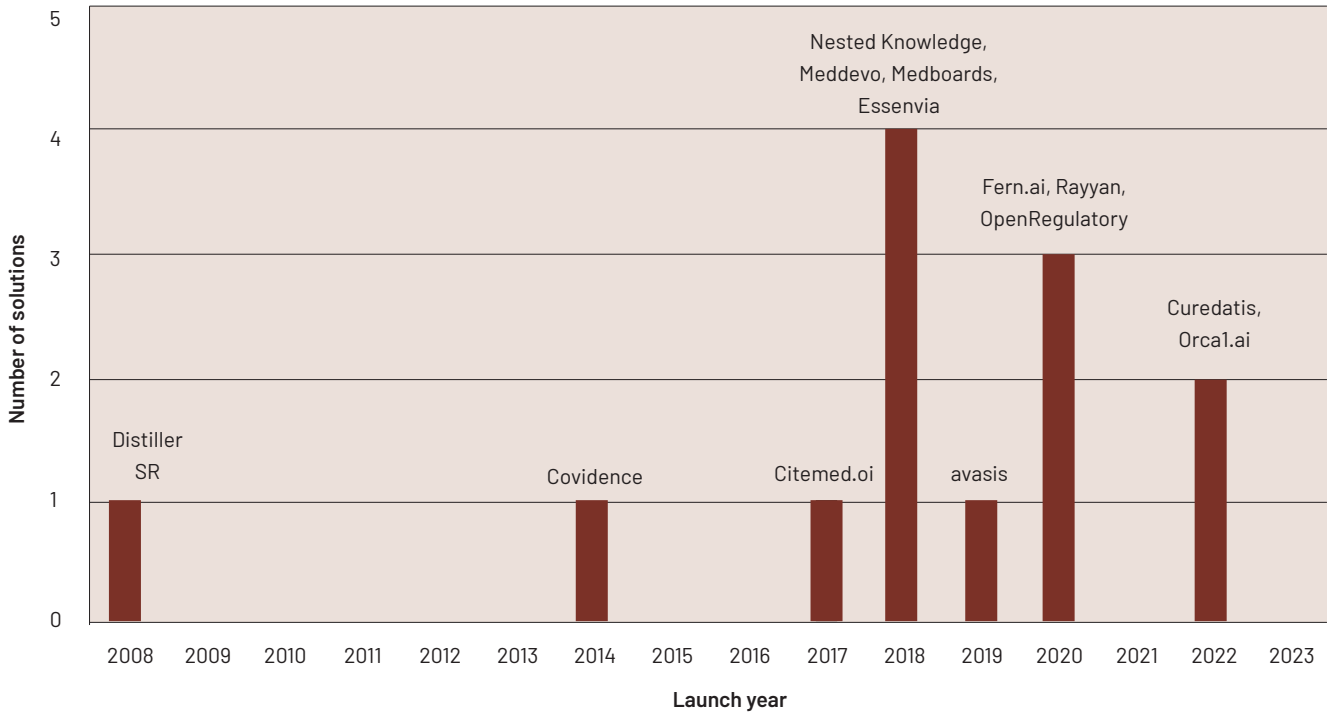

Figure 1. The timeline of the release of regulatory and medical writing tools

This infographic demonstrates the release of tools and platforms aimed for conducting systematic literature reviews and providing assistance for technical documentation of medical device life cycle between 2008 and 2023.

different processes (e.g., for harms in the risk analysis). These codes can be used to identify trends and signals in PMS and to categorise publications identified during literature reviews, ultimately contributing to PMS reporting. The use of IMDRF AE codes for adverse event coding is an international requirement, playing a crucial role not only in vigilance (serious adverse event reporting) but also in various activities such as cause investigation, complaint handling, and clinical evaluation, all of which contribute to effective risk management.

DistillerSR

DistillerSR, one of the pioneers in the field of digitalising literature reviews, optimises the processes of both pre-market approval and post-market compliance evidence management.[4] This platform can be customised to match the complexity of each specific use case, with configuration options available at every key step of the literature reviewing process.

One of the time-saving features of DistillerSR is its smart quarantine functionality, which automates the deduplication process while giving users control over the level of confidence processes at which the AI should consider a reference as a duplicate. Users also have the option to manually review these references at any point.

With its AI capabilities, DistillerSR enables reviewers to find references more efficiently by continuously assessing their relevance and comparing them to pre-screening records. This results in updated rankings and reprioritised order of the reference list. Additionally, DistillerSR plays a role in quality control by double-checking inclusion and exclusion decisions and automatically categorising references.

Workload triage is another aspect of DistillerSR's design that clearly distinguishes the platform. This feature allows project leaders to assign specific portions of the review process to certain reviewers while keeping track of their progress in real time. Through comprehensive traceability, a project leader's task is further facilitated by the access to details of the actions and decisions taken throughout the reviewing process. A specific action or search can be traced back not only to the user, but also to the date and time of execution and is linked to a certain query. This also ensures that any project completed in the platform is audit-ready.

CuratorCR, a recently developed add-on module, serves as a research knowledge centre within the platform. It consolidates and dynamically manages the workflow of evidence-based research, enabling reviewers to continuously curate, share, update, and reuse data across multiple teams, modules, and product portfolios.

Fern.ai

Fern.ai™, previously known as Giotto Compliance, is a comprehensive platform for clinical evidence review that offers an intuitive interface.[5] Fern.ai employs AI models trained by medical writers with a human-in-the-loop approach which deliver recommendations during the title and abstract screening and the extraction steps with high sensitivity and accuracy.

With a literature review-based structure that lends itself well to a wide range of use cases, the platform has built-in features that align with the guidelines set by the EUMDR and EU In Vitro Medical Device Regulation for clinical evaluation and performance evaluation purposes. The platform ensures thorough documentation of all steps, facilitating auditing and ensuring traceability. Users have the flexibility to customise the generated documents, available in various formats, at the end of each step. Academic research, epidemiological studies, and health economics and outcomes research are a few more examples of use cases for Fern.ai.

At the outset of each literature review, Fern.ai allows users to define their research strategy in the project workspace through the Population, Intervention, Comparison, Outcomes and Study (PICOS) framework. These data are subsequently used by the AI as the basis for its recommendations for that specific project. Fern.ai facilitates a seamless transition between the query, screening, appraisal, and data extraction steps through its intuitive workflow.

By leveraging the AI's inclusion and exclusion recommendations, users can optimise their screening process, offering the flexibility to customise the degree of automation in their decision-making. Users can also specify the exclusion reasons on which these recommendations should be applied, giving them greater control over the screening outcomes. Duplication, language type, and missing abstracts are among the common exclusion reasons where a high degree of automation is often used, resulting in significant time reduction during screening. In a similar fashion, Fern.ai plays a central role in improving efficiency and data quality during the data extraction steps. Using natural language processing and customisable data extraction templates, users can directly extract relevant data from selected articles through an intelligent tagging interface. Moreover, users can locate relevant data with the help of the AI's suggestions. The link between the extracted data and their original location in the article allows a "one-click" revision and audit process. The data extraction functionality of Fern.ai is one of the strongest features of the platform.

> Given the stringent nature of the regulatory domain, such software solutions go through repeated assessment and validation processes to align with regulatory and legal expectations.

MedBoard

MedBoard is a multipurpose platform consisting of six digital modules integrated with a large, curated information portal through a powerful AI search engine for MedTech, Pharma, and Digital Health.[6] These modules include: MedBoard Search, Databases and Analytics, MedBoard profiles, Intelligence (Clinical and regulatory), Systematic Reviews, and Product portfolio and country registrations management.

MedBoard encompasses a wide range of information, covering clinical trials, literature, recalls, adverse events, approvals, guidelines, regulatory news, market news, technical standards, documents, and safety alerts. Equipped with advanced search filters, and an analytics studio, these databases offer the capability to slice and visualise data, providing instant new insights.

MedBoard Search, databases and other trusted data sources are at the core of the platform delivering regulatory, market and clinical intelligence to the other modules. The "Systematic Reviews" module harnesses the extensive database capabilities of the platform. In addition to scientific literature, this module can help users tap into other data resources such as: technical standards, market information, and clinical trials. Furthermore, the Systematic Review module offers features such as automated updates, customisable appraisal criteria, automated PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses), and identification of similar reviews. Additionally, an "AI Reviewer Assistant" is available to assist users in their tasks. In keeping with their strategy of placing the user at the centre of the decision-making process, the role of the AI tool is providing assistance, intelligence, and automating manual, repetitive work.

The platform's modules and functionalities come together to expediate various key activities, including PMS clinical reviews, SOTA (state-of-the-art) analysis, and competitive market analysis by leveraging its extensive database of manufactures and medical product profiles.

Nested Knowledge

Nested Knowledge is an evidence synthesis tool designed to transform the way the scientific community gathers and interacts with clinical data.[7] It offers various functionalities, such as finding, filtering, extracting, and analysing data from diverse sources for different purposes. While its primary use case is health economics and outcomes research, as well as academic meta-analyses, it is also highly effective in early stages of medical device and drug research and development, clinical study design, and compiling data for regulatory submissions.

There are notable differences between publicly available AI platforms and those designed for professional use, particularly in terms of training, testing, and validation.

A significant challenge addressed by Nested Knowledge is the laborious and continuous process of updating existing reviews. Unlike other tools that produce static documentation, Nested Knowledge provides interactive, AI-assisted living systematic reviews and meta-analyses that can be updated in real-time.

Structurally, Nested Knowledge consists of two main modules: AutoLit and Synthesis. The AutoLit workflow serves as the foundation, allowing users to search, screen, and extract content from published studies. AI assistance is available at each step, but an expert review is required for accuracy confirmation. The platform also utilises AI during the screening process, serving as a third reviewer by learning from the user's screening decisions.

Synthesis is a robust analytical component of the platform that provides evidence-based insights into the data collected using AutoLit. These insights are presented through web-based interactive data visualisations that dynamically change as the underlying data are updated. Synthesis offers functionalities such as Quantitative, Qualitative, Manuscript, Critical Appraisal, and PRISMA.

The qualitative Synthesis function of Nested Knowledge enables users to collect and classify data through a tagging hierarchy to review the population and endpoints of trials, and compare interventions and comparators. These data can be used to define the standard of care and compare intervention outcomes when conducting SOTA reviews. On the quantitative side, Synthesis provides a network meta-analysis environment where the data can be reviewed at the summary level using the data elements of interest. Dynamic visual outputs such as forest plots with calculated odds ratios and funnel plots are generated and can be reviewed directly on the platform. Furthermore, heterogeneity and risk of bias are assessed through automatically calculated r-squared value and and risk of bias visual representations.

Conclusion

At the end of this technically packed exploration, I would like to emphasise a key message: Automations are designed to tackle challenges encountered during technical documentation. Despite having a common goal, they employ alternative implementation strategies and thus prioritise different features. As a result, they empower their users through improving data quality, minimising repetitive tasks, and eliminating versioning issues. By providing template and customisable exports and ensuring traceability, they enhance compliance and audit-ready documentation. Digitalisation sets the stage for a highly streamlined collaborative and organisational project management processes. Collectively, these advantages make medical writers more efficient, reduce errors and audit deficiencies, and ultimately alleviate frustration. In the long run, reliable processes foster the delivery of medical devices with enhanced safety and performance profiles, paving the way for innovation and better patient care.

Here are a few additional takeaways:

- Features and functionalities of automation tools can vary significantly. While some focus on content authoring and analytical synthesis, others put more emphasis on data reusability, automated data extraction, and curated global intelligence.
- Considering the diverse profiles of automation tools, there is no one-size-fits-all solution. Users should invest time to determine which tool best suits their specific use cases.
- Not all automation tools incorporate AI and those that do utilise it as an additional feature to facilitate certain activities, while keeping the user in the driver's seat.
- There are notable differences between publicly available AI platforms and those designed for professional use, particularly in

terms of training, testing, and validation.
- When approaching a new tool, it is advisable to employ multiple methods and sources to thoroughly understand its functionalities. Engaging in discussions with long-term users and conducting adequate testing are essential.

As I have only scratched the surface of this group of technologically sophisticated solutions, and given the rapidly evolving nature of this sector with new products and features being introduced regularly, I would like to encourage readers to use this review as a starting point, conduct further research to gain a deeper understanding of the tools covered in the article, and explore additional options that I may not have been able to discuss due to space limitations. Noteworthy automation tools for reviewing clinical evidence include CiteMed.io, Covidence, Curedatis, Meddevo, and Rayyan. For generative AI-based tools in regulatory intelligence, consider Dr.Evidence, Huma.AI, Orca1.ai, and Yseop.

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Disclaimers

The opinions expressed in this article are the author's own and not necessarily shared by her employer or EMWA. This article is neither a promotional piece nor a systematic comparison of the showcased tools. EMWA and the author do not endorse any specific automation platform.

Disclosures and conflicts of interest

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AI language models are transforming the medical writing space – like it or not!

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Abstract

Whether you're an early adopter, an occasional user, or yet to acknowledge its transformative potential, artificial intelligence (AI) – specifically generative AI applications underpinned by large language models – is undeniably shaping our present and destined to influence the future of medical writing. Achieving a comprehensive understanding of these models can pave the way for their optimal application in areas where they excel. Additionally, this understanding helps to maintain a realistic, balanced perspective, allowing us to avoid the pitfalls associated with excessive or unfounded fear stirred by the current AI hype and related exaggerated promises.

A selection of AI applications offers insights into specific tasks for which generative AI can be effectively utilised. These applications can truly make a difference by saving time, streamlining workflows, and potentially enhancing the quality of the resulting outputs.

Introduction

In an era of rapid technological progression, artificial intelligence (AI) language models have emerged as transformative forces, significantly altering traditional workflows and methodologies across many fields, including medical writing.

As medical writers preparing for an AI-dominated future, we need to understand how these AI language models work. It will allow us to truly leverage their potential, comprehend their capabilities and limitations, and integrate them effectively into our writing processes.

Many of us tend to view the quantity of training data and parameters as crucial determinants of a model's performance. Indeed, we get all hyped up when respective players announce that the next-generation AI language model will be trained on x amount more data or are tailored towards a more specific subject, additionally claiming enhanced speed, reliability, and accuracy. Yet, are these factors truly game-changing? Maybe not exclusively. The intrinsic nature of the model, the underlying algorithms, and their data processing methodologies hold equal significance.

Therefore, let's aim to grasp the mechanics of AI language models before delving into their practical applications.

These applications can truly make a difference by saving time, streamlining workflows, and potentially enhancing the quality of the resulting outputs.

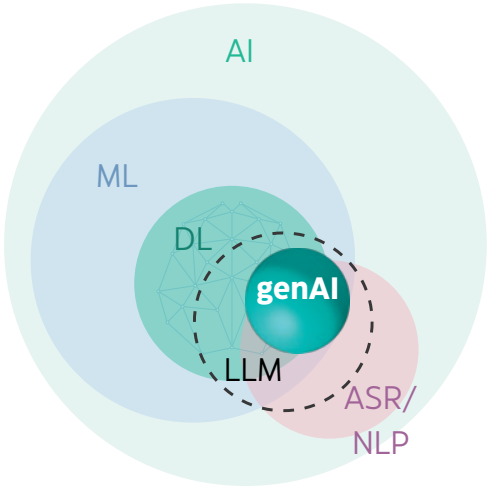
Understand AI language models and their limitations

Behind the scenes – Terminology

A **large language model (LLM)** is a deep learning technique, and a subset of machine learning, that uses artificial neural networks to analyse immense volumes of data, unveil intricate patterns, and guide decision-making. Through extensive training on massive datasets, LLMs develop an unparalleled capacity to recognise, comprehend, predict, and generate novel content spanning myriad domains (Figure 1).

The term **generative AI (genAI)** refers to all AI tools that use LLMs to primarily create content such as images (e.g., Midjourney or Stable Diffusion), text (e.g., GPT-4, PaLM, or Claude), code (e.g., Copilot), or audio (e.g., VALL-E or resemble.ai) in response to short **prompts**. To process a prompt, its words need to be converted into a model-readable input format, such as vectors or tokens.

Tokens can be as small as individual characters or punctuation symbols, or as large as words or even whole sentences, depending on the model and tokenisation method (e.g., rule-based, statistical, neural). This process of breaking down text into individual units is called **tokenisation** (Figure 2).



AI	Artificial Intelligence
ML	Machine Learning
DL	Deep Learning
ASR/NLP	Automatic Speech Recognition/Natural Language Processing
LLM	Large Language Model
genAI	Generative AI

Figure 1. Large language models (LLMs) and generative AI (genAI) as a subset of artificial intelligence (AI)

Tokens are processed by assigning each token a numerical ID as AI models can only process numerical data.

Modern LLMs and hence genAI tools successfully apply **transformer architecture** (Figure 3). Two key features define transformers: the *encoder-decoder* structure and the *attention mechanism*. The encoder processes the input data and generates a set of context vectors. Using these vectors, the decoder generates the output by selecting the token with the highest probability in a sequence of tokens. The attention mechanism, a crucial element in transformers, assigns a weight to an input token, guiding the model on where to focus during output generation. This process enables the model to manage long-range data dependencies, effectively equipping the model with long-term memory (Figure 3).

In simple terms, these models are mathematical functions supported by powerful computing capabilities, but they cannot think.

When a prompt is submitted to an AI language model, it generates the response by selecting the most likely next token based on calculated context and specific rules/settings. That means tokens/words are chosen based on their likelihood to follow.

In simple terms, these models are mathematical functions supported by powerful computing capabilities, but they cannot think. This is an important factor to consider when assessing the results produced by these AI tools, setting your expectations, and highlighting their limitations.

Sophisticated **prompt engineering**, which involves giving specific and detailed instructions to guide the model in its decision-making or prediction process, can enhance a model's performance. Depending on the task, methods such as **few-shot prompting**, which provides a few input-output examples, **chain of thought**

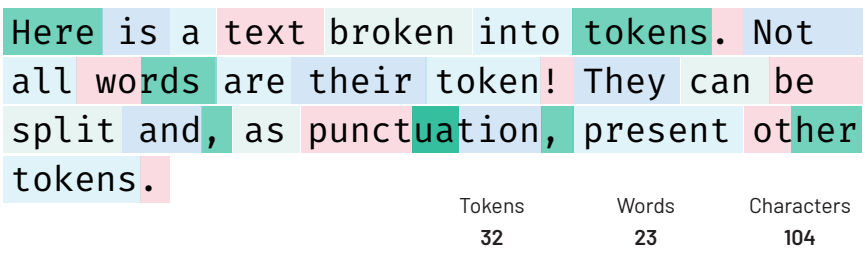


Figure 2. Example of tokenisation

Can genAI assist medical writing? Yes it can.

GenAI, and ChatGPT in particular, can be used to assist with many tasks, including:

- Paraphrasing
- Reformatting references to different styles
- Rewriting materials and methods sections
- Explaining statistical tests
- Rewriting abstracts
- Extracting article highlights
- Suggesting keywords
- Writing submission letters
- Summarising scientific articles or medical information for various audiences
- Writing lay summaries
- Repurposing available information for different formats and various audiences
- Creating educational and other training materials such as courses, webinars, presentations, hand-outs
- Compiling product and safety information
- Generating responses to customer inquiries
- Generating scripts for chatbots/virtual assistants and much more.

prompting (CoT), which uses sequential prompts to encourage reasoning or guide the model through complex tasks, and **prompt iteration**, have been found to be most successful in elevating a model's performance.

To avoid confusion, the term LLM/AI language model is used in conjunction with a range of natural language processing tasks, including text generation, translation, content summary, rewriting content, classification and categorisation, sentiment analysis, and conversational AI and chatbots.

OpenAI's GPT-series (the GPT stands for Generative Pre-trained Transformer) is widely recognised as one of the most extensively utilised LLMs at present. ChatGPT, along with its respective plugins, stands out as a prominent representative within this series.

In the following sections, we will focus on text-generating AI tools and use terminology such as LLM, AI language model, AI assistant interchangeably.

Limitations of AI language models

Despite being trained on increasingly larger datasets, using more parameters and unprecedented computational power, current genAI models are primarily sophisticated "prediction engines". While their performance consistently improves, it is important to remember that their output lacks true comprehension, critical thinking, or consciousness. Consequently, the generated texts have a tendency to be lengthy and articulate replies that could potentially include plausible but inaccurate or biased information. Therefore, it is mandatory that users review the output critically and always check its accuracy, appropriateness, context, and actual usefulness before accepting any result.

Especially in medical writing, text-generating AI tools should be regarded as assistants or a tool in the toolbox supporting workflows, providing a starting base, or helping to overcome writer's block. The human ability to comprehend context, strategise, critically evaluate, and convey nuanced emotions remains irreplaceable.

It is also essential to address privacy concerns when using text-generation tools. Careful consideration should be given to the inclusion of safe input data to prevent the inadvertent sharing of confidential or proprietary information.

The potential disruptiveness of this technology is not going unrecognised. Many journals and organisations have published guidelines with the intent to regulate the use of text-generation tools for publications (Springer-*Nature*,[1] Elsevier,[2] Taylor & Francis,[3] JAMA Network,[4] the World Association of Medical Editors [and *British Medical Journal*],[5] and the International Committee of Medical Journal Editors[6]).

With a grasp of these basics, you're well-prepared to begin or continue your journey with AI language models. Embracing an open mind and adopting a trial-and-error approach will facilitate exploration, learning, and the development of an AI-driven mindset. Establishing a clear understanding of these models will enable their effective use in workflow areas where they truly excel. This knowledge also helps to maintain a realistic perspective, preventing undue fear or over-enthusiasm sparked by the current AI hype and its associated promises and expectations.

> Embracing an open mind and adopting a trial-and-error approach will facilitate exploration, learning, and the development of an AI-driven mindset.

AI tools that can assist medical writers

Besides **ChatGPT** and its respective plugins, hundreds of AI-assisted, text-generating tools are launched weekly or integrated into existing applications as AI assistants. Keeping track of these numerous tools can be daunting for a busy professional. Therefore, below is presented a curated selection of widely accepted tools which could prove valuable to the majority of medical writers (see also Figure 4).

Don't forget

- ✓ Text-generating AI applications are sophisticated prediction engines; they predict words or tokens based on their likelihood to follow.
- ✓ Think of them as "word calculators" that use mathematic functions and mechanisms to fill in the gaps/blanks in a data set with the intental ways to provide an answer.
- ✓ Their performance depends not only on the quantity and quality of their training data or parameters, but also on factors such as model characteristics (transformer architecture, fine-tuning, combination of models), tokenisation method, and human skills (e.g., prompt engineering).

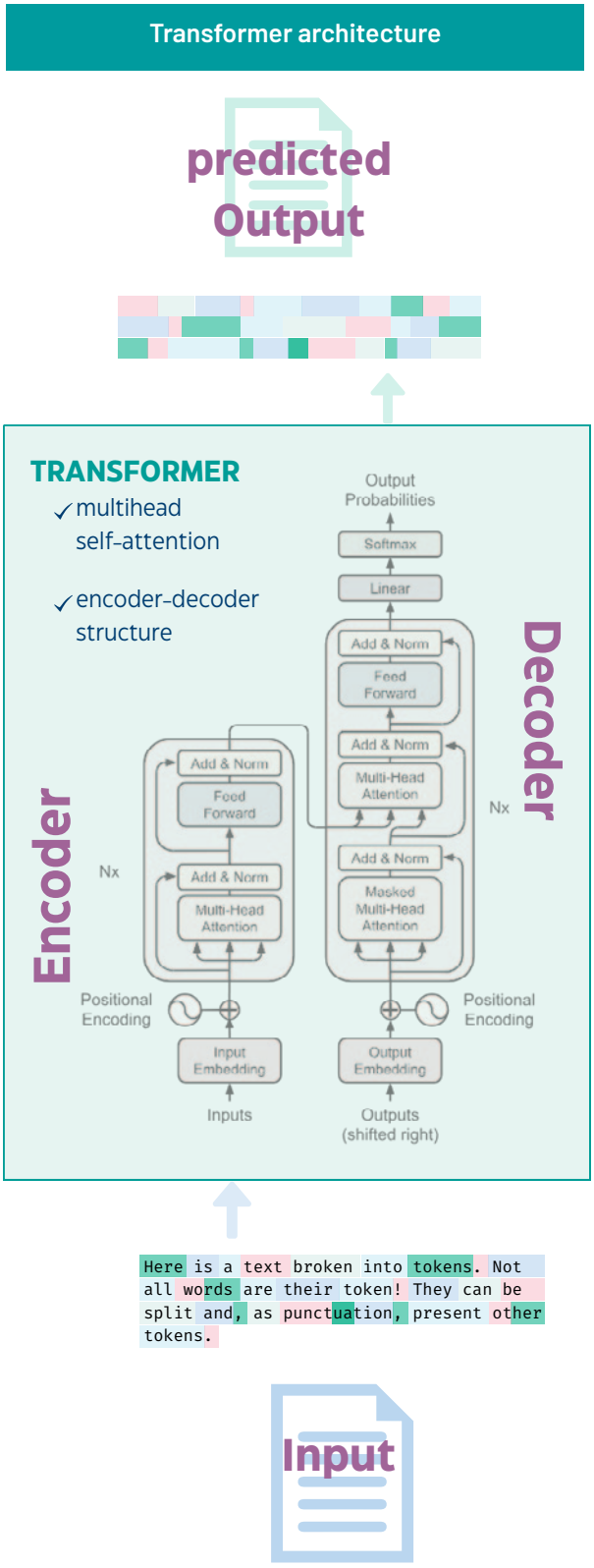


Figure 3. Illustration of transformer architecture

Writing and rewriting assistants

Let's start with **Quillbot** and **Wordtune**, two AI-rewriting assistants. Quillbot is a comprehensive paraphrasing tool targeted at improving grammar and enhancing wording; it also features a summariser tool. Its smaller alternative, Wordtune, helps you rephrase, improves tone and word choice, and is able to shorten or expand given text.

Conversation

Another extremely useful application and time-saver is **ChatPDF**. It allows you to chat with uploaded pdfs, such as scientific articles. It can answer specific questions and, when prompted correctly, returns structured responses.

Research plus writing assistance

scite_ is a platform that helps discover and evaluate scientific articles via Smart Citations. Smart Citations allows users to see how a publication has been cited by providing the context of the citation and a classification describing whether it provides supporting or contrasting evidence for the cited claim. Importantly, scite_ offers an integrated conversational AI Assistant, based on GPT-3.5. It can answer questions from a database of 180 million articles, book chapters, and data sets. Just like ChatGPT, it can assist you in the writing process for a plethora of materials.

SciSpace, an AI research assistant, is not only able to read, understand, and explain uploaded scientific literature, but it also comprises a citation generator, paraphraser, and AI detector.

SciSpace Copilot, available as Chrome Extension, can help understand technical language, math, and tables in PDFs, and allows you to organise and annotate materials to keep track of important information. This one is to watch!

Another free AI research assistant is **Elicit**. It assesses publications from Semantic Scholar and helps expedite the literature review process. When queried, it retrieves relevant papers and summarises key information in table format.

In addition, the AI tools **ResearchRabbit** and **Connected Papers** are definitely worth checking out. For these tools, the user provides specific citations (seeding) and the models search and visually map similar work. This greatly speeds up and deepens the discovery phase, no matter what research phase you are in.

Summary plus writing assistance

Scholarcy is an online article summariser tool for articles, reports, and book chapters. It highlights key sections for users to easily save and export summaries to return to at a later date.

Figure 4. Selection of AI-assisted applications that can support a medical writer's workflow

Unlike Elicit, it can only summarise one publication at a time but in much more detail. It extracts key concepts, a synopsis of the full-text, comparative analysis, and more.

An alternative AI-assisted research and summary tool is **genei**. It is designed to help users improve productivity by quickly extracting key information from articles, analyzing research, and summarizing articles. The paid subscription has the usual GPT-3 capabilities.

Generative AI tools excel in marketing support

GenAI tools have long been embraced in content marketing, where they outperform classical copywriters. From blogs, and website content, to social media posts, email marketing campaigns, newsletters, ads, and much more – genAI is widely adopted.

I recommend trying out **Jasper.ai**, a powerful all-in-one content generation platform trained to write original, creative content for all sorts of marketing assets. It also builds on OpenAI but adds other models to provide tailored solutions to specific content marketing needs. A big plus is that it comes with templates that help you structure and detail your prompts and a plagiarism checker.

Copy.Ai is a valid alternative to Jasper. Another tool, **AI-writer**, searches, writes content, and adds valid references to this content.

Every week, more than 100 new AI tools are released, and it is up to us, the users, to stay informed and check their feasibility to enhance our workflows. Only the most valuable applications will get adopted and survive. It is impossible to predict what the next developments and releases will be and how the tools will integrate and complement each other. Exciting times are ahead!

Only the most valuable applications will get adopted and survive.

Future-proof yourself and let AI amaze you!

AI language models and applications are set to reshape the medical writing space, redefining traditional workflows and methodologies in the process. Navigating this shift requires an open attitude, curiosity, and a commitment to continuous learning. Consider genAI applications as tools in your arsenal. Merely possessing a toolbox isn't enough; you need to know which tool to use for which task and how to use it effectively.

Our unique human abilities – understanding context, strategic thinking, critical evaluation, and conveying nuanced emotions – remain invaluable. They set us apart and play a crucial role in moderating and refining AI-generated output. Harness the potential of these AI tools to boost your productivity and elevate the quality

of your work instead of fighting them.

Crafting credible, evidence-based materials that are accurate, clear, and compelling still demands the expertise of a skilled medical writer. Remember, AI tools are not substitutes but powerful allies in our writing journey. Let's leverage these advancements to build a promising future in medical writing.

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I used ChatGPT (OpenAI, model GPT-4, version May 24, 2023) to rephrase some passages. I reviewed the AI-generated text and edited it as needed. I take full responsibility for the generated content.

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The opinions expressed in this article are the author's own and are not necessarily shared by EMWA. This article was prepared in May 2023 and reflects the status quo at that time. It is intended to provide understandable and memorable background information on AI language models. The importance of the selected tools may have changed by the time of publication.

Disclosures and conflicts of interest

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Narratives for a clinical study report: The evolution of automation and artificial intelligence

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Abstract
Automation and artificial intelligence (AI) are useful tools that are rapidly progressing in many fields within the clinical trial landscape, and their use in the production of narratives for clinical study reports is no exception. Technology and processes for efficient narrative production have evolved – but what may the future hold now that we are in the era of AI?

The generation of narratives for clinical study reports (CSRs) can be a complex, time-consuming, and costly task. The International Council for Harmonisation (ICH) E3 guidance indicates individual patient narratives should be included in Section 14 of a CSR for patients "describing each death, each other serious adverse event, and those of the other significant adverse events that are judged to be of special interest because of clinical importance".[1] The number of narratives required for an individual CSR can be as high as 1000 or more, depending on the phase of the clinical trial, and the work required to generate a narrative for each participant can necessitate a large team of dedicated medical writers (MWs).

> Best practices for creating CSR narratives have evolved over time, and continue to do so, with processes becoming increasingly efficient.

The majority of the work involved in generating CSR narratives needs to occur when final data for the trial are available (after database lock and when the tables, figures, and listings have been generated for the CSR); the narratives must be final and ready for inclusion in the final CSR. To perform this work efficiently and within the required timelines, strategies have to be employed to reduce time and effort and increase efficiency, which we will discuss in this article.

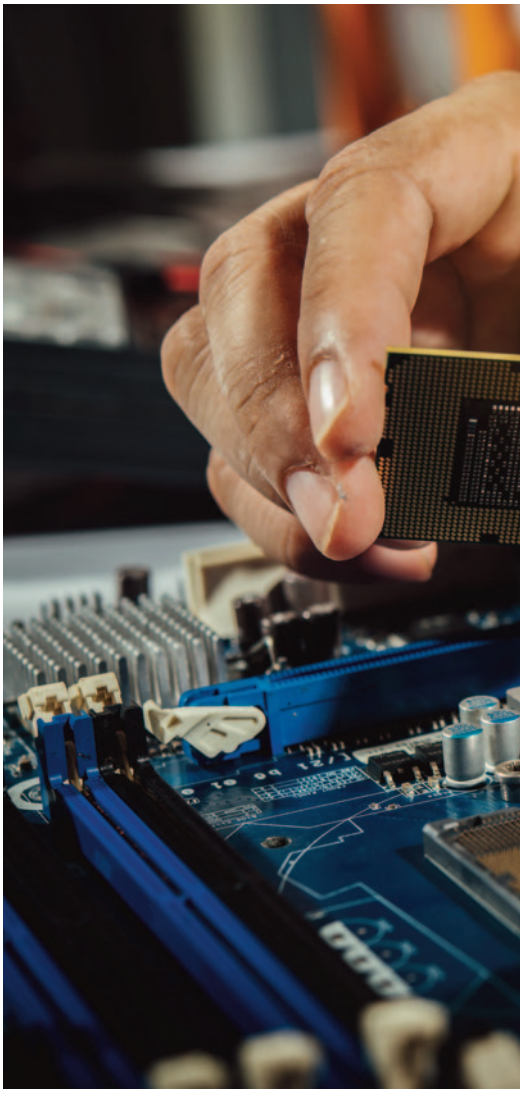
Where we have come from – a time-consuming and tedious manual approach

Best practices for creating CSR narratives have evolved over time, and continue to do so, with processes becoming increasingly efficient. Many of us will be familiar with a more manual approach to medical writing; whether preparing narratives, CSRs, or other regulatory documents, MWs used to spend a huge amount of time simply copying and pasting data from multiple sources.

Before any form of automation, narratives were created manually, in that MWs started from a template and populated it with data from various listings provided for the CSR. The complexity of a narrative can increase significantly in cases where the trial participant has a complex disease status, with a large amount of information needed to describe the disease or clinical status, concomitant medications, and the course of events that fully describe the event(s). Manually retrieving data from each listing for each narrative was a time-consuming task and increased the chance of human error. This, in turn, required a full, thorough quality control (QC) check of all data within the narrative to catch errors. When a CSR required the inclusion of hundreds of narratives, the manual process was a huge undertaking, and hence created the need for a more streamlined approach.

Where we are now – various tools for more efficient narrative production

Moving on from manual production of narratives, the process-driven automation approach is currently widely adopted and involves populating a narrative template containing placeholders or fields where data from



the clinical database can be inserted programmatically. As MWs are not trained programmers, we do not write the programming code ourselves – rather, we can use software or employ the assistance of trained programmers to perform the task. In large, multi-service organisations, where there is a department of programmers, the MW assigned to the narratives can work with a programmer to tailor the narrative template to the specific requirements for the trial. Essentially, we set the rules within the template for what actions follow: an automated trigger or a manual intervention, and the programmer can run narratives with text-based sentences populated with the data points required using the trial data captured in the case report form (CRF) fields. The programmer can generate as many narratives as needed for a CSR, producing consistent and accurate outputs. With the data having been inserted into the narrative programmatically, the QC check of each item of data by the MW is not necessary.

Alternatively, software can be purchased and installed on the MW's computer and used to generate narratives, using data from the clinical database. The MW can load the clinical data into the software package, and set the criteria for the narratives: which narratives should be run, which data should be included, and hence, how they will look. At the click of a button, the software will generate the required narratives.

Manual intervention by MWs in these narratives (either produced with a programmer or by using software) is, however, still required. The primary data source for drafting narratives is the clinical database, but supplementary data sources include data from the safety database (including the Council for International Organizations of Medical Sciences [CIOMS] forms or MedWatch forms), which still need to be inserted manually.[2] These secondary sources aid in providing additional details for building the story of the events being described. This, in turn, then merits a QC check of the manually incorporated text to the programmed output. That aside, it is clearly a benefit to writers to use automation to save time and effort in generating large numbers of narratives.

It is clearly a benefit to writers to use automation to save time and effort in generating large numbers of narratives.

The future of automation – AI

We say *the future*, but we are already in the era of artificial intelligence (AI). The use of AI is a phenomenon that is an ever-growing reality and many healthcare companies are now employing AI.

AI is defined as the ability of a digital computer or computer-controlled robot (or *bot*) to perform tasks commonly requiring human intelligence. Popularity of free-to-access AI tools like ChatGPT is growing and the use of AI tools to generate text within our industry is developing rapidly. AI can save MWs more than 30% of their time spent on QC processes and up to 80% of their time overall.[3,4]

AI is a promising tool to automate the narrative writing process beyond the programmed approach.

So where does AI come into play when generating CSR narratives? AI devices mainly fall into two major categories: the first being machine learning techniques that analyse structured data and select the desired information, and the second being natural language processing methods (of which ChatGPT is a form) that extract and analyse information from unstructured data such as clinical notes, to enrich structured data.[5] When we look at these two methods in the context of patient narrative preparation, AI is a promising tool to automate the narrative writing process beyond the programmed approach. An AI tool can automatically interpret the type of input data (CRFs, clinical database listings, CIOMS and MedWatch forms) and self-generate a full narrative output.[6]

Table 1. What are the benefits and potential challenges of AI in narrative production?

Benefits	Potential Challenges
✓ Increases efficiency of MWs	• AI detects and analyses patterns, so needs to be trained on large volumes of content to generate human-like text
✓ Raises the overall quality of the documents	• Adherence to laws and regulations, particularly privacy laws such as GDPR
✓ Re-use of tool to generate narratives after the first project can reduce overall costs	• Adherence to AI-specific laws in the process of being enacted such as the EU AI Act
✓ Reduces risk of errors	• Ethical issues remain largely unaddressed – such as biases in algorithms and protection of patient privacy[8,9]
✓ Reduces the number of reviews required	• Accuracy of output generated – AI tools used to generate text are based on patterns rather than facts, often resulting in factual errors[10]
✓ Maintains consistency between narratives	• Requirement of new skill set for MW using AI tool
✓ AI tool can be tailored closely to project-specific requirements	• Selecting only the relevant data may be a challenge – may include all data rather than just relevant data
✓ Allows MW to focus on data interpretation and messaging	• The narrative cannot be fully automated – MW input still required to ensure highest quality narratives • No efficiencies in medical review of the narratives

Abbreviations: AI, artificial intelligence; GDPR, General Data Protection Regulation; MW, medical writer

Production of narratives using AI still relies on a template being used as a starting point, with the MW adapting the template to meet the needs of the particular trial. This step is an early investment in time that subsequently saves time when the narratives are generated using the AI tool. If narratives are required for more than one trial, but following similar client or product specifications, generation of narratives for subsequent trials is even more efficient as less work is required in the initial template generation step.

The concept of using AI to generate narratives is still emerging, however, and there are a number of restrictions to consider when using AI tools (Table 1). For now, the programmed approach is still well-suited for generating standardised, repetitive documents such as patient narratives.

Will using AI replace MWs in narrative generation?

It is understandable that people feel anxious about the future of their careers when AI tools have quickly become more accessible and especially when a news outlet releases an article titled "Which Jobs will AI Replace?" stating that around 300 million jobs could be affected by generative AI.[7]

As with the introduction of any new process or tool, employing the use of AI will inevitably cause a change in the role of the MW. It will require learning a new skill set to be able to understand and use AI. As much as AI can collect large amounts of data and generate *human-like* text, it can't generate outputs or documents that don't need a human's input, at least to some degree. When preparing CSR narratives, MWs would be alleviated of the repetitive tasks required to manually incorporate data into each narrative and perform a full QC check for errors, and would instead be able to focus on the flow of the story of events for each participant and to use their scientific expertise. With each narrative project being less labour-intensive, MWs would also have the capacity to work on more projects concurrently, meaning refining skills in prioritisation and management of multiple projects at the same time. A medical review of the narrative, and incorporation of any comments, would still be necessary – AI could not replace this valuable part of the work.

> Rather than fearing that AI will replace MWs, we can use AI to our advantage to replace some of our most tedious tasks.

We have discussed the use of AI in the generation of narratives for CSRs, but what uses might it have beyond generation of narratives? In this rapidly evolving area, might we see its evolution heading towards AI tools creating the template used for the narratives by taking the structure of the clinical database and converting it into paragraphs with fields for the data to be inserted? Or further down the line, when narratives are final, could we see AI performing redaction or anonymisation of narratives to maintain patient confidentiality?

AI is quickly becoming a useful tool for MWs

but, at least for the foreseeable future, any output produced using AI tools would still be an initial draft that pulls together content from a variety of sources. As MWs, we need to adapt to using AI tools, just as we often have to adapt to working with updated processes or working to new regulatory guidelines. Rather than fearing that AI will replace MWs, we can use AI to our advantage to replace some of our most tedious tasks.

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Unlocking new efficiencies:

How structured content authoring is streamlining the production of clinical documents for the pharmaceutical industry

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Abstract

Current practice requires clinical and regulatory documents to be created and updated manually by medical writers throughout a product's development. Conventionally, document content is unstructured, with free-form text, figures, and tables that the medical writer can arrange in any configuration. By structuring and standardising clinical and regulatory content, the pharmaceutical industry can shift from a document-based to a content-based approach. This transition will require adopting structured content management tools and common structures, and standardising content. In tandem, medical writers must evolve their skillset and ways of working, primarily through planning and producing content and adopting structured content authoring practices to facilitate content creation and reuse. This article introduces structured content authoring and outlines how the medical writing role in the pharmaceutical industry may soon evolve.

The hidden value of structuring content

The burden of unstructured information

In clinical research, medical writers create and update clinical and regulatory documents at multiple points throughout a product's clinical development. Conventionally, document content is unstructured, with free-form text, figures, and tables that the medical writer can arrange in any configuration. In terms of structure, aside from high-level section headers defined in the table of contents, medical writers are free to organise content as they see fit – provided they fulfil content requirements described in the authoring guidance.

As medical writers often develop clinical and regulatory documents independently of one another, each document contains unstructured information that is created and organised differently. For example, if one medical writer prepares a briefing document while another medical writer prepares a clinical study protocol, similar information is created and managed independently. Ultimately, if the writers do not have a tool or process to ensure consistency between the two documents, then an additional step is needed before finalisation where the medical writers need to align content between the two documents to avoid discrepancies.

As medical writers often develop clinical and regulatory documents independently of one another, each document contains unstructured information that is created and organised differently.

Another limitation of unstructured information occurs during document revisions. As the information in each document is not linked, independently revising documents can result in changes to the information's meaning that leads to the same information in different documents becoming increasingly divergent over time. Resolving this "information drift" is inefficient as this requires repeated, and deliberate, consistency checks that can be especially burdensome for authors working on tight timelines.

Harmonising between-document information involves additional complexity in that if only one piece of information requires revision, then the entire document must be checked and updated. Unless sections not undergoing alignment are locked, checking an entire document introduces the risk that stakeholders will reconsider content in sections that do not require revision. This, in turn, can lead to further cases where information starts to diverge among documents.

What is structured content and how does it work?

Rather than creating the same content across separate documents, a structured content approach is based on the "create once, use often" principle where information is created once as a content component (Table 1) and reused often across multiple documents.[1] To enable this, teams define, create, manage, and archive individual content components using a centralised structured content management tool (Figure 1 and Table 1). The tool tags defined content components with metadata, which allows users to identify and retrieve components for a particular purpose or deliverable. Much in the same way that metadata fields (e.g., recruitment status, age groups, phase, or funder type) can aid study search and retrieval efforts using the US ClinGov register (https://clinicaltrials.gov), metadata-tagged content facilitates its reuse capability and allows writers to perform a more targeted search.

Once these structures and tools are in place, a medical writer can generate a deliverable using

Table 1. Table of definitions

Term	Definition
Content components	Individual content components (e.g., the study design, participant characteristics, study interventions, etc.) which are defined, created, managed, and archived in a centralised repository and with minimal formatting details for the purpose of reusing the components across clinical and regulatory documents
Content standards	The set of rules and guidelines that govern content, including how sentences are put together to make paragraphs, how paragraphs are put together to make sections or components, and how components are put together to generate a deliverable
Structured content authoring	The process and rules by which an author creates content using defined structures that can be easily reused, repurposed, and automated
Structured content management tool	A centralised, platform that allows for creation, management, and reuse of digital content

a structured content authoring (Table 1) approach by populating the document structure with content that is either created *de novo* or reused from the tool's content repository.

Using content standards to improve authoring

When considering content standards and reuse, inspiration can be drawn from data standards as for data to flow between systems it needs to have certain standards for reuse. The four guiding data principles were designed and jointly endorsed by a set of stakeholders representing academia, industry, funding agencies, and scholarly

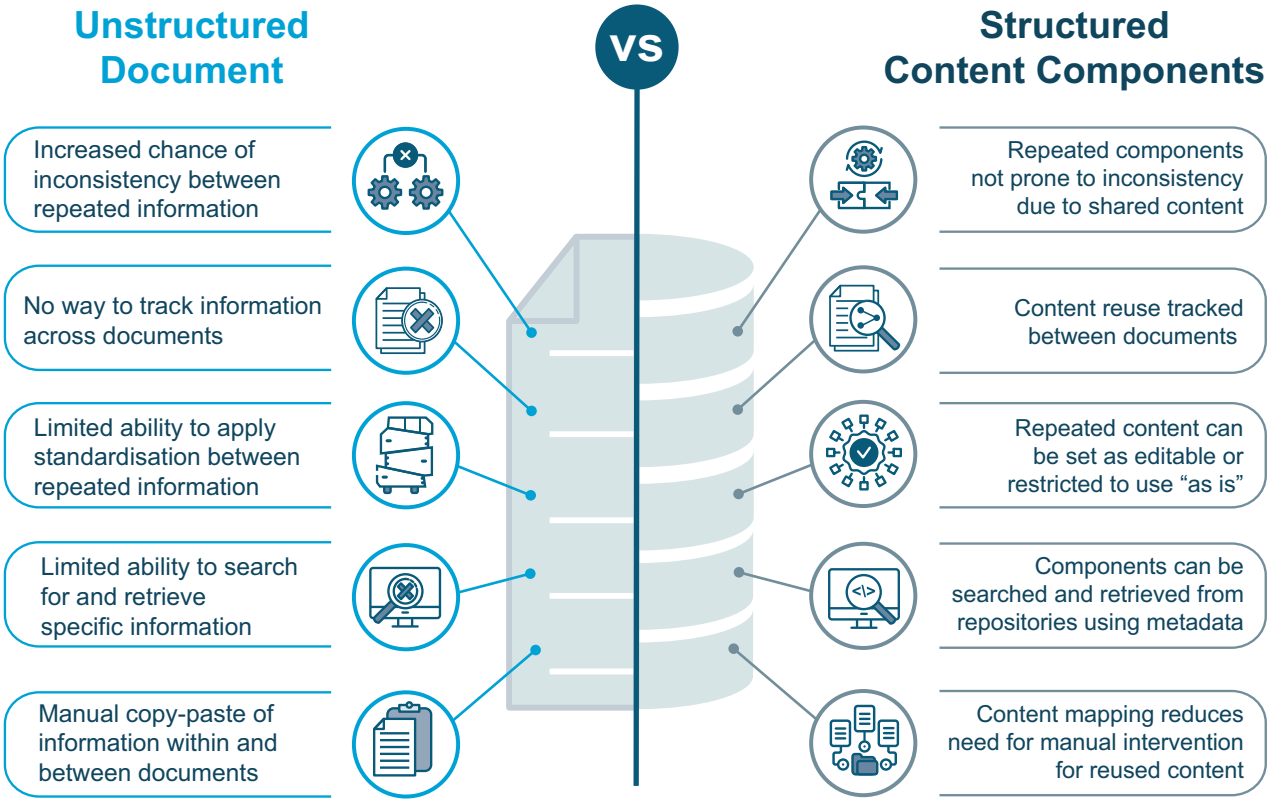

Figure 1. A comparison of information stored in unstructured documents vs. structured content components

publishers. These principles are commonly called the FAIR Data Principles: Findability, Accessibility, Interoperability, and Reusability.[2]

These same FAIR Data Principles can also be applied to structured content. By structuring content and adopting content standards (Table 1), the pharmaceutical industry can reduce document development time by enabling reuse of defined standard content. For example, TransCelerate Biopharma Inc.'s Clinical Content & Reuse Solutions include content libraries that provide select content standards that can be used in clinical study protocols and then reused in downstream documents.[3]

An example of structured content authoring

How an organisation defines content components will depend on how the organisation intends to use the content in the future. Our example of how structured content authoring can be applied to a clinical study starts with a study outline (Figure 2), a document that provides a high-level summary of the proposed clinical study. It includes sub-sections such as study design, overall rationale, study interventions, statistical methods, and so on. Using a structured content management tool, the individual subsections of a study outline can be defined as distinct content components. Once the team finalises the study outline, the medical writer can generate a draft protocol that is partially completed by automatically incorporating the study outline information based on a pre-specified content reuse plan and rules. In such a case, no manual manipulation is needed by the medical writer in copying and pasting content from one document to another. Furthermore, if the study development team has approved the study outline, the outline components can be locked for subsequent reviews, allowing for a faster and more targeted review process.

Similarly, when writing a clinical study report, the medical writers can populate the report shell by automatically pulling in relevant protocol components, e.g., background information, such as the study design, key participant characteristics, study interventions, and so on.

What does this mean for medical writers?

Medical writing skillset

As the clinical research landscape modernises and pharmaceutical companies deploy structured content management tools, the medical writer skillset will need to evolve to include content management principles. Medical writers will need to be trained on how to use structured content models, content standards, and content reuse authoring strategies in their everyday work. In turn, this will help medical writers concentrate on creating the unique *de novo* content rather than searching for or recreating content that has been developed elsewhere. Ultimately, the goal is to cut down on the manual intervention by medical writers in finding and transferring content. Furthermore, adopting automated content reuse will reduce errors and the need for consistency checks, thus allowing medical writers to focus on other tasks, such as interpreting clinical data or communicating with stakeholders.

The way we work

Much like a medical writer's skillset, the way in which medical writers work will also evolve to include new ways of approaching content development. Instead of developing information that resides in a single document, medical writers will need to work with content that is used throughout a product's development. This will require greater adherence to content standards as well as resisting editorial requests from stakeholders to rephrase content in a manner they prefer. Medical writers may be tasked with developing a protocol that contains content that will be used downstream, for example in a briefing document or a clinical study report. This content must be clear, easy to understand, and use agreed standards for terminology and acronyms. Similarly, the content must be devoid of any positional phrases, such as "see below" or "as mentioned above", or cross-references to other content sections that will not apply to downstream documents as these will be out of place in the location where the content is reused.

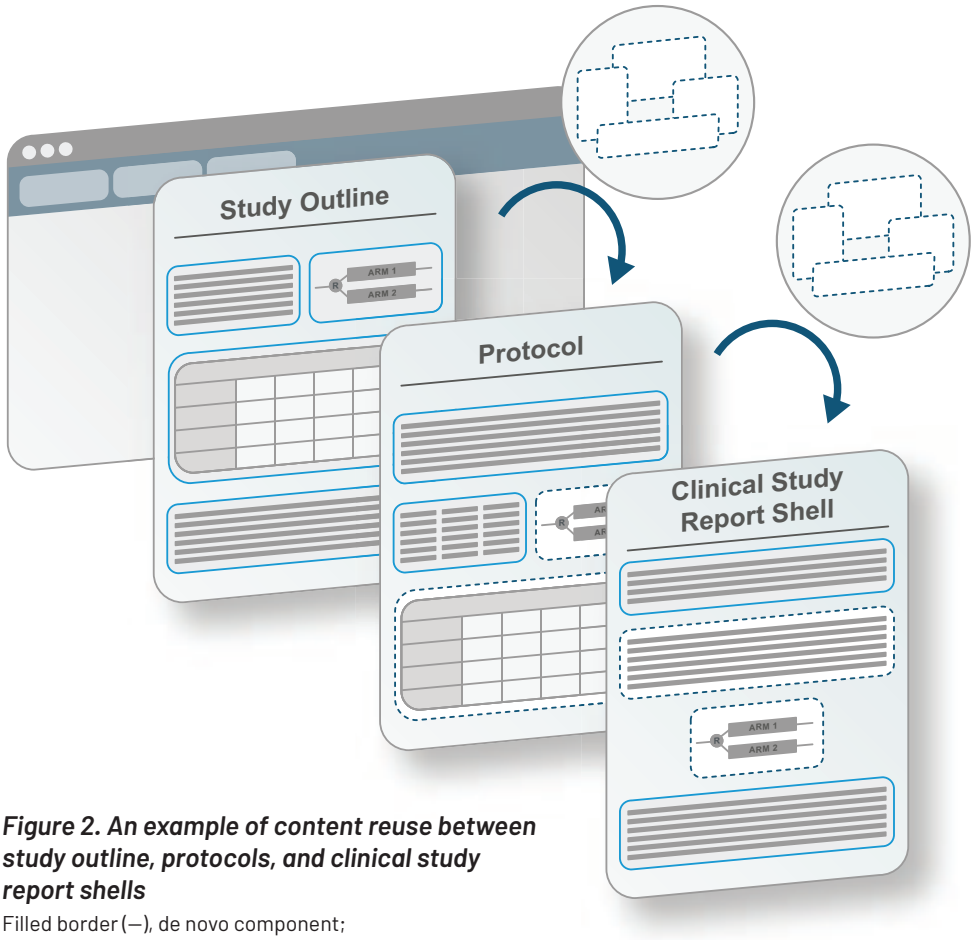

Figure 2. An example of content reuse between study outline, protocols, and clinical study report shells

Filled border (—), de novo component;
Dotted border (...), reused component.

Outlook

Technology has evolved to a point where the pharmaceutical industry has the capability to modernise the process of creating clinical and regulatory content. Technology-enabled content reuse allows organisations to facilitate the authoring process by using a "create once, use often" approach to develop clinical and regulatory documents.

> Technology enabled content reuse allows organisations to facilitate the authoring process by using a "create once, use often" approach to develop clinical and regulatory documents.

Although data standards are widespread in clinical development, structuring and standardising content is still in its infancy. Only some organisations have implemented initiatives to standardise content and increase content reuse. In the future, as structured content authoring matures, it is likely more cross-organisational coordination will emerge between pharmaceutical companies sponsoring clinical trials, contract research organisations, and regulatory authorities. To this end, the TransCelerate Biopharma Inc. Clinical Content & Reuse Solutions and more recently, the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) M11 draft guideline (Clinical electronic structured harmonised protocol – CeSHarP) are important steps in this direction.[3,4,5] For the former, TransCelerate Biopharma Inc. has longstanding, publicly-available, technology-enabled templates and reusable library content. For the latter, the recent ICH M11 guideline provides a more global reference for the structure and technical properties of protocols, with the aim of enabling consistent and efficient exchange of protocol information between sponsors of clinical studies, investigational sites, independent review boards, regulators, ethics committees, and other related stakeholders.

At the organisational level, implementation of agreed standards such as the Clinical Content & Reuse Solutions and ICH M11 technical specifications will level the playing field, which will increase the likelihood of harmonisation of documents between stakeholders. In parallel, to effectively embed structured content authoring, organisations will need to implement authoring process changes, and content governance structures to adapt to content creation, reuse, and management practices in structured content management tools.

In addition, for true adoption success, time and resources must be allocated to ensure adequate training and support for users new to structured content management tools and content-based working practices. As organisations create, review, approve, revise, manage, archive, and, if needed, retire each piece of content individually, the requirement for users to manually perform these activities will diminish. Ultimately, structured content management tools

will facilitate the medical writer's ability to find, reuse, and repurpose content that will enable organisations to create content faster than developing unstructured content in individual documents.[6]

Conclusions

By structuring and standardising content, the pharmaceutical industry can shift from a document-based to a content-based approach for creating clinical and regulatory content. This transition will require adopting structured content management tools and common structures, and standardising content. Thus, medical writers must adopt content planning, structuring, and production practices to facilitate content creation and reuse. Ultimately, structured content will enable medical writers to save time by streamlining the writing process, allowing them to focus on tasks that require deliberate thinking, interpreting clinical data, and communicating with stakeholders.

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Can readers spot the AI impostor in healthcare writing?

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Abstract

The use of artificial intelligence (AI) writing assistants in the healthcare industry is becoming increasingly prevalent. These tools can help medical writers to generate content more quickly and efficiently, but they also raise concerns about the accuracy and completeness of the information that is produced. This study investigated whether readers can distinguish between health-related texts written by humans and those generated by AI writing assistants. A survey of 164 respondents found that slightly more than half could correctly identify the source of the healthcare text. Differences between healthcare professionals and non-healthcare professionals were not statistically significant. Medical writers were better at recognising that a text had been written by an AI model than were non-medical writers ($P<.05$).

These findings suggest that it is important for organisations to establish clear guidelines regarding the use of AI writing assistants in healthcare. The authors of health-related content should be required to identify whether their work has been completed by a human or an AI writer, and organisations should develop processes for evaluating the accuracy and completeness of AI-generated content.

This study has several limitations, including the small sample size. However, the findings provide valuable insights into the need for organisations to develop clear guidelines for their use.

Artificial intelligence (AI) writing assistants are large language models (LLM) trained to generate text based on prompts by the user. ChatGPT, GPT-4, Bing Chat, and Google Bard are some recent AI writing assistants to enter the marketplace. The AI writing assistant market has been forecast to grow by 14.2% compound annual growth rate between 2021 and 2028.[1] Due to the growing popularity of LLMs, it is inevitable that more medical writers will start using them. This trend is already apparent based on surveys I conducted in March 2022 and then again in May 2023.

Based on a survey I conducted on Formaloo in March 2022, 19.5% of medical writers (17 of 87) had tried using an AI writing assistant to help with their healthcare write-ups. In May 2023, I repeated the question in another survey to try to identify any fluctuation that may have occurred over the previous year. Out of 76 medical writers who responded to the most recent survey, 52% indicated that they use an AI writer occasionally, whereas 17% use it regularly. Only 17% of the medical writing respondents have never tried using an AI writing assistant. This suggests that 69% (52% + 17%) of medical writers use AI to assist their writing at some level. That represents four times more medical writers using an AI writing assistant in May 2023 compared with March 2022.

Confidence in ability to identify AI vs human-written content is generally high

As the use of AI writing assistants becomes more prevalent in the healthcare industry, it is increasingly crucial for readers to be able to spot indicators that will help them identify the source of health-related articles. AI writing assistants, such as Generative Pre-trained Transformer (GPT) and ChatGPT, generate text based on input from the human user. However, writers in regulated industries, such as healthcare, may not gain as much benefit from AI writers due to the requirements for accurate and complete information. Improved patient care is the primary goal for all written healthcare content, and low risk for all stakeholders, including patients and healthcare professionals (HCPs), must be achieved.[2] Inaccurate or incomplete healthcare information could be harmful to a patient. It has been recognised that language models generate incorrect statements and even fabricate false information.[3] Such fabrications are unintended text generations not supported by the input data or the context, yet they are stated with utmost confidence. These are called "hallucinations", similar to when humans experience something through the senses that seems very real, even though it is not based on anything in the outside world. Evaluating and mitigating hallucinations within an LLM is challenging because evaluating a hallucination is subjective and based on user expectations. Also, mitigating hallucinations could come at the cost of reducing fluency or naturalness in the generated text, which can negatively affect the user experience.[4]

Writers in regulated industries, such as healthcare, may not gain as much benefit from AI writers due to the requirements for accurate and complete information.

Considering the increased experience of AI language models by medical writers, one can expect that a greater volume of healthcare-related content written to some degree with AI will emerge. Thus, it will become more challenging for consumers and healthcare professionals to know if a human or an AI writer wrote the content they are reading. This is a concerning issue due to the potential for inaccuracies or incomplete data in text generated by AI. In my research, one objective was to identify how common it is for people to believe they could discern between content written by a human and an AI writer.

I conducted a LinkedIn poll to ask respondents (n=66) if they thought they could tell if a human or an AI writing assistant wrote healthcare copy.[5] In the survey, 39 people (59%) were confident they could tell the difference, whereas 19 (29%) did not believe they could,

and 8 (12%) were uncertain. Several who responded "yes" also commented that it would be highly evident to them. Of the uncertain group, several commented that they were not sure what was meant by an "AI machine".

In related research, my main objective was to test readers' abilities to correctly identify whether a selection of health-related texts had been written by a human or by an AI writer. The human-written healthcare passages originated from websites published before June 2020. GPT-3 was released in June 2020; therefore, by selecting texts published prior to this date, this ensured that GPT-3 was not involved in creating the content. Moreover, to increase the likelihood that the content was accurate, each chosen text had to be written by an author with a healthcare designation such as "MD" or "pharmacist". I selected parts of the text that explained the basics of the disease. For the AI-written texts, I used several large language models, such as Rytr, WordHero, Nichess, ContentBot, Texta.ai, and Creator.ai.

In March 2022, 164 respondents were asked to read the medical texts and identify whether they thought it was written by a human or an AI writer. The readers were blinded to the source of the text.

Table 1. Percentage of correct responses regarding human or AI-generated text for all respondents and subgroups

	Healthcare Professional (Yes or No)		Medical Writer (Yes or No)		Neither HCP nor MW	TOTAL
Human or AI author	**HCP Yes** *n*=59	**HCP No** *n*=105	**MW Yes** *n*=58	**MW No** *n*=106	*n*=75	*n*=164
Text 1 Human	44.10%	53.80%	43.10%	53.80%	58.70%	**50.00%**
Text 2 AI	40.70%	41.90%	39.70%	42.50%	46.70%	**41.50%**
Text 3 AI	84.70%	77.10%	89.70%	74.50%	70.70%	**79.90%**
Text 4 Human	91.50%	77.40%	79.30%	84.00%	80.00%	**82.30%**
Text 5 Human	57.60%	50.90%	53.40%	52.80%	50.70%	**53.00%**
Text 6 AI	74.60%	73.30%	77.60%	71.70%	70.70%	**73.80%**
Text 7 AI	33.90%	28.60%	36.20%	27.40%	25.30%	**30.50%**
Text 8 Human	30.50%	34.90%	32.80%	33.00%	32.00%	**32.90%**
Text 9 AI	35.60%	34.30%	43.10%	30.20%	32.00%	**34.80%**
Text 10 AI	61.00%	63.80%	70.70%	58.50%	61.30%	**62.80%**

Differences in responses between HCP and Non-HCP were not statistically significant.
For AI-generated text, the differences in responses between MW and non-MW were statistically significant (Chi-square, $P<0.05$).

Abbreviations: HCP, healthcare professional; MW, medical writer

Results

Each respondent was shown 10 text examples – four human written and six AI written. Overall, respondents correctly identified the writer 54% of the time (358 of 656 human-written texts [54%] and 530 of 984 AI-written texts [54%], Table 1).

The respondents included 59 healthcare professionals (HCPs) and 105 who were not HCPs. Of the examples of *human-written* text that were shown, 55.9% and 54.1% were correctly identified by HCPs and non-HCPs, respectively. There was no significant difference between groups (Chi-square, non-significant). Of the *AI-written* texts 59.5% and 50.8% were correctly identified by HCPs and non-HCPs, respectively. There was no significant difference between these groups (Chi-square, non-significant).

Try the Test!

The Guest Editors for this issue of *Medical Writing* participated in one of the surveys to try to guess the AI-written sentences. Daniela Kamir correctly guessed 4 of the 6 AI-written sentences. Shiri Diskin was unable to identify any.

Try it yourself at: https://marketing4health.formaloo.net/AIorHuman

An analysis was also done to compare the ability of medical writers (n=58) and non-medical writers (n=106) to identify text that AI or humans wrote. Medical writers and those who do not write medical content demonstrated no difference in identifying text written by humans. However, medical writers identified text written by an AI model significantly more than non-medical writers (Chi-square, P<0.05).

A more recent study with the same objectives is underway, but the data have not been analysed as of this publication. The difference between the new survey vs. the 2022 survey is that the new survey uses AI texts written by ChatGPT, Google Bard, and GPT-4. The data will be published once available. In the meantime, the survey has been left open so anybody can test their skill at identifying AI vs. human-written healthcare texts. It is free, online, and confidential. Your score and the answer sheet will be available at the end of the survey. Aggregate data may be used for ongoing research. You can try it at: https://marketing4health.formaloo.net/AIorHuman

Identifying text generated by AI is an important issue due to the potential for inaccuracies or incomplete data in such text.

Conclusions

As the number of individuals with experience using AI writing tools continues to grow, it will become increasingly important for organisations to establish clear guidelines regarding the acceptable use of such technologies to address the potential for misuse or abuse of these tools, and the need for transparency and accountability in their use, particularly in the healthcare field. The authors should be required to identify their work as having been completed by either a human or an AI writer.

Disclaimers

A human author wrote the content of this article. AI was used for grammatical corrections and phraseology suggestions.

Disclosures and conflicts of interest

The author declares no conflicts of interest. No monetary or non-monetary incentives have been provided.

Data availability statement

Please contact the corresponding author for inquiries about data and other supplemental information.

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Don't miss!

The March 2024 edition

Translation

Medical translation is a complex and demanding field requiring specialised knowledge, skills, and expertise. In this issue, we explore a range of topics, including the role of medical translation in clinical trials and regulatory affairs, the importance of terminology management, the use of technology and machine translation, ethical and legal considerations, the impact of cultural differences, quality assurance and risk management, and the emerging trends and challenges in the field. This issue provides valuable insights into medical translation and its contribution to enabling communication with different audiences from different backgrounds.

Guest editors: Ana Sofia Correia and Claire Harmer
The deadline for feature articles is December 1, 2023.

Essential principles towards improving clinical risk assessment tools: A conversation with Uri Kartoun, PhD

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Abstract

Uri Kartoun (PhD in robotics, Ben Gurion University of the Negev, Israel) is a Staff Research Scientist and an IBM Master Inventor, co-developer of technologies such as MELD-Plus, EMRBots, Memory-memory (M2) Authentication, and Subpopulation-based Feature Selection. Prior to joining IBM Research in 2016, Kartoun worked at Microsoft Health Solutions Group and at Massachusetts General Hospital.

EMWA Guest Editor Daniela Kamir, PhD, interviewed Kartoun about clinical risk assessment tools, organ transplant allocation disparities, and how the Model for End-Stage Liver Disease (MELD) score is used to allocate livers for transplantation. The conversation has been edited for brevity and clarity.

Daniela Kamir: What factors are potentially predictive in developing effective clinical risk assessment tools, and how can unbiased feature selection techniques help in this regard?

Uri Kartoun: To develop effective clinical risk assessment tools to help better manage a disease, clinicians and data scientists must select patient characteristics that are potentially predictive, such as a subset of laboratory values, co-morbidities, medications, and genetic profiles. This selection process should incorporate both practical experience and knowledge acquired from scientific manuscripts. With the advancement of machine learning–based technologies,

unbiased feature selection techniques can help recommend which characteristics should be incorporated into these tools.[1,2] Additionally, novel metrics, such as those related to fairness, can aid in designing the next generation of risk assessment tools, beyond just assessing the tools by using traditional metrics such as prediction performance and calibration.

DK: The MELD score is used to prioritise patients on the liver transplant waiting list, with higher scores indicating greater illness severity and thus greater urgency for transplant. What guided the development of the Model for End-Stage Liver Disease 3.0 score?

UK: In a recent announcement, the Organ Procurement and Transplant Network (OPTN) Board has decided to replace the MELD-Na (MELD + serum sodium) with the Model for End-Stage Liver Disease 3.0 (MELD 3.0) score for determining organ allocation priorities in the United States.[3,4] This move comes after the co-creators of the MELD 3.0 score were congratulated for their efforts.[5] The cocreators outlined several principles that guided the development of the new score. These principles included the requirement that all features included in the score must be measurable in an objective fashion, generalisable, devoid of unnecessary volatility without biological significance, and reportable to the OPTN without causing an undue burden. OPTN's decision is expected to have a significant impact on organ allocation in the United States as the MELD 3.0 score is a more refined and accurate way of determining organ allocation priorities and is expected to result in better outcomes for patients in need of liver transplants.

DK: Why does the MELD 3.0 score incorporate sex as a variable?

UK: The MELD 3.0 score has incorporated sex as a variable for two reasons: mitigating sex disparity in access to transplantation and improving prediction performance. The inclusion of sex differences in the MELD 3.0 score corrects for sex disparity caused by creatinine and differences in risk of death, among other factors.[3,6] The primary objective of adding the new sex variable, as well as revising the creatinine coefficient, was to improve fairness across the sexes. Note, however, that assessing fairness quantitatively was not thoroughly discussed in related manuscripts.

DK: What is the significance of using fairness-related metrics to assess the performance of risk assessment tools as used in organ allocation?

UK: As a more modern score that accounts for fairness, it is crucial to assess the performance of the MELD 3.0 using metrics specific to fairness.[5] If performance of fairness-related metrics may be found unsatisfactory then a revised version must be developed urgently (i.e., MELD 4.0). Standard metrics such as discrimination and calibration have been used to assess the performance of the new score, but it is also important to use measures such as statistical parity difference, true positive rate difference, and true negative rate difference to assess fairness within the context of patient characteristics such as sex, race, and age.[7] Overall, the incorporation of sex into the MELD 3.0 score is a step towards improving access and fairness in organ allocation. As further assessments of its performance continue to emerge, it will be interesting to see how this new approach to liver disease assessment and transplantation impacts patients and medical professionals alike.

DK: Can you give an example of how fairness should be assessed?

UK: IBM Research and the Broad Institute of MIT and Harvard have collaborated on a recent study that assessed the performance of widely used risk scores in cardiology, namely the Cohorts for Heart and Ageing in Genomic Epidemiology Atrial Fibrillation (CHARGE-AF) score for AF and the Pooled Cohort Equations (PCE) score for Atherosclerotic Cardiovascular Disease (ASCVD).[8] The study evaluated performance by using standard metrics such as discrimination, calibration, and standard hazard ratios, as well as fairness-related metrics considering sex, race, and age ranges.

Evidence was found of potentially unfair performance, with significant differences in fairness metrics for sex and race in both scores. The study considered three large independent datasets, including the Explorys Life Sciences Dataset, Mass General Brigham, and the UK Biobank.[9] Notably, the sensitivity difference of both scores was much lower for females than males in the intermediate-age subgroups, suggesting that current scores may miss more females at high risk for events, potentially worsening existing sex-related treatment gaps.[10] The findings underscore the importance of evaluating prognostic models across specific subpopulations to better understand the accuracy and potential unfairness of the prognostic information used to drive clinical decisions at the point of care.

This study highlights the importance of assessing the performance of prognostic models using metrics specific to fairness and calls for continued evaluation of widely used risk scores to better understand their impact on patient outcomes across various subpopulations. The collaboration between IBM Research and the Broad Institute of MIT and Harvard provides important insights into the limitations of current risk prediction models and paves the way for more equitable and effective approaches to cardiology risk assessment. Similarly, future versions of the MELD score must exhibit small to non-existent bias across all age ranges and characteristics such as sex and race. These findings underscore the importance of developing healthcare scores that are not biased and that accurately reflect the severity of patients' conditions.

DK: Can you give an example of a method that you developed that could aid in identifying additional features for risk assessment tools and reduce bias?

UK: Subpopulation-based feature selection that was developed as part of another collaboration (between IBM Research and MIT) is an iterative machine learning–based technique used to identify the most important features for risk assessment in specific subgroups of patients and was proved to be superior compared to notable widely used feature selection methods.[1] Incorporating novel covariates that improve performance and fairness is expected to provide clinicians with more accurate and unbiased patient risk assessments. Within the context of liver, new versions of MELD are expected to better fairly rank patients on the liver allocation list, once they incorporate novel features that are also adjusted to optimise fairness-related metrics. Combining these principles with the principles specified is expected to yield better performing and more equitable risk assessment tools in heart, liver, and beyond.[4]

Disclaimer

The views and opinions expressed in this interview are those of Uri Kartoun and do not necessarily reflect the views or positions of IBM.

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AI-based plagiarism detectors: Plagiarism fighters or makers?

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Abstract

Plagiarism damages the biomedical academic publication domain. Artificial intelligence (AI) is a rising hope in academic plagiarism hunting. However, new AI-based tools are available online to assist with plagiarising! This article presents plagiarism throughout history, especially in medicine, and the promises of AI to detect a new type of plagiarism, namely Aigiarism. The danger of the above-mentioned AI-based services to help in paraphrasing copied texts is also highlighted, including some proposed solutions.

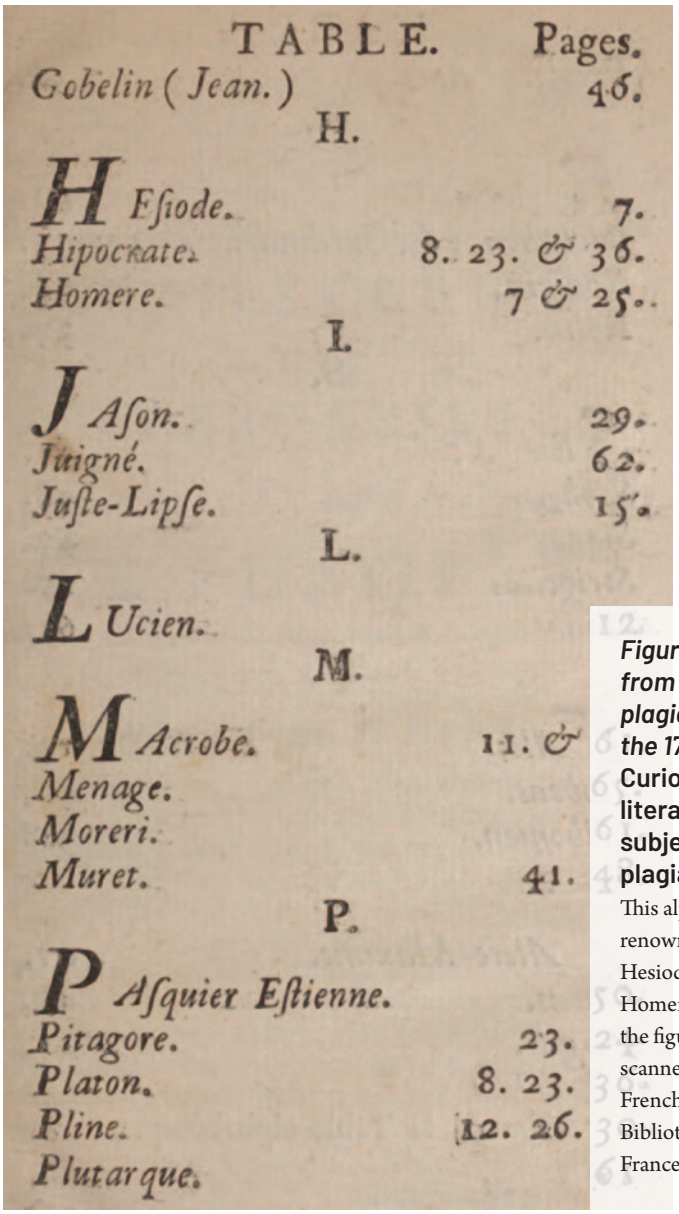
Introduction

Automated medical report writing supported by artificial intelligence (AI) is gaining ground in clinical regulatory writing. Therefore, challenges and opportunities regarding streamlined medical writing software are rising. Such matters are also faced in the academic publication field. The most famous story is about the Swedish researcher Almira Osmanovic Thunström who asked Globally unique identifier Partition Table-3 (GPT-3) to write an academic paper about itself.[1] The paper was accepted by a journal, with ChatGPT listed as an author. More disturbingly, according to the structure of the sentences, it was demonstrated in 2021 that about 500 papers published in *Microprocessors and Microsystems* may have been written by GPT. This investigation was made possible by another machine learning engine, the RoBERTa base OpenAI Detector for GPT-2 output.[2]

While providing tools for unauthentic medical writing, one of the first academic automated software programs – now becoming more effective thanks to AI-guided functions – was used to detect plagiarism in theses or university assignments. Thus, AI is an efficient weapon against false works and plagiarism. More precisely, plagiarism is in fact the use or imitation of the language and thoughts of an author, without any authorisation or credit to the original author.[3] Although AI clearly represents a future hope in academic plagiarism chasing, free and new AI-powered services are spreading on the internet to help in plagiarising! This article presents aspects of plagiarism throughout history, especially in medical science, before debating two sides of the AI coin, both combatting and favouring plagiarism.

Plagiarism: *The Never-Ending Story*

For this section, we borrowed the title from the famous fantasy movie by Wolfgang Petersen,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Juſte-Lipſe. 15.

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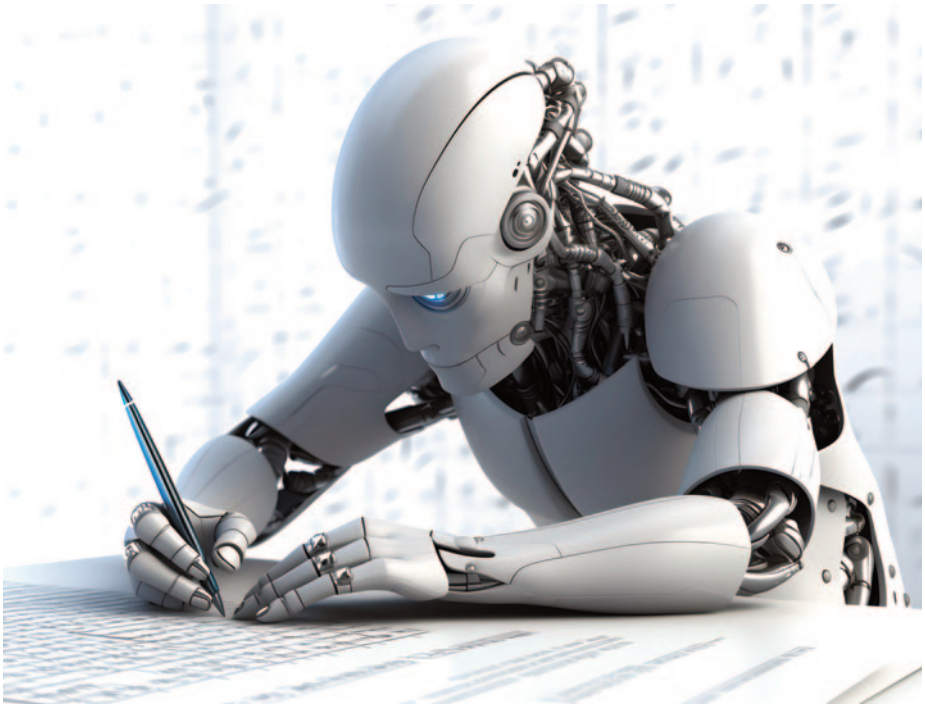
Moreri.
Muret. 41.

P.

P Aſquier Eſtienne.
Pitagore. 23.
Platon. 8. 23.
Pline. 12. 26.
Plutarque.

***Figure 1. Alphabetic table, from H to P, of the plagiarists mentioned in the 1741-dated book* Curious details on literature diverse subjects. First article: plagiarism.**
This alphabetic table displays renowned plagiarists, such as Hesiod, Hippocrates, and Homer. The book from which the figure comes was numerically scanned and diffused by Gallica, French database of the library Bibliothèque Nationale de France.



itself based on a German novel, for which the movie producer obviously bought copyrights. *The Never-Ending Story* is an amusing way to illustrate that plagiarism is as old as written culture. The 1741-dated book *Curious Details on Literature Diverse Subjects. First article: plagiarism* displays a table of plagiarists (Figure 1), in which some well-known writers are listed.[4] Despite the theme of this book, it is rather funny to note that it was written by an unknown author.

Plagiarism comes from the Latin word *plagiarius*, itself derived from *plagium*, meaning the theft of a human being.[5] A *plagiarius* is the crime of stealing a slave. The Latin poet Martial used such a metaphor to accuse another poet of verses imitation.[6] Yet, Figure 1, a 1741-edited document, is a good example that plagiarism, currently being a juridic ethical offence, is an 18th-century concept. Following the spread of the printing press, authors earned their lives without the support of arts and literature's generous benefactors. In the 18th century, plagiarism became juridically distinct from counterfeiting, and copyrights appeared for the first time in France under the initiative of dramaturgist Pierre-Augustin Caron de Beaumarchais.

The 1741-published book mentioned above is divided into chapters, including "Bought plagiarism"; "Free plagiarism"; "Involuntary plagiarism"; "Maimed plagiarism", etc. Well, nothing original. Plagiarism truly is a *Never-Ending Story*, which plagiarises itself for centuries.

Science is cool but cruel!

Although plagiarism emerged from the literary world, it also concerns science and is even included in academic misconduct. More precisely, it is one of the three reported frauds: Falsification, Fabrication, and Plagiarism (FFP).[7] The first two (FF) are misconduct involving the scientific data. If FFP is detected within a published academic paper, the editor is required to retract the article. In 2021, Professor Gonzalo Marco-Cuenca and his collaborators revealed that in Europe, 60.83% of the articles retracted due to FFP are from the Life Science and Biomedicine field.[8] The biomedical field is especially competitive regarding funding, and the pressure to publish more and more creates bad practices in biomedical research.

60.83% of the articles retracted due to FFP are from the Life Science and Biomedicine field.

Some prestigious researchers were plagiarists, such as the French chemist and microbiologist Louis Pasteur. He plagiarised his works on silkworms from Dr Antoine Béchamp; on anthrax from Dr Henry Toussaint; and "his" worldwide famous rabies vaccine from Dr Pierre-Victor Galtier.[9] Pasteur filed a patent for the rabies vaccine without having mentioned Galtier. Pasteur deposited his notes to the French "Académie des sciences", having instructed them not to open them before a hundred years following his death. (All of his plagiarism was publicly disclosed with his notes.[9]) Additionally, the scientific working environment exacerbates sociological disparities. For instance, the Matilda effect is the minimisation of the contribution of women scientists, whose works are credited to men, and was first described by feminist Matilda Joslyn Gage. One of the most widely known cases is British physicochemist Rosalind Franklin, never cited for her significant achievements in the DNA structure discovery.[10] Those examples are plagiarism of ideas or denial of contributions. Such stories tend to hide what science is: *a collective work*.

Very importantly, due to the "Publish or perish" situation in academia and "copy-paste" bad habits, another category of plagiarism, namely the plagiarism of text, became one of the top reasons for biomedical retractation. This was divulged in an Indian study,[11] and recently confirmed by a Brazilian analysis.[12] Plagiarism of text may include self-plagiarism, which is the reuse of work previously submitted as a strategy to increase the number of publications.

AI-based plagiarism detectors: tools against Aigiarism...

First, let us discuss plagiarism detectors. Software for academic plagiarism detection has been used by universities since the nineties. In some institutions, master's theses are mandatorily screened by antiplagiarism algorithms before being submitted for evaluation.[13] These internet-based university detection systems are not accessible to students. Such evaluation applications encourage students to insert quotation marks, cite sources, and mention authors in their essays. Nowadays, this kind of software is also routinely run by academic biomedical editors, like Elsevier or Springer Nature.[14] An issue is emerging: the use of AI in medical writing. The above-mentioned plagiarism detectors are now combined with machine learning operations to identify and quantify AI writing within a text. Nevertheless, these AI-driven options are mostly available to lecturers.[15] The story plagiarises itself: the problem originated in universities and then spread to academic biomedical publications.

Undoubtedly, AI-based AI writing detectors will be an extraordinary tool to uphold the

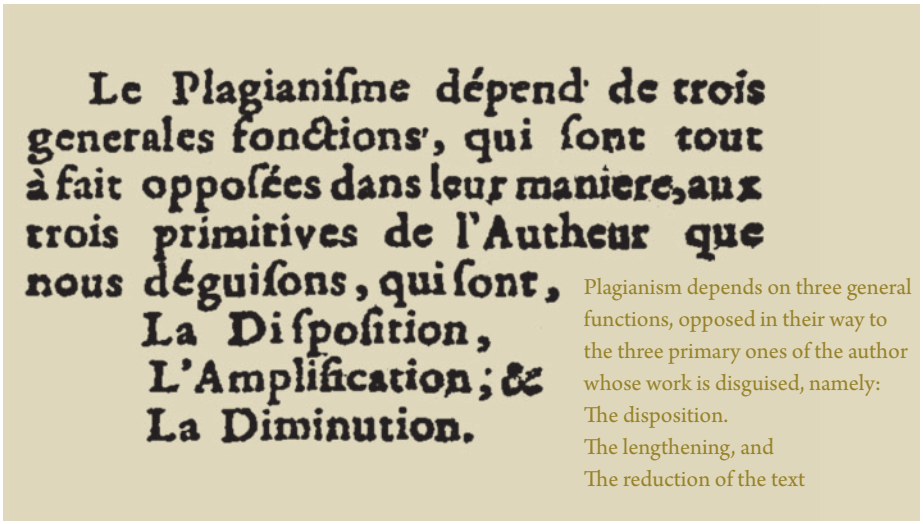


Figure 2. An extract of the French 1667-published book* The mask of speakers or the manner to easily disguise any sort of speech, *translated into English.
On the left: the screenshot extract defines *plagianism*, a French word invented by author Jean de Soudier de Richesource. On the right: translation into English of the screenshot extract. The translation has been done without any AI-based assistance. The book from which the figure comes (left part) was numerically scanned and diffused by Gallica, French database of the library Bibliothèque Nationale de France

writing integrity of medical articles. Furthermore, as they hunt AI-written texts, in which AI is not cited as an author, they unveil a new type of plagiarism: Aigiarism, meaning the use of AI to generate content and present it as one's own work. "Aigiarism" is a word created by American manager Mike Waters. To fight against Aigiarism, again, AI will help. The research company OpenAI is working on a watermarking scheme, to make it harder to take any GPT output without mentioning it.[16] AI technology is thus the best way to combat AI-mediated violation of biomedical literature ethics.

... Or plagiarism promoters?

Let us try to understand the "work" of a plagiarist. In the 17th century, Jean Oudart opened in Paris a school of *plagianism*, a term he had invented. In 1667, he published his method under the pseudonym of Jean de Soudier de Richesource, "The mask of speakers or the manner to easily disguise any sort of speech".[17] A pseudonym containing the word "source" is quite ironic for writing a book that provides advice to plagiarise! Figure 2 illustrates what plagiarism (*plagianism*) has been over the centuries.

The 1667-edited method, from which comes Figure 2, is divided into sections. One explains how to change the order of words (The disposition). This section contains specific paragraphs that praise synonymy with examples: courage can be replaced by virtue to disguise a text. Other sections teach how to lengthen a speech, for example by adding definitions of several words, or how to cut some parts. Now, imagine that AI was able to perform these time-consuming tasks, done for centuries (Figure 2). This is currently possible with recent online AI-guided "plagiarism fixers". For example, the platform ©Check-Plagiarism.com offers a free AI-powered paraphrasing service,[18] as well as the website ©Plagiarismremover.net.[19] In 2021, the YouTube™ channel Insights4UToday released two videos to demonstrate the use of such tools, with provocative titles like "How to avoid plagiarism while copying" or "Copy & paste and not get caught".

This could have remained a sad and insignificant story, except that YouTube™ channels promoting AI-driven paraphrasers are openly designed for researchers, themselves producing scientific literature. One of the above-mentioned videos starts this way, "This video is purely for educational purposes. Plagiarism is very unethical. You must cite all sources used."[20] However, the engines for rephrasing supported by machine learning are fast, free or cheap, easy to use, and attractively interfaced.

With the pressure to publish, such problems are affecting academic medical writing. In the future, watermarking schemes and the juridic requirement not to take any output from these tools without mentioning them might be the answer. This component would be technically hard to apply, but – once again – the issues may be solved thanks to AI innovations.

Other AI challenges in medical writing

As AI promotes plagiarism and helps against Aigiarism, as discussed in the previous sections, other AI challenges in medical writing are rising. Above all, we must keep in mind that AI is definitively valuable for all its perspectives in biomedical discoveries. For instance, in Germany, the group of Professor Peter Krawitz developed a deep learning machine to improve the diagnosis, in terms of speed and objectivity, of leukaemia.[21] In addition, AI is becoming the new paradigm in drug discovery, especially because it can predict the features of a compound.[22] That said, concerns are growing about scientific papers entirely written by AI. As aforementioned, AI helps against Aigiarism, but AI technologies are getting more sophisticated and ultimately, will be undetectable to AI writing detectors.

> The submission and publication of content created by AI, language models, machine learning, or similar technologies is discouraged, (...) and is not permitted without clear description of the content that was created.

The smartsciencecareer.com platform published an article on methods to more quickly write scientific papers. Professor Sven Hendrix, author of the article and founder of smartsciencecareer.com, cites cactus.ai, a Large Language Model (LLM) text generator able to include references in academic essays, even as he warns that it is not precise enough for scientific publication.[23] Yet, Hendrix says that these functions are going to improve soon. Coping with this generalised utilisation, the Journal of the American Medical Association (JAMA®) recently updated its publication policy to discourage authors from submitting AI-generated text, as quoted below.[24]

Another kind of Aigiarism may exist, based

on Generative Adversarial Network (GAN) AI, through the creation of fake biomedical pictures, such as microscopy, endoscopy, and biochemistry images.[25] This scientific misconduct is hard to detect,[26] which makes it unquantifiable. Some researchers are warning the scientific community that this misconduct will be the next data fabrication stratagem, and call for preventive solutions from machine intelligence algorithms.[25]

Concluding remark

This article has been written without any AI support. The Editor option of Microsoft® 365 Word, an AI-enabled writing assistant, displays 86% of correct writing for the whole text. It seems an AI decided that the article you just finished was good enough to be read!

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Disclosures and conflicts of interest

The author declares no conflicts of interest.

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A survey on current use of software tools for systematic literature reviews

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Abstract

Adoption of the EU Medical Devices Regulations and In Vitro Diagnostics Regulations has led to increased demand for systematic literature reviews. This article reports on a survey investigating the current use of software platforms and tools by regulatory medical writers and others involved in conducting systematic literature reviews. The survey was completed by 125 respondents from 31 countries, evenly spread across different levels of experience. Most respondents use a partially automated (35%) or fully manual process (59%). Familiarity with specific software to conduct systematic literature reviews was low, with most respondents (61%–84%) indicating they were unfamiliar with five software applications and tools. Data extraction was named as both the most time-consuming and error-prone step in the process. Process improvement, improvement of data extraction, and time saving were seen as topics where systematic literature review software could make the most valuable contribution.

The EU Medical Device Regulations (MDR) and In Vitro Diagnostics Regulations (IVDR) require a systematic literature review of clinical data for every device to evaluate the clinical safety and performance, which need to be updated periodically throughout the lifetime of the device.[1,2] The adoption of EU MDR and IVDR has greatly increased the demand for systematic literature reviews. In combination with the ever-increasing volumes of literature published each year, the workload of regulatory writers in the medical devices and in vitro diagnostics industries is soaring. An important strategy to deal with this is the adoption of software packages and tools aimed at improving the efficiency of retrieving, identifying, analysing, and synthesising information from the literature.

The purpose of this article is to investigate current practices and the use of software tools by medical writers and other professionals involved in systematic literature reviews for medical devices and in vitro diagnostics using an internet survey.

Methods

Survey details

An anonymous, online survey (see Appendix 1) was conducted using SurveyMonkey (https://www.surveymonkey.com/) from April 3 to May 9, 2023. All EMWA members were invited to participate via email. A reminder email was sent shortly before the closing date. To solicit additional responses, members were encouraged to share the link and the link to the survey was also posted on LinkedIn (https://www.linkedin.com/).

Data processing

The survey tool allows submission of incomplete responses, but querying of missing or inconsistent responses was not possible. A data cleaning process removed obviously inconsistent or irrelevant responses, and additional categorical variables were created for free text responses. When a range was provided for the time spent on a literature review, the highest estimate was used for analysis. Responses in weeks, days, or months were converted to hours using the assumption of 8 hours/day, 40 hours/week, and 184 hours/month. A categorical variable was added to indicate whether respondents provided a time estimate and, if not, whether this was because the question did not state the volume/size of the literature review or because respondents were not able to estimate the time needed for a literature review.

The number of software packages used per respondent was calculated per type of software (word processor, spreadsheet, reference manager, PDF software, graphical software, and databases) and overall.

Statistical analysis

Descriptive statistics included frequencies and percentages for categorical variables, and mean, standard deviation, median, and range for numerical variables.

Statistical analyses were performed using SPSS 28.0 (IBM Corp, Armonk NY, USA). The Kolmogorov-Smirnov test indicated that numerical variables were not normally distributed. Therefore, non-parametric tests were used: Mann Whitney U-test and Kruskal-Wallis H-test, as appropriate. Bonferroni corrections were used for multiple comparisons. For categorical variables, Pearson's chi square test was used. A value of $P<0.05$ was considered significant.

The adoption of EU MDR and IVDR has greatly increased the demand for systematic literature reviews. In combination with the ever-increasing volumes of literature published each year, the workload of regulatory writers in the medical devices and in vitro diagnostics industries is soaring.

Results and discussion

Characteristics of survey respondents

The survey was completed by 125 respondents (Figure 1) from 31 different countries, with respondents from Germany (n=22, 17.6%), France (n=9, 7.2%), Belgium (n=9, 7.2%), United States (n=8, 6.4%), the UK (n=7, 5.6%), and Canada (n=7, 5.6%) accounting for more than half (n= 69, 55.2%) of the responses.

Responders were mostly female (n=89, 71.2%), and working as employees (n=78, 62.4%). Freelancers made up 23.2% (n=29) of the respondent population, whereas 8.8% (n=11) are in a hybrid employment situation, and 5.6% (n=7) of the respondents are small business owners.

Respondents predominantly conduct literature reviews as medical writers (n=73,

Figure 1. Population characteristics of survey respondents

Distribution of survey respondents per country, role, experience level, and employment type.

Abbreviations: RA, regulatory affairs; SB, small business

58.4%), but 22.4% (n=28) of respondents have a clinical/regulatory affairs manager role, 10.4% (n=13) are researchers, whereas 8.8% (n=11) do so from another role. Other roles included clinical affairs (clinical trial coordinator, clinical evaluation specialist, medical advisor), regulation specialist, consultant or management-related roles (performance evaluation manager, client portfolio manager), statistician, and librarian. Survey responders were spread quite evenly over all experience levels.

Literature review process

Only 6% of respondents conduct systematic literature reviews using an automated process, whereas 35% use a partially automated process and 59% use a fully manual process without specific software or tools for conducting literature reviews (Figure 2). Of the respondents who use specific software tools for at least part of the literature review process (n=40, 32%), 19 (47.5%) use a commercially available desktop or self-hosted software package, 15 (37.5%) use a software-as-a-service (SaaS) platform, whereas 6 (15.0%) use a custom or self-created tool or application. About a third of respondents perform different steps of the literature review in duplicate. Screening in duplicate was reported by 38.1%, appraisal in duplicate by 37.1%, and data extraction in duplicate by 27.8% of respondents.

A valid numerical time estimate for conducting new or updated literature reviews was provided by 78 respondents. Time estimates averaged 84.8 hours (SD 71.2, IQR 37.5–105.0) for new literature reviews and 45.9 hours (SD 70.4, IQR 13.75–50) for updates of literature reviews. Eight respondents reported time estimates of at least 200 hours for new

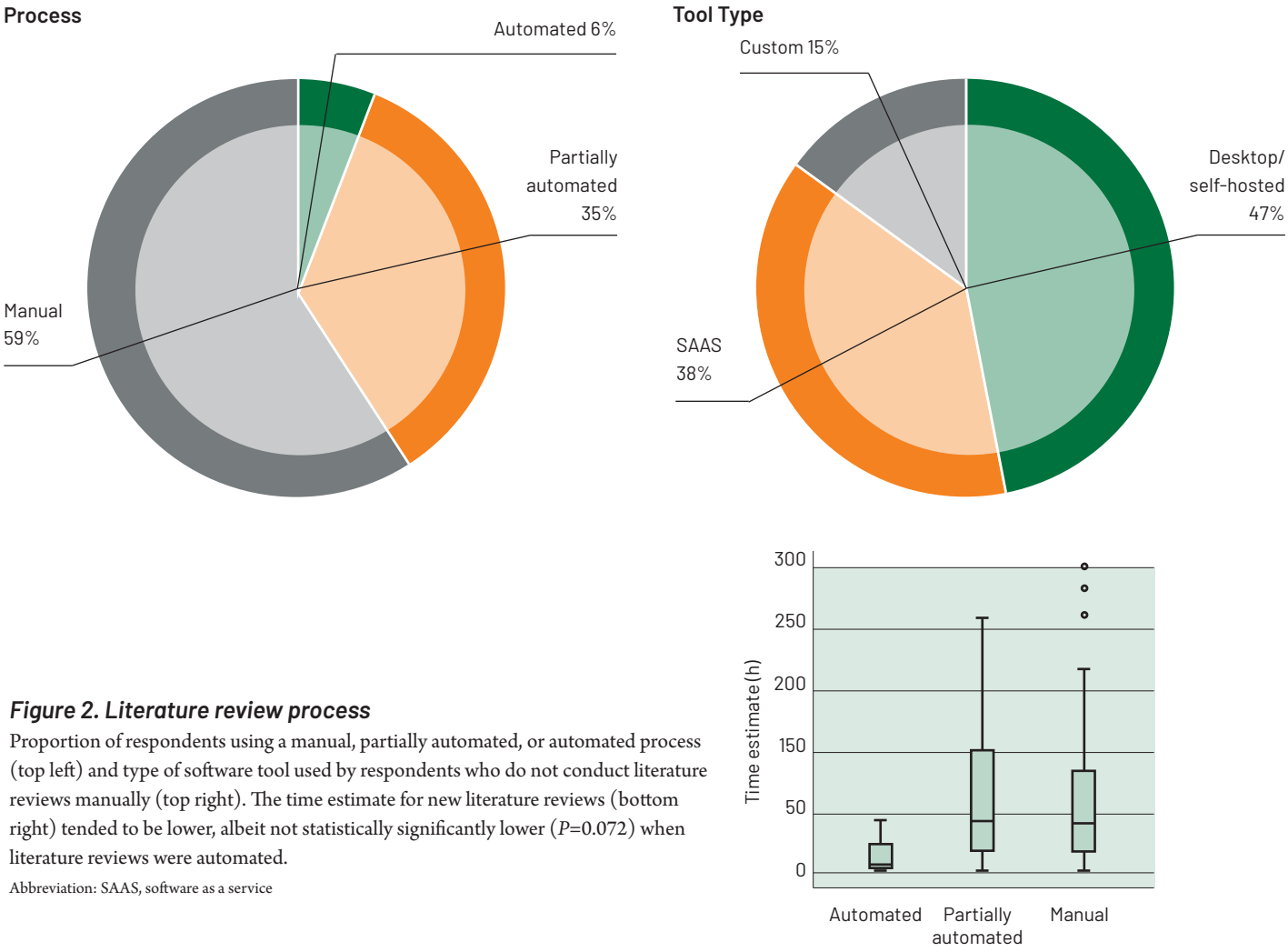

Figure 2. Literature review process

Proportion of respondents using a manual, partially automated, or automated process (top left) and type of software tool used by respondents who do not conduct literature reviews manually (top right). The time estimate for new literature reviews (bottom right) tended to be lower, albeit not statistically significantly lower (P=0.072) when literature reviews were automated.

Abbreviation: SAAS, software as a service

literature reviews (the maximum being 500 hours), whereas 14 respondents reported typically spending less than 8 hours on a new literature review. These data either point to domains where no or very limited data are available or to possible misreporting where the unit intended by the respondent may have been days or weeks.

Several (n=10, 8%) respondents correctly indicated that the time needed is dependent on the volume of literature retrieved, and the survey question did not contain a size indication for the retrieved literature. The question on the time needed to perform a new literature review or an update to a literature review was skipped by 35 (28%) respondents, and of those who did not provide a valid numerical estimate, 10 (8%) indicated volume of retrieved literature as reason, whereas 4 (3.2%) indicated they had no idea of the time typically spent on a literature review.

The number of hours spent on either new or updated literature reviews did not differ significantly by employment type, role, or level of experience. Time estimates did not differ significantly according to the type of process used (manual, partially automated, or automated) for either new or updated literature reviews, but the difference neared significance for new literature reviews (P=0.072) (Figure 2).

Use of dedicated literature review software

Respondents' answers on their use of and familiarity with software tools specifically intended for conducting systematic literature reviews are displayed in Table 1. On average, 4.6% of respondents were currently using one of the software tools in the survey; these software tools had been used in the past by 3.4% of respondents, 2.2% were planning to use them in the near future, 12.7% were aware of their existence, and 77.1% of respondents were unfamiliar with them. DistillerSR is the most widely used and known package. Medboard and Polarion were named as additional software packages by one respondent each via the "Other (please specify)" option.

Other software packages

Respondents used a median of 5 (interquartile [IQR] 4–7, range 0–15) other, general purpose software packages. The total number of software tools used was significantly lower for respondents who did not use a manual process or used a SaaS package for conducting literature reviews (Kruskal-Wallis P=0.03), whereas respondents with custom/self-made applications reported using a higher number of database applications (P=0.009).

Figure 3 presents an overview of the most frequently used software tools in different categories. Word processing software is used by 89.4% of respondents, spreadsheets by 86.9%, reference management software by 73.2%, PDF handling software by 79.9%, graphical software by 61%, and database software by 18.3%.

Microsoft Office tools are the most frequently used software packages in every category in which they are represented, and Acrobat is dominant for PDF handling. Two respondents indicated using the Mac OS Preview application

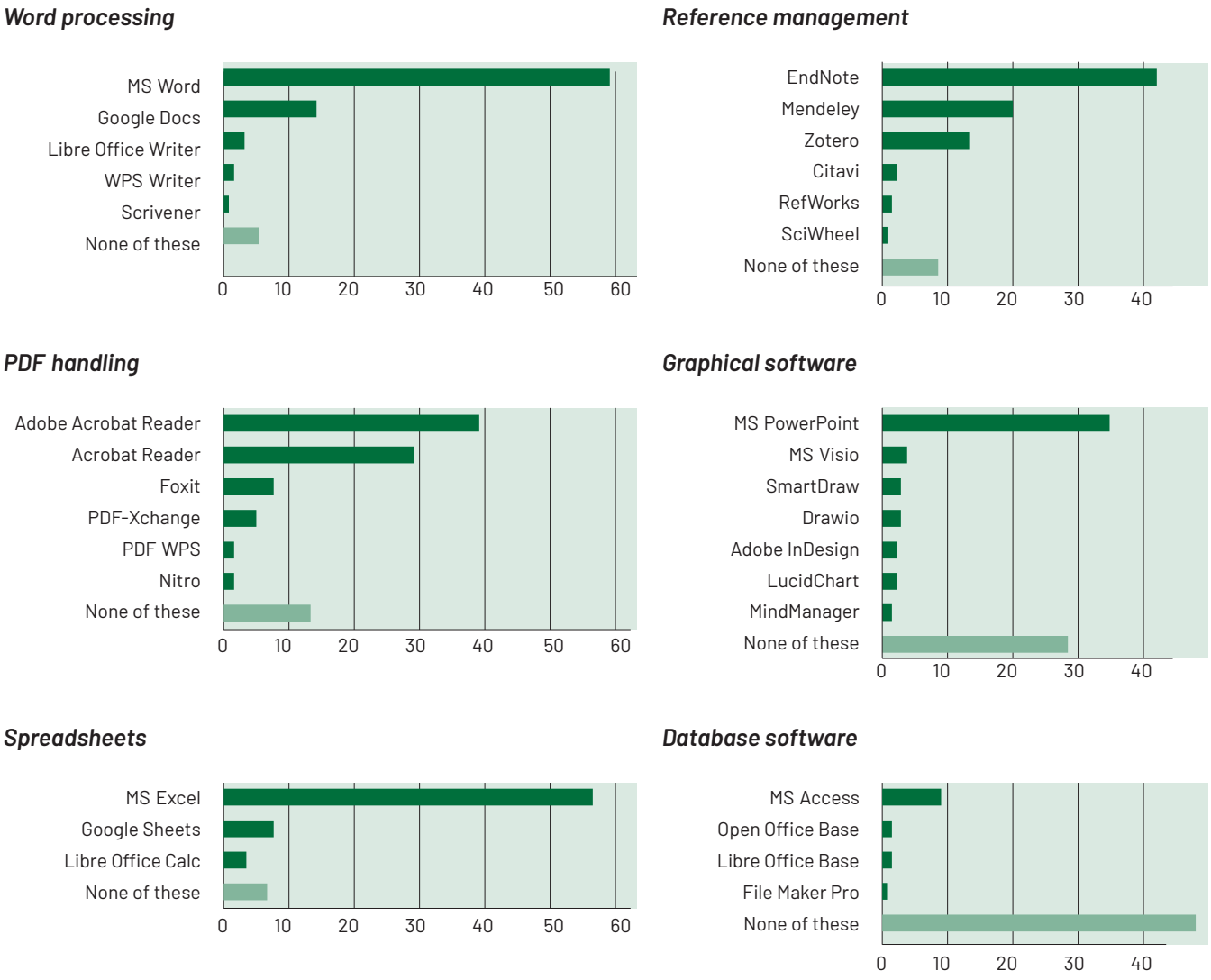

Figure 3. Current use of other software tools

Bars indicate the % of responses.

Abbreviations: MS, Microsoft; PDF, portable document format; WPS, Writer, Presentation, and Spreadsheets

Table 1. Familiarity with software tools for systematic literature reviews

	Currently using	Used in the past	Planning to use in the near future	Know it exists/ heard or read about it	Not familiar with it
Covidence	3.7% (3)	3.7% (3)	2.4% (2)	13.4% (11)	76.8% (63)
Rayyan	8.5% (7)	2.4% (2)	1.2% (1)	3.7% (3)	84.2% (69)
DistillerSR	8.5% (7)	7.3% (6)	1.2% (1)	22.0% (18)	61.0% (50)
Giotto Compliance	1.2% (1)	1.2% (1)	2.4% (2)	15.9% (13)	79.3% (65)
Systematic Review Accelerator	1.2% (1)	2.4% (2)	3.7% (3)	8.5% (7)	84.2% (69)

The question was answered by 82 respondents. Additional software packages named via the "Other (please specify)" option of this question were Medboard and Polarion, each named by one user.

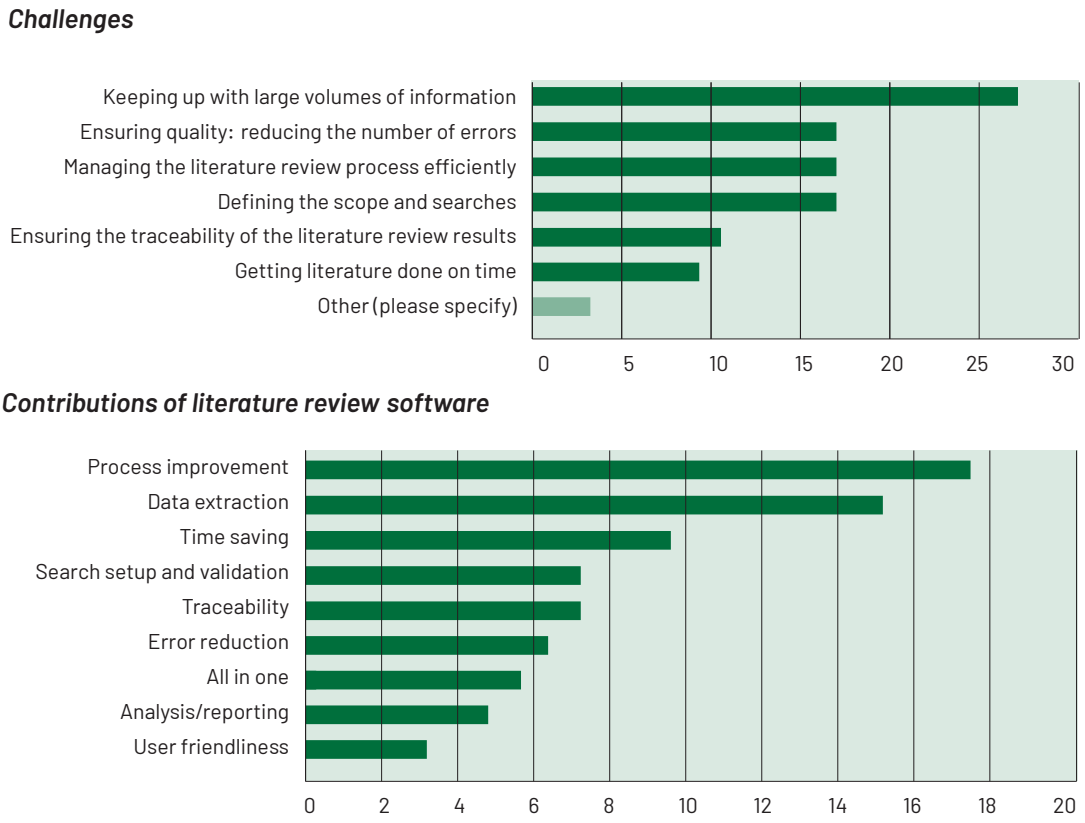

Figure 4. Current challenges and most valuable potential contributions of software to the literature review process
Bars indicate the % of responses.

for handling PDFs. In addition to the graphical software listed in the survey, three respondents use MS Word for creating Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) charts, three others indicate that this functionality is built into the literature review software they use, and one respondent reported not creating PRISMA charts.

The role of software in the literature review process

The main challenges perceived by respondents in conducting systematic literature reviews are shown in Figure 4. Responses in the "Other (please specify)" category were getting full texts of included articles and meeting client/employer expectations while maintaining quality.

Data extraction was reported as both the most time-consuming and error-prone step of the literature review process. Data extraction, screening, and data analysis were indicated as the three most important aspects where the use of software tools could most help to reduce the error rate and improve traceability of literature review results. Process improvement, improvement of data extraction, and time saving were the most valuable topics addressed by systematic literature review software, according to respondents (Figure 4).

Limitations

Some of the limitations are inherent to the nature of anonymous internet surveys. It is hard to estimate how representative the respondent population is and impossible to query missing or inconsistent results. The question on the estimated time needed for conducting a systematic literature review did not include a standard volume of retrieved literature, causing several respondents not to provide a valid numerical estimate.

As the objective of the study was to investigate current practices and familiarity with existing software tools, the survey did not question the motivation or reason for using or not using certain systems. Questions on specific features respondents require or look for in systematic literature software packages were not included either.

Data extraction, screening, and data analysis were indicated as the three most important aspects where the use of software tools could most help to reduce the error rate and improve traceability of literature review results.

Although the SurveyMonkey tool used to distribute the survey prevents a respondent taking the survey more than once from the same device, it cannot check whether the same respondent filled out the survey from multiple devices.

Conclusion

The majority of respondents (59%) conduct systematic literature reviews manually, without the aid of dedicated software packages, and most (61%–84%) are unfamiliar with the literature review tools queried in the survey. Data extraction was both the most time-

consuming and error-prone step in the literature review process.

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Disclosures and conflicts of interest

The author declares no conflicts of interest.

Disclaimer

Any interpretations and opinions in this article are the author's and are not necessarily endorsed by EMWA.

Data availability statement

For inquiries about data and other supplemental information, please contact the corresponding author.

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Appendix

Appendix 1. Survey questions

Demographics

What is your gender?

a. Female
b. Male
c. Non-binary
d. Prefer not to say

In what country do you live?

(List of countries to select from)

What is your employment type?

a. Freelancer
b. Employee
c. Hybrid (a mix of employed and freelance)
d. Small business owner (<10 salaried or subcontracted team members)

In what role do you perform systematic literature reviews?

a. Medical Writer
b. Researcher
c. Clinical/Regulatory Affairs Manager
d. Other (specify)

How many years of experience do you have in your current role?

a. <3
b. 3–5
c. 6–10
d. >10

Process

Are you currently conducting your literature reviews manually?

a. Yes b. No c. Partially

What tool do you use for your literature reviews?

(Only available when answer to previous question was not *a. Yes)*

a. Commercially available desktop/ self-hosted software
b. Commercially available web application (SaaS)
c. Custom/Self-made application(s)

Do you perform screening in duplicate (every paper screened by two people)?

a. Yes b. No

Do you perform appraisal in duplicate?

a. Yes b. No

Do you perform data extraction in duplicate?

a. Yes b. No

Time

How many hours do you (and your team) typically spend in total on a (new) systematic literature review?

How many hours do you (and your team) typically spend on an update of a systematic literature review?

Use of dedicated literature review software/ tools

How familiar are you with the following platforms for conducting systematic literature reviews?

- Covidence
- Rayyan
- DistillerSR
- Giotto Compliance
- Systematic Review Accelerator
- Other (please specify)

a. Currently using
b. Used in the past
c. Planning to use in the near future
d. Know it exists (heard or read about it)
e. Not familiar with it

Use of other software tools

Which other software tools do you use in for conducting a literature review?

(check all that apply)

Word processor

- MS Word
- Google Docs
- LibreOffice Writer
- WPS Writer
- Scrivener
- None of these

Spreadsheets

- MS Excel
- Google Sheets
- LibreOffice Calc
- WPS Spreadsheet
- None of these

Reference management software

- EndNote
- Mendeley
- Zotero
- SciWheel
- Paperpile
- Papers
- RefWorks
- Citavi
- Qiqqa
- Docear
- None of these

PDF software

- Adobe Acrobat Reader
- Adobe Acrobat
- Foxit PDF Reader
- Nitro
- PDF-Xchange
- WPS PDF Reader
- None of these

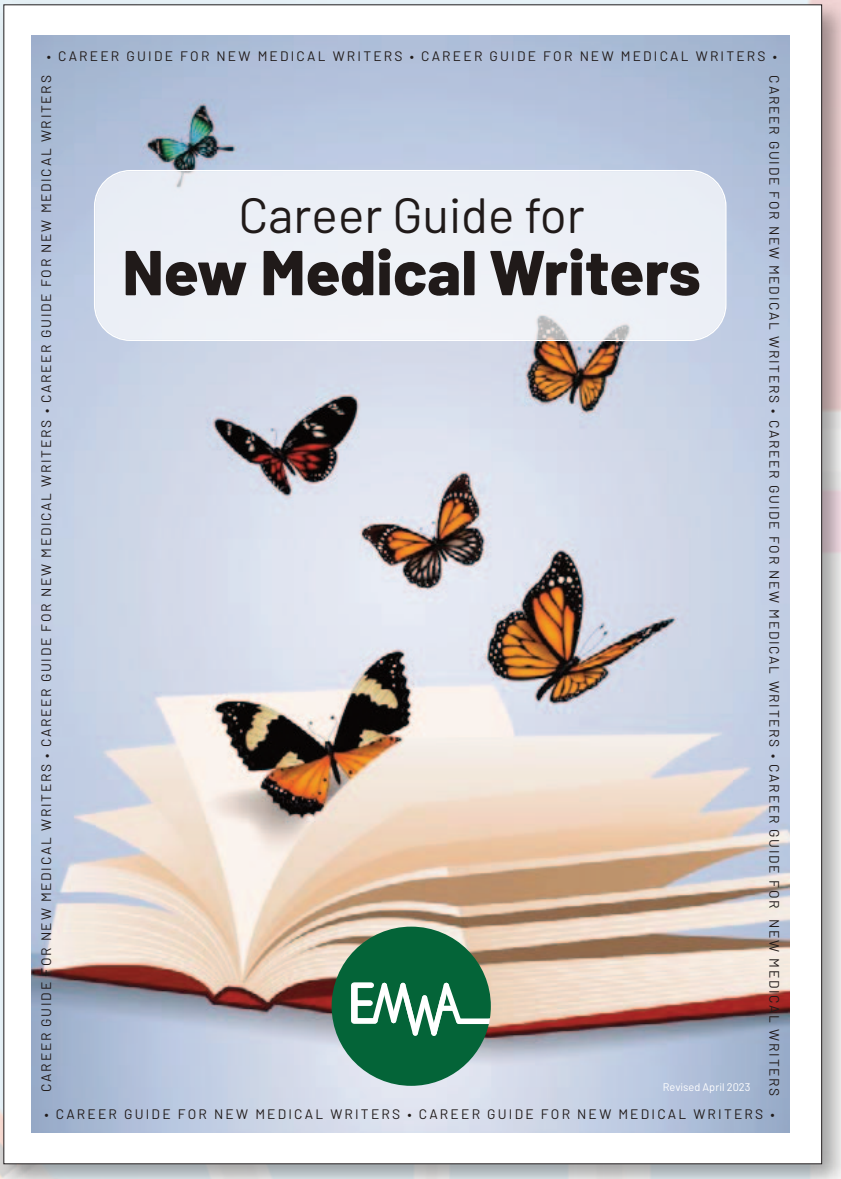
Graphical/flowchart software

- MS PowerPoint
- MS Visio
- Drawio
- LucidChart
- SmartDraw
- Adobe InDesign
- MindManager
- None of these

Database

- MS Access
- FileMaker Pro
- LibreOffice Base
- OpenOffice Base
- Memento Database
- Airtable
- None of these

Abbreviations: MS, Microsoft; PDF, portable document format; SaaS, software as a service; WPS, Writer, Presentation, and Spreadsheets



Career Guide for New Medical Writers

EMWA's Getting into Medical Writing group announces an updated *Career Guide for New Medical Writers*, which is available on the EMWA website. If you're new to medical writing, it's a useful resource that will help you take your first steps on this rewarding career path. You can email us at gettingintoMW@emwa.org with comments.

Writing reports of modelling and simulation analysis: Our experience in the field of pharmacometrics

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Abstract
Pharmacometric analyses generate mathematical models that can describe and simulate the pharmacokinetics and pharmacodynamics of drugs. The role of these modeling and simulation (M&S) analyses is growing both in drug development and regulatory assessment. Reporting M&S analyses can be technically challenging given the large amount of input and output data that need to be summarised and accurately described in regulated reports. Therefore, reproducibility, automation, traceability, and standardisation are considered key aspects of this process. We present here a system that, using a combination of software, meets these challenges and improves the efficiency, accuracy, and reliability of our work.

Introduction
Pharmacometrics, an emerging field in drug development, combines information from biology, physiology, pathology, and pharmacology, into mathematical models that can quantify the interaction between drugs and patients. Modeling and simulation (M&S) of drugs' pharmacokinetics (PK) and pharmacodynamics (PD) are used to inform drug development, support regulatory assessments and trial design, and extrapolate predictions for specific populations. Altogether, this information can contribute to better patient care and support regulatory decisions. M&S analyses for regulatory submission are characterised by short timelines, large input data sets, and extensive output files; all these processes need to be tracked, organised, and interpreted in regulated reports. We describe here a reproducible reporting system developed to meet these challenges: a combination of several software programs (R, RStudio, knitr, and LaTeX) that integrates analyses and partly automates report writing.

A natural need for automation in reporting pharmacometrics results
Like many other areas of regulatory writing, the field of pharmacometrics also benefits from some level of automation and standardisation during report writing. To understand where this need comes from, we should first consider how the role of M&S analysis developed over the years.

The evolving role of modelling and simulation analysis in drug development
The role of M&S in drug development and regulatory assessment has grown in the last few decades. The benefit of using M&S is demonstrated by the integration of this type of analysis in the regulatory guidelines, as well as the creation, and continuous development, of "good practices" documents.[1-7] An extensive overview of these documents, as well as the scientific articles published on recommendations for model building and its documentation, is provided in a white paper from 2016.[8]

Given a closer look, the role of M&S in drug development has rapidly grown beyond the sole internal decision-making within pharmaceutical companies. What we nowadays call "model-informed drug development" (MIDD) is used, among other aims, to support regulatory assessments, trial design, dose selection, and extrapolation to special populations. Moreover, in some cases, the authorities have used M&S studies to approve a variation of indication even in the absence of clinical data (e.g., in paediatric studies).[9,10]

This expanding role of M&S has led to more pharmaceutical companies applying these analyses to complement their submission packages and/or to inform the subsequent phases of drug development. Pharmaceutical companies either perform these analyses in-house, when competences and resources allow for it, or request them from specialised contract research organisations (CROs).

Pharmacometrics, an emerging field in drug development, combines information from biology, physiology, pathology, and pharmacology, into mathematical models that can quantify the interaction between drugs and patients.

Why automation in reporting?
Very often, time is key for M&S analyses. When these analyses need to be performed immediately after clinical data become available, either to inform internal decision or to support regulatory submissions, results are expected within short timelines.

In pharmacometrics, not only the analysis phase but also the phase of documentation/reporting is regulated, and the produced documents need to conform to specific requirements.[8] For example, original data files, data transformations and the associated code, computation and coding of the final model and simulation files all need to be made available. Furthermore, data and results need to be shown in specific types of plots, and the validity of the developed models must be demonstrated using suitable "model diagnostics".

It goes without saying that reporting such type of analyses benefits from a clearly organised, structured, and reproducible system. By "reproducible" we here refer to a system that, if

starting from identical input data analysed with the same methods, should give the same output and lead to an essentially identical report. This implies that the final analysis report can be more in line with the internal organisational standards and less dependent on the single individual.

Tools for report-writing

There are many ways to achieve the main goals of consistency, traceability, and standardisation of reporting. The one that we chose is using a combination of:

- The statistical computing program and modelling software **R** (v4.2.2; R Core Team, 2019)[11] together with RStudio, an integrated development environment (IDE) for R, published by Posit[12]
- The document preparation system for typesetting **LaTeX**[13]
- The R package that enables integration of R code into LaTeX, called **knitr**[14-17]

These 3 tools are used in combination in the process that is described in Table 1.

This type of approach makes the whole process (after data collection) traceable and reproducible, thus complying with the principles of "reproducible research".[18,19]

Importantly, while this system needs to be solid and standardised to comply with regulatory

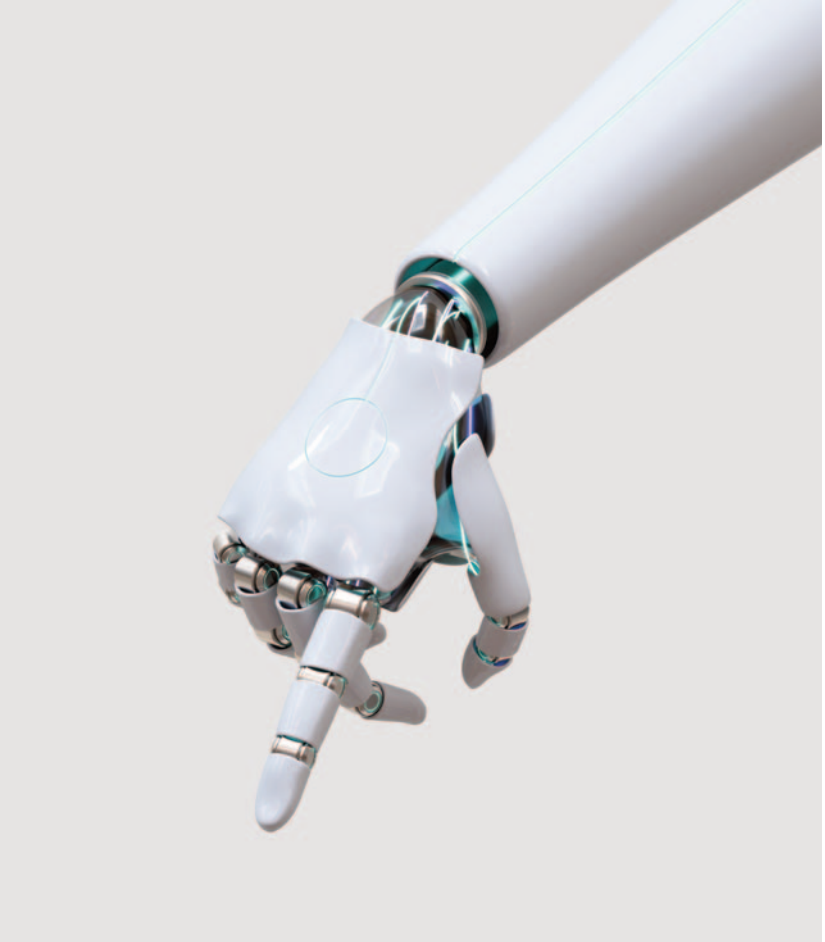


Table 1. Process of pharmacometric analysis and reporting: Typical main steps and examples of the actions that can be performed during each step

Main steps of analysis and reporting	Examples of actions performed during the step
1. Data transformation	Create a variable that groups subjects by type of underlying disease
2. Data exploration	Observe trends in the data, e.g., subjects with a specific disease type eliminate the drug faster
3. Model building	Develop a model that describes the PK profile of a drug while taking into account possible sources of variability, such as type of underlying disease, age, genotype
4. Description of the model results	Results are generated by an external software (e.g., NONMEM®, ICON plc); results are then analysed to demonstrate the validity of the models (e.g., by generating plots, such as visual predictive checks) and to draw conclusions on the endpoint analysed
5. Simulations	If results are further used to perform simulations, this allows making predictions of how a drug is expected to behave, e.g., in specific patient populations
6. Creation of submission-ready reports	Reports are generated, peer reviewed, and quality controlled; when finalised, the report and all supporting documentation are included in an e-submission package that is ready for regulatory submission

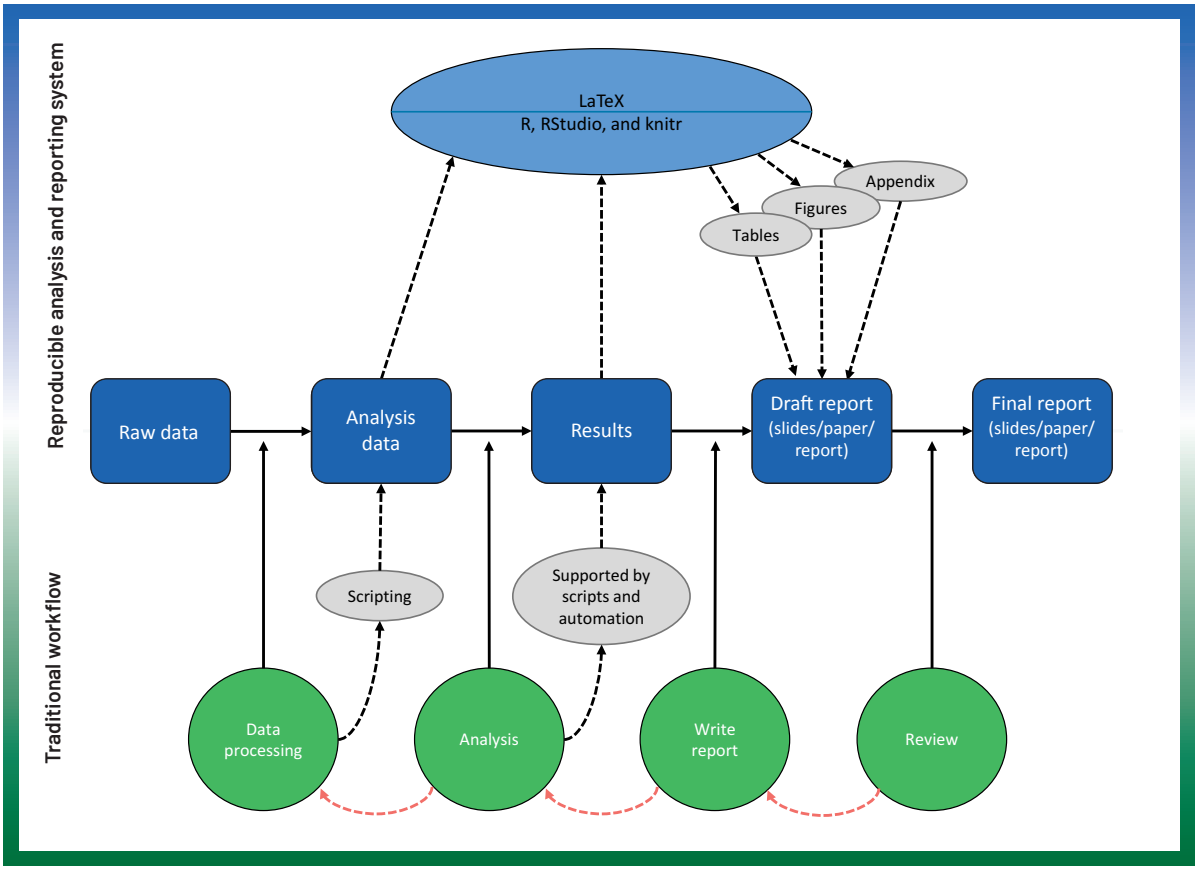


Figure 1. Analysis and reporting workflow

The blue boxes (central part of the figure) represent the typical workflow of pharmacometric analysis, from access to raw data to the phase of reporting the performed analysis. The lower part of the figure (green circles) describes the traditional workflow, in which analysis and reporting consist of consecutive steps and where review feedback (red dashed arrows) needs to be implemented manually for every single step. The upper part of the figure (light-blue ellipse) describes the tools used in the reproducible analysis and reporting system that we describe in this paper. The integration of analysis and report generation creates a seamless chain between raw data and final report. Incorporation of review feedback and correction of data errors is done in one place and then automatically propagated throughout the report.

requirements, it also needs to be sufficiently fit-for-purpose and flexible so as to adapt to the specific type of analysis (e.g., a PK-PD analysis concerning an oral-delivered drug and its active metabolites or an intravenously-infused drug, a PK-PD analysis of a time-to-event endpoint, or an endpoint measured as a continuous variable).

Setting up such a system and defining all its technical details, as well as creating user-friendly instructions for each step, requires the collaboration of a multidisciplinary team (pharmacometricians, system developers, data programmers, medical writers, quality control reviewers, etc.). Despite its technical complexity, once set up, this system is rather straightforward to use. The process makes use of R and its literate programming capabilities:[20] according to this principle, the system not only delivers a user-friendly PDF document, but is also more robust and easily maintained. With regards to the latter, when pitfalls are identified by users and when new methodologies or software updates are released, the system can be updated and refined. In this way, new versions of the system can be released, where standard code is adapted and dependencies across programmes are revised.

> The reporting system represents the point in which scientific analysis, automation/ scripting, and medical writing meet.

Brief description of the system

When a CRO performs pharmacometric analysis for a pharmaceutical company, a typical project starts with discussions with the client about the objectives, project planning, and definition, to reach an agreement on the analysis plan. When data from clinical studies become available, large data files, possibly also in different file formats, are delivered by the client to the CRO. These data are explored and transformed to create data files that can be read and used as input by a modelling software (such as NONMEM®, ICON plc)[21] (Figure 1). Pharmacometricians then analyse the data, develop models that appropriately describe the data, and possibly perform simulations in accordance with the purpose of the analysis (Table 1).

The hands-on process starts with specific input files and generates large amounts of output files and output data, in different formats, that should be summarised and interpreted. Therefore, already during the analysis, modelers need to gradually put all this information

Case study

This case study exemplifies the advantages of shifting the time spent on report writing to the early analysis phase. A pharmaceutical company requested our CRO to perform pharmacometric analyses on data from a phase III study of a drug used for cardiovascular diseases. Our company performed much of the work during the preparation phase: planning the analysis in detail, creating data files of dummy data, generating a dummy report with simulations to prepare for several alternative study outcomes, and performing scientific review and QC of the analysis and the report. As soon as the clinical study was completed and final study data were made available, scientists could spend time on actual data analysis rather than on extensive writing and editing of the report. This resulted in a 7-week turnaround time from final data access to regulatory submission of the M&S report.

together in a clear, structured, and understandable way (Figure 1). By the end of the analysis, this bundle of information needs to be organised in a report that should not only be consistent with the CRO's and clients' standards, but also conform with the content and quality requirements imposed by the regulatory authorities.

To support this process, the reporting system represents the point at which scientific analysis, automation/scripting, and medical writing meet. From a user perspective, the reporting system appears as consisting of 3 main "blocks" for each report section:

- **Instructions** on which specific information to include, how to include it, and which output files to append, allowing to deliver a "structured content";
- Section-specific verified **scripts** and functions that generate standard figures and tables in accordance with regulatory requirements (of note, R scripting uses R-packages validated to comply with good clinical practices);
- **Standard text** to help describe and clarify methods and processes typically used; in addition, optional standard text is provided to describe the most common alternative analyses.

The full product of this reporting system is a few hundred-pages-long PDF document ready for regulatory submission. However, the system can also generate shorter reports if leaner documents are better fit for the specific purpose. For such alternative cases, the system we developed allows tailoring the length and the subsections of the report to the client's requests. This can be done before report writing begins by selecting the specific document template and the type of analysis. This way, reports of different sizes or with specific subsections, as well as slide decks, can easily be produced using the same, flexible reporting system.

Advantages

The advantages of this reporting system are related, on the one hand, to the more "technical" aspects of the process and, on the other hand, to the characteristics of the final document.

The most evident technical advantage is probably the fact that, despite using several different file formats as input, the product of this system is a PDF document. This is often the format that clients prefer for final reports. Besides, a PDF is convenient since it does not allow accidental modifications and can easily be signed with official e-signing software. Additional advantages of this system are the type of software involved (LaTeX+ R + RStudio + knitr), which are open source, and thus available to everyone at no cost. Furthermore, these software programs are not specific to pharmacometrics, and thus can profit also by developments in other fields. In addition, these programs can handle large and complex technical documents. Finally, RStudio offers an environment that integrates code for statistical analysis and regular text for document preparation (Figure 2). In simple words, when RStudio receives the command to compile a PDF, it will automatically:

- Execute the R code and replace it with the appropriate LaTeX code;
- Typeset the LaTeX document into a PDF;
- Update the bibliography numbering and references list (according to the information in a file named bibtex);
- Update the glossary and correctly include all abbreviations according to the company standards.

> In pharmacometrics, not only the analysis phase but also the phase of documentation/reporting is regulated, and the produced documents need to conform to specific requirements.

Another advantage is that, as already pointed out earlier, this system allows for reproducibility of reporting and traceability of data sources, data transformation, and analysis. Additionally, instead of having to type all the content manually and having to create plots and figures from scratch for each new project, the use of validated R-scripts is more efficient and much less error-prone. With coded content, possible errors can be efficiently corrected by changing a value (or code, filename, or directory) only once in the master document: code dependencies generate a cascade of changes that will automatically propagate the corrected item in the rest of the report. These are all factors that are known to reduce the overall time and money spent on performing, writing, and QC reviewing these analyses.[22] Other authors have previously emphasised the effects of using automation tools to accelerate document writing, in some cases also quantifying them in terms of time saved.[23,24]

Another factor contributing to the efficiency of this system is that reports can be prepared even before clinical trial data are accessible and before final models are generated. In a sort of "preparation phase", the main analyses can be performed (e.g., using dummy data or previously published data from a similar study), and the report can be shaped (and already partly QC reviewed in the relevant sections). Then, when final study data become available, one can focus most of the effort on the outcome-related aspects that need to be interpreted and reported. This preparation phase allows shifting the time spent on report writing from the final and time-critical stages to an earlier and more convenient phase of the analysis. The case study described in the box gives an example of the possible time gain.

Another advantage of this system is the possibility to deliver "structured content", i.e., a document in which information is placed in the appropriate section. This specific aspect has been defined by some authors as a labour-intensive and "the most time-consuming, tedious task" for a medical writer.[23,25] Besides the use of standard text and instructions, another tool contributing to this is given by the use of technology (e.g., scripts) that retrieves information from different parts of the document (or even separate documents) and combines it in the appropriate

Input

```
\section{Demonstration of  \LaTeX and \knitr}

\LaTeX is a markup language that allows authors to focus on the content of their
document while the system takes care of formatting and layout. With simple commands
, text formatting such as \textbf{bold font} and \textit{italics} can be applied.
\LaTeX syntax can also be seamlessly combined with program code, such as the
statistical program R. This can be achieved through inline equations, such as
writing "10 + 10 = \Sexpr{10 + 10}" or more complex code chunks as illustrated
below.

<<Rcode,results='asis',fig.env="figure",fig.cap="This is a figure based on the Iris
data set",fig.pos='H'>>=

ggplot(data=iris,mapping=aes(x=Petal.Length,y=Petal.Width))+
  geom_point(aes(color=Species,size=Sepal.Width))+
  xlab("Petal lenght") + ylab("Petal width") +
  labs(size = "Sepal width")+
  theme(legend.position="top")

@
```

Output

1 Demonstration of LaTeX and knitr

LaTeX is a markup language that allows authors to focus on the content of their document while the system takes care of formatting and layout. With simple commands, text formatting such as **bold font** and *italics* can be applied. LaTeX syntax can also be seamlessly combined with program code, such as the statistical program R. This can be achieved through inline equations, such as writing "10 + 10 = 20" or more complex code chunks as illustrated below.

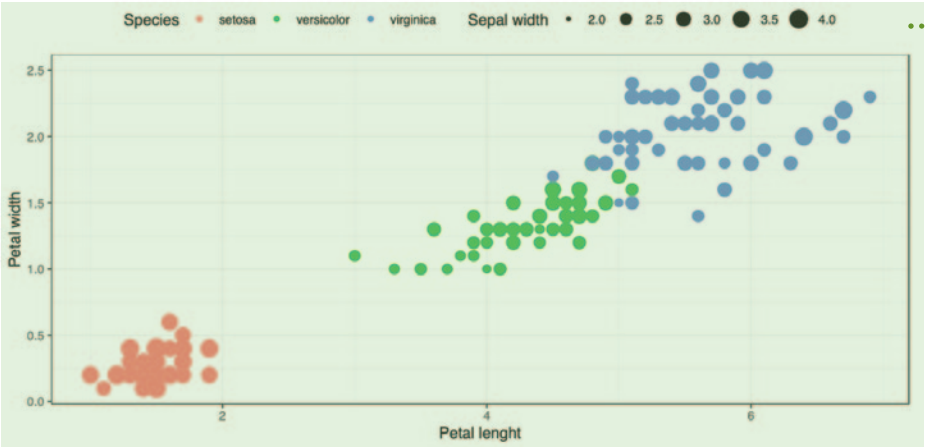


Figure 1: This is a figure based on the Iris data set

Figure 2. Example showing how the tools in the reproducible reporting system (R, RStudio, LaTeX, and knitr) allow the integration of the analysis and reporting processes.
On the upper panel (input), an example of LaTeX syntax (in blue) and R code (in green); on the bottom panel, the output PDF document that includes the respective text generated by LaTeX syntax (in blue) and the figure generated by the R code (in green).

sections, with only minor manual adaptations needed.

From a more linguistic point of view, an additional advantage is that by using guiding text and standard sentences for alternative scenarios, the formatting, tone, and language style are more consistent across scientists; this, additionally, supports professionals that are less focused on the linguistic aspects of reporting. Consequently, less time needs to be spent by a medical writer rephrasing entire paragraphs to adjust language style and formatting.

Limitations

The main drawbacks of this reporting system relate to the technical complexity of the tools that are employed. The less IT-skilled professionals may find the interface rather unfamiliar and somewhat "archaic". An example of this complexity is linked to the use of LaTeX instead of Microsoft (MS) Word as software for document preparation. Although most users may be largely familiar with MS Word, this software does not allow the programmatic integration of text, plots, tables, and abbreviations generated with standard code, yet this can be done using LaTeX, in combination with R and knitr. Of note, when developing this system, we also considered using R Markdown (RStudio, PBC) instead of LaTeX, where R Markdown is more user-friendly; however, R Markdown may not produce PDF documents meeting all the requirements of regulatory agencies, and thus LaTeX remained the preferred software. A second example of technical complexity is the need to understand most of the R code that generates tables and figures so as to be able to adapt it when certain functionalities need to be modified (e.g., a standard plot shows the subjects' median drug concentrations over time, but the client requests showing the mean values instead). A final example of complexity is related to the phase of report revision and finalisation: the document generated by the system is in PDF format instead of MS Word. Once again, users may be more familiar with the review functions in MS Word, implying that adding comments and revisions in a PDF document may require some training. All these technical aspects, together with the need to learn and adapt to the company-specific standards of analysis, lead to a steep learning curve for those using this system.

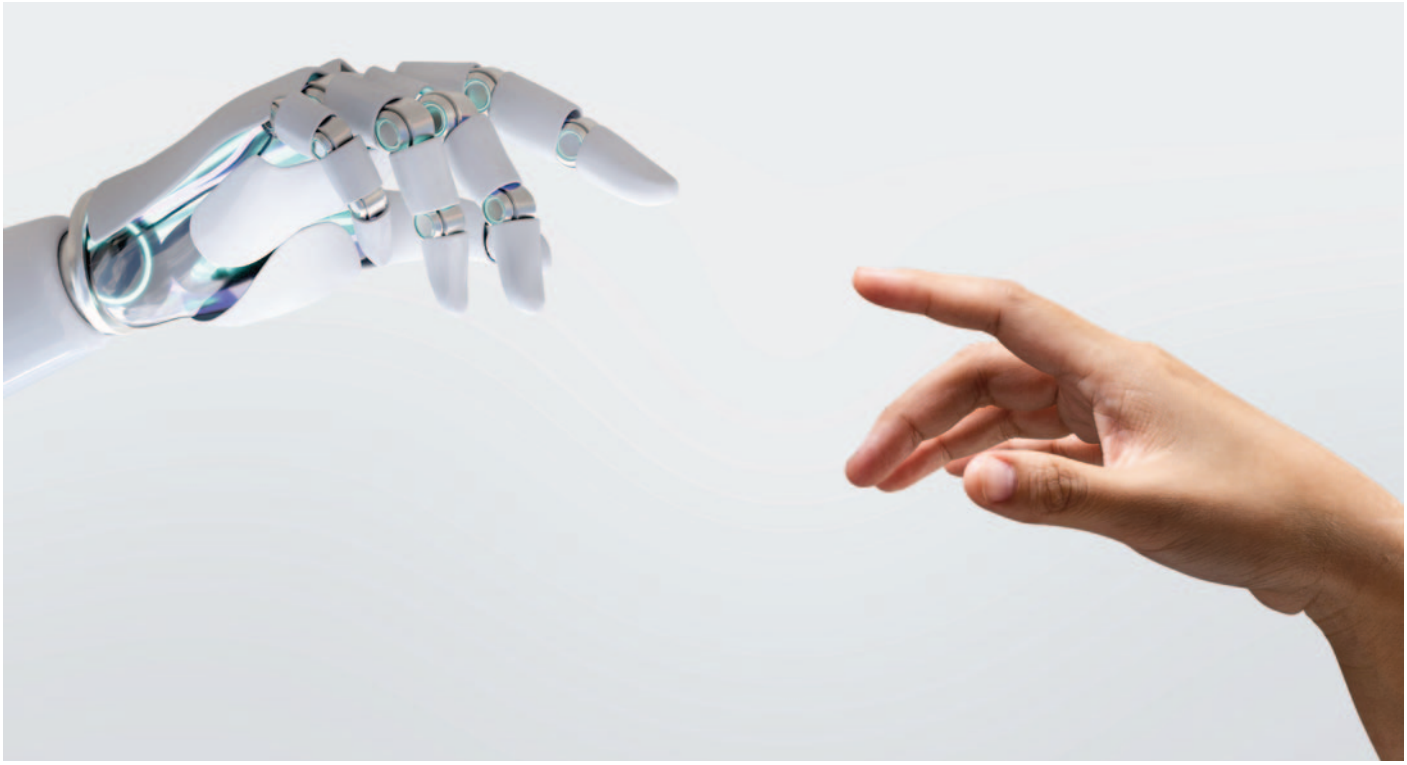
Another technical disadvantage is that all the tools listed (R, RStudio, LaTeX, and knitr) need to be correctly integrated into the existing IT environments in use at the company. Furthermore, any process adaptations or program updates need to be compatible with the rest of the system.

Regarding the final document delivered by this system, the main drawback is probably the fact that the resulting report is more template-oriented than project-oriented. In practical terms, this implies that sometimes particular client requests or project-specific needs may require additional effort to implement.

Finally, a challenging aspect is that the whole system needs to be accurately installed, so as to protect business confidentiality, information security, and access to confidential regulatory documents.[22]

Conclusions

In conclusion, despite not being free from challenges, the reporting system that we developed has increased the efficiency, accuracy, and reliability of our work. Moreover, in line with the principles driving our analysis within pharmacometrics, this reporting system contributes to the reproducibility, automation, traceability, and standardisation of our deliverables.



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Disclaimers

The opinions expressed in this article are the authors' own and not necessarily shared by their employer or EMWA.

Disclosures and conflicts of interest

The authors are current employees at Pharmetheus AB, where the reproducible reporting system discussed in this article was developed. The authors have no connection or affiliation with the companies that created or developed any of the software used in this reporting system.

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AI for medical writers: Friend or foe?

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Abstract

Artificial intelligence (AI) is beginning to affect almost every industry, and medical writing is no different. But how does this relate to our industry? How will AI affect medical writers? What's already available and what is in the pipeline? Should medical writers be happy and embrace the technology, or should we resist as much as we can, assuming that we will all be replaced by machines? This article discusses the current state of the art of AI in medical writing and asks the question: AI for medical writers – friend or foe?

How did we get here?

What a year it's been for artificial intelligence (AI) already! The pace at which the conversation around AI has accelerated in just a few short months is unprecedented. However, AI is certainly not new. As a term, AI was coined back in the 1950s,[1] and ever since then, the technology, models, and processing power have advanced. With ChatGPT leading the way, along with Google, Meta, and a host of other tech companies, the paradigm is shifting so rapidly that in the time between writing this article and publishing it, there could be something new to discuss in the world of AI.

But what led us to this point? What triggered this explosion? AI is not new nor are language models such as those employed by ChatGPT. As we enter the age of AI, and with ChatGPT competing with the behemoth of Google, the success is best explained by Google's own history.

In the early days of the internet, conducting a "search" seemed like something of a dark art. Companies would invest their marketing budgets in promoting their URL because the idea of just being able to search for the company seemed to be a pipe dream. Even with the advent of the first search engines, if you did not know how to write queries using Boolean logic, getting any meaningful results felt like a lottery.

And then Google came along: no pop-up ads, no confusing page layout, just a simple search box. And it worked. Effortlessly. The beauty was in how they made something so complex incredibly simple and accessible. And the rest, as they say, is search history. And now history repeats itself: AI is not new, but a simple, well-designed-interface such as ChatGPT makes it appear effortless and provides powerful results. This has captured the imagination of the world. It is certainly impressive and has prompted a flood of examples demonstrating its power. As Arthur C. Clarke famously said, "Any sufficiently advanced technology is indistinguishable from magic".[2]

> What was once a niche domain for data scientists and AI technologists has suddenly become widely accessible.

What was once a niche domain for data scientists and AI technologists has suddenly become widely accessible. We now see everyone leveraging its power for everything from drafting emails to answering exam questions. This explosion has been so large and rapid that it has outpaced working practices and even legislation. This has led to the kind of concerns that triggered the open letter from tech leaders in which they urged a pause in development of AI to allow some checks and regulations to be put in place.[3]

What AI is and how it works in a writing context

In a rapidly changing sector, what is already available and for what purpose?

The term AI is very broad. Different branches of it often get conflated, but there are disciplines within the discipline. At its highest level, AI is a catch-all term for any computational technique that enables machines to mimic human behaviour. This could be as simple as a macro in excel that automatically performs a set of calculations or procedures or as advanced as a facial recognition algorithm.

The next layer of detail is referred to as "machine learning", which is a subset of AI that uses statistical methods to improve a model based on experience. For example, for image recognition, this could be a system that improves the accuracy of recognising a certain animal under increasingly ambiguous scenarios.

The next deeper level is so-called "deep learning". It is a subset within machine learning, where a neural network is used to make connections. Incredibly large, multi-layered networks create computational systems that work more like the human brain. Many deep learning algorithms are actually closer to "black box systems", in which the outcomes may be incredibly accurate but difficult to explain. This is one of the areas that makes some groups pause because they often show emergent behaviours that were not predicted by humans and can be unsettling, adding to concerns that AI is out of control.

This is where the notion of "explainable AI" comes in.[4] Being able to reverse-engineer outcomes and explain the results of AI models creates a more comforting outcome, although this may mean sacrificing some of the computational power provided by deep learning models.

Where does ChatGPT fit in?

ChatGPT uses neural nets to support the computation power of its outcomes. As a large language model, it retains a degree of "explainability".[5] Large language models generally use statistical models. In simple terms, a language model uses a set of training data to create a probability of the next word or series of words in a sentence. ChatGPT's power comes from access to perhaps the largest corpus of training data of any language mode. However, even ChatGPT has shown emergent behaviours. For example, it can be used to solve maths problems, for which it was not specifically designed, and although it can "solve" maths problems, it cannot interpret statistics.

Language modelling also cannot assign probabilities to linguistically valid sequences that may not have been in the training data. This is a positive in the sense that in can create novel texts, but it also can produce results that are grammatically correct but factually incorrect. That is, it can assess the probability of word sequences but cannot understand their meaning. In this way, language models differ from cognitive models, which, as their name suggests, are closer to our own abilities to solve problems.

The challenge of interpreting new concepts is an important consideration for AI. This has been illustrated using the "Monty Hall" problem from the medium of gameshows.[6] The Monty Hall problem is a brain teaser, in the form of a probability puzzle, loosely based on the American television gameshow "Let's Make a Deal" and named after its original host, Monty Hall.

The challenge of interpreting new concepts is an important consideration for AI.

Imagine that you are given the choice of three doors: Behind one door is a car; behind the others, goats. You pick a door, say number 1, and the host, who knows what's behind the doors, opens another door, say number 3, which reveals a goat. He then says to you, "Do you want to pick door number 2?" Is it to your advantage to switch your choice?

Most people's intuition is to stick with their original choice. However, the correct response is, counter-intuitively, to switch. Switching gives a two in three probability of winning a car, while sticking with your original choice gives only a one in three chance. If you do not believe it, there are plenty of referenceable articles on this topic that can be found on Google.

If you pose this question to ChatGPT, you will receive the correct response, suggesting that you switch. This is due to the training data, which most likely included a written reference to how this problem is solved. However, what if we made this a "dumb" problem, where the answer is much more obvious? In this case, we pose the same problem but with a small change: This time the

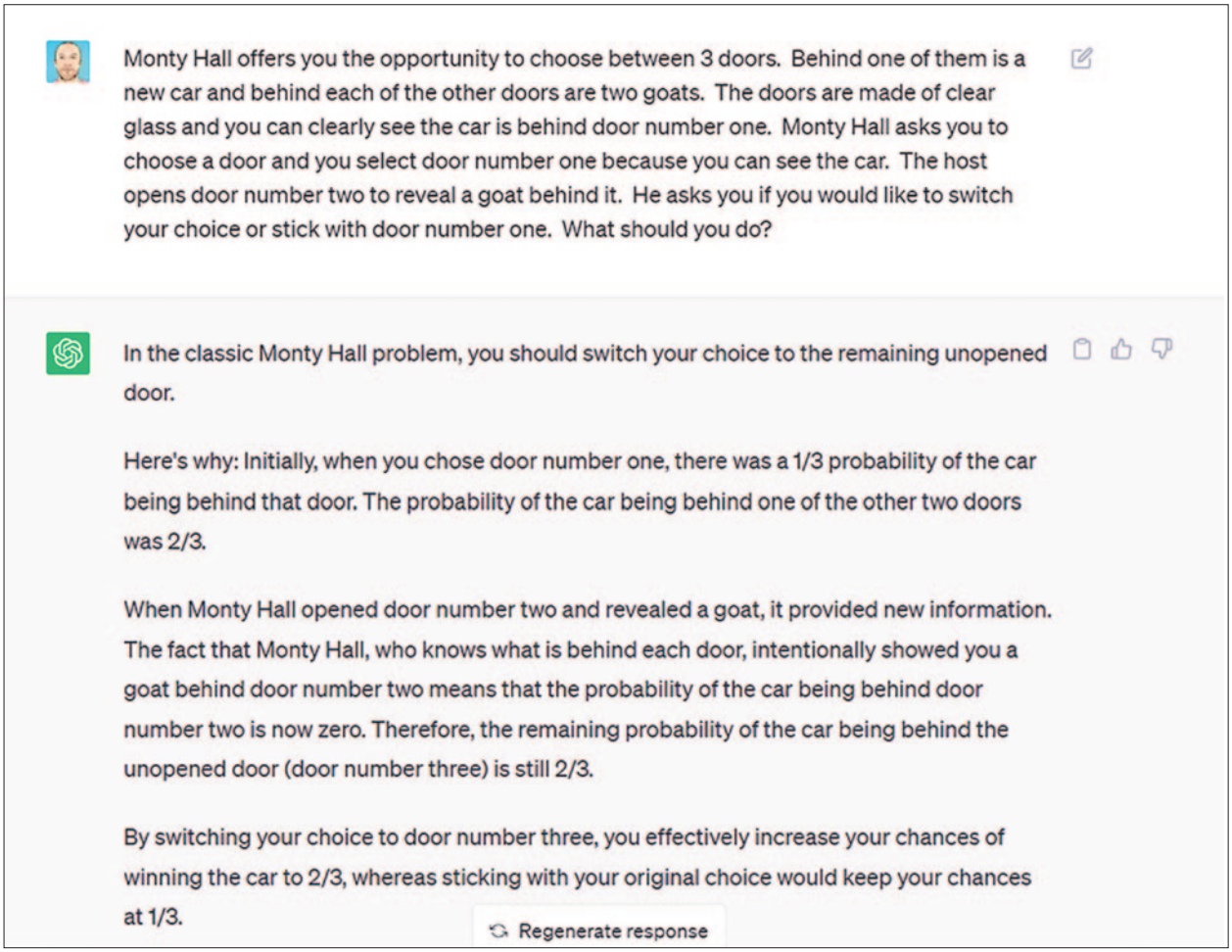

Figure 1. GPT prompt and response to the "dumb" Monty Hall Problem

With thanks to Colin Fraser, Data Scientist at Meta.

doors are made of clear glass so that you can see behind every door. Under these conditions, you can easily pick the door with the car behind because you can see it, and when asked to switch this time, you would clearly stick with your choice. However, when posing this challenge to ChatGPT, it always suggests switching your choice (Figure 1).

This is a reflection of the language model's inability to reason in the same way as a human – to make deductions from premises or to process insights rather than to make probabilistic inferences from word frequencies. This explains why making new inferences from data can be challenging, and it is exactly the kind of challenge we face in interpreting statistical data from new drugs. The margins for error in this context are significantly smaller so we cannot rely on language models alone.

> The challenge of interpreting new concepts is an important consideration for AI.

Like any technology, ChatGPT is just a tool. As with any tool, it is only as good as the person using it. ChatGPT is incredibly powerful, but to build products around it, its underlying working models, nuances, and other details need to be understood.

How could AI help medical writers?

Many generic language models are able to create authentic content, but they do not always perform well when the content is novel or its frame of reference is new, as was the case with the dumb Monty Hall problem previously mentioned.[6] This is simply a result of the training data used because language models can only produce content related to the data they have been trained on. A well-documented downside of generic language models is "computer hallucinations", where a language model "makes up" information or cites references when it has no information. This is obviously a major concern for the field of scientific writing.

To address this, some niche tools have been specifically trained on and produce content relating to scientific information. An example is Ferma ai,[7] which searches the abstracts of papers to answer specific text-based questions and can support research scientists. Another is BioGPT,[8] which is a spin off from ChatGPT designed specifically for life sciences and produces more relevant biological text. Our own tool, TriloDocs,[9] combines a sector-specific language model with a core of expert rules to provide a set of "guiderails" and only interprets relevant information from clinical trial data in relation to specific best practice criteria.

It seems that the future of AI in the medical writing sphere may not be as stand-alone tools but rather within platforms that use it in the context of wider rules and other elements. Using AI tools in the medical writing space as more of a "walled garden" makes sense because of reluctance to upload intellectual property, personal data, or other sensitive information to open platforms, where data ownership and data protection are currently being debated. Regulatory authorities need to be confident in the accountability and traceability of raw data and documents supporting any claims. GDPR (General Data Protection Regulation), protection of commercially sensitive information, and "AI hallucinations", not to mention the specific context of medical writing, remain major concerns.

Like any technology, ChatGPT is just a tool. As with any tool, it is only as good as the person using it.

Nonetheless, language models are undoubtably powerful tools for creating authentic-looking texts from certain prompts, rewriting texts for different audiences (e.g., in other languages), and producing simplified summaries. Most medical writers would be delighted to pass on routine, mundane, and repetitive tasks to a computer, which can do them more efficiently, accurately, and quickly. This could liberate writers to concentrate on the highly skilled tasks of contextualising and interpreting clinical data and allow them to have meaningful data discussions with clinical teams much earlier than is currently possible. In the medcomms and medical journalism worlds, AI tools can help writers more quickly and accurately create time-sensitive documents and sift through huge amounts of literature.

What are the risks of AI?

We have already touched on some of the key risks involved in using AI. **Data privacy** is often the main risk that springs to mind. However, this is an inherent risk of any technology and not specific to AI. Some AI platforms present a risk of being internet-based. Also, "open" systems present a risk even in a non-AI context. Some emerging options allow developers to build a language model within a secure environment (although the training data are publicly available). How this develops in the medical writing arena will be interesting.

A well-documented downside of generic language models is "computer hallucinations", where a language model "makes up" information or cites references when it has no information.

Risk of errors. In our experience with TriloDocs, the risk of human error has been significantly reduced, if not eliminated. Important data that humans may miss are identified by the tool, and we have not yet found an issue raised during quality assurance that was not already identified by the technology. The problem of AI hallucination is a cause for real concern because there is no room for false data, inferences, or references when dealing with clinical and scientific data. The more niche platforms will have to specifically eliminate this risk, which may pose a significant challenge. From a medical writing perspective, a conservative approach is always best. Our experience is that it is better for the tool to highlight where something is missing or interpretations cannot be made, flagging data points for the medical writer to investigate rather than having a tool that produces a "complete" but misleading draft.

Other considerations include the **ethical debate** about AI, which is far outside the scope of this article. Jamie Bartlett,[10] a journalist and author specialising in technology and a regular speaker on the topic of futurism, has warned that only three things can be guaranteed about the future of technology: firstly, that data storage capabilities and demand will continue to grow at an exponential scale; secondly, that the processing power of computing will also continue to grow, which along with the ability to store huge amounts of data, has powered this latest AI revolution; and thirdly and most importantly, that human drives and behaviours will not change.

The limiting factor to AI is how we implement these tools and how ethically we can introduce checks and balances to manage them. There is almost an AI paradox playing out in front of us: We all want AI to help us to do our jobs better or at least take away the more menial parts of our work without replacing us altogether. Unfortunately for some, that choice will not be theirs to make.

The limiting factor to AI is how we implement these tools and how ethically we can introduce checks and balances to manage them.

What does all this mean for medical writers?

One thing we always stress when talking about our own platform, TriloDocs, is that it does not replace the medical writer. TriloDocs simply accelerates and enhances the writer's ability to have meaningful data discussions with the clinical team and speeds crafting of the report. We have not yet met anyone who actually enjoys trawling through data with a highlighter pen and interrogating tables for information; crafting a strong narrative around the data, however, is an entirely different proposition.

Highly skilled medical writers bring value as critical thinkers as they create study reports and related documentation. We are still some way off from the ultimate goal of AGI (Artificial General Intelligence), which moves AI into the realm of human-like thought. Until that point, critical thinking can only be done by humans. In the short time that tools like Chat CPT have captured our imagination, there is already an adage that describes where things could be going in the short term: AI might not take your job, but someone who uses AI will.[11]

AI is not going away – medical writers cannot influence that – but we can influence how we approach and use AI. If we view AI as a tool that can supplement our work, make us more efficient and accurate, and relieve us of some of the heavy lifting, then it can become a powerful resource, freeing us to focus on the more valuable work of critical thinking and crafting a strong narrative in our highly complex and vital work.

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Lisa Chamberlain James is a CEO of Trilogy Writing & Consulting Ltd. Following a PhD and postdoctorate at the University of Cambridge, in 2000, she began a medical writing career. She has since been involved in EMWA as a member of the Educational Committee, mentor, leader, and assessor of workshops, and she teaches and reviews workshops for the American Medical Writers Association. Lisa holds an EMWA Professional Development Certificate, is a visiting lecturer for Kings College, London, initiated and chaired the EMWA Pharmacovigilance and Communicating with the Public Special Interest Groups, is Chair of EMWA's Geoff Hall Scholarship Committee, Section Editor for *Medical Writing*, and a Fellow of the Royal Society of Medicine.

EMWA Future Conference

Virtual Conference

November 9–16, 2023

The EMWA spring and autumn conferences provide a medium for networking, active discussions, and extensive cost-effective professional training. They also provide a wealth of opportunities for participants to benefit from the experiences of other medical writers.

The venues, facilities, and training programmes are chosen to offer the best possible learning environment. In addition to the formal training sessions, a relaxed, friendly conference atmosphere provides for ideal networking opportunities and enables all those attending to meet medical writers and communicators at all stages in their careers.

Watch for news about in-person local hubs for the virtual conference!

https://www.emwa.org/conferences/future-conferences/

Introducing EMWA's new AI Working Group

Sarah Tilly[1], **Slavka Baronikova**[2], **Martin Delahunty**[3], **Namrata Singh**[4], **Claire Harmer**[5]

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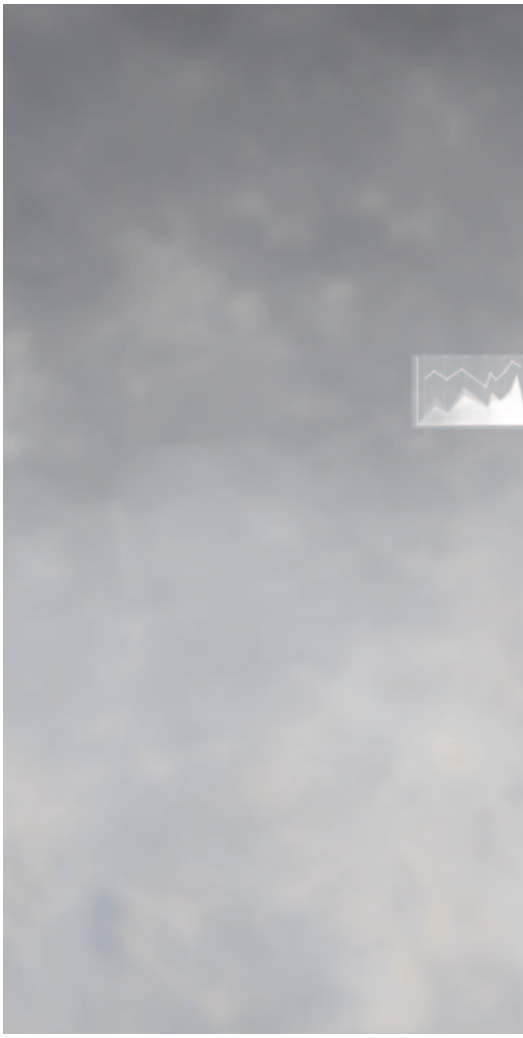
Abstract

Artificial Intelligence (AI) is a broad umbrella term that refers to the use of computer algorithms to perform tasks that typically require human-like intelligence, such as reasoning, learning, decision-making, and perception. The new EMWA AI Working Group, designed to keep our organisation abreast of AI developments in our industry, will initially focus on writing, editing, and analytical tools and include literature and data analysis. For the moment, the group will exclude image creation, and diagnostic and analysis tools. In this article, each member will answer some questions about our group and AI in our industry.



An interview with the members of the AI Working Group

Q1 What is the EMWA AI Working Group?

Sarah Tilly: The AI Working Group was formed at the May 2023 EMWA conference in Prague in response to the need to serve our members and ensure that EMWA stays ahead of the curve as this area rapidly evolves. The working group consists of four members: Sarah Tilly, Slavka Baronikova, Martin Delahunty, and Namrata Singh. We serve as a hub to liaise with EMWA Special Interest Groups (SIGs), organise activities and events regarding AI in medical writing, as well as serving as a voice for EMWA and our members to external bodies as regulations will undoubtedly develop in this field.

Q2 Why is an AI Working Group needed now?

Slavka Baronikova: Since the release of ChatGPT-4 at the end of 2022, most of us with even a slight interaction with social media and the news quickly realised that AI was no longer just for technical researchers and that it would soon impact, to a large extent, our professional lives (many now also realise how far AI had already subtly penetrated into the personal and professional realms). And we medical communicators are no exception. The sessions and exhibitors at the 2023 EMWA Spring conference in Prague gave insight on the need for understanding and education of our EMWA members on AI and its use and limitations. And so emerged the conception of the AI Working Group.

> One of the major fears … is whether AI tools will replace what medical writers are doing now.

Q3 What do medical writers understand about AI-powered tools and which ones are they using?

Martin Delahunty: A majority of medical writers have a level of understanding about AI-powered tools and most notably, ChatGPT. However, only a minority are using ChatGPT and related tools in their work. Examples of other tools mentioned by EMWA members include Triliodocs, Grammarly, Quillbot, Writefull, and Perfectit.

Q4 What are medical writers' fears about AI?

Namrata Singh: One of the major fears that the medical writing community faces is whether AI tools will replace what medical writers are doing now. Also, the writers are sceptical about the evolving skills that will be required to be

employable now and that certain routine tasks/activities that they had been working on recently might become redundant.

Q5 What activities does the AI Working Group plan over the next year?

ST: For the virtual conference in November 2023, we are planning an educational seminar, where our members can gain an excellent foundation on AI in medical writing, rewind a little and understand the difference between Deep Learning, large language models (LLM), and natural language generation (NLG), and start to get an idea of the do and do-nots that are being established regarding the ethical use of AI in each of the medical writing fields. At the May 2024 EMWA conference, in Valencia, Spain, we will have a full-day symposium on AI and automation where we will go into more depth. In between the conferences, we will be reaching out to understand your views and uses of AI, to liaise with external bodies, and we will begin to generate a framework within which medical writers can begin to feel more comfortable with embracing these tools whilst also understanding their limitations and risks.

Q6 What bodies are you connecting with to collaborate and to promote EMWA's voice in the use of AI in medical communication and writing?

SB: Use of AI in scientific and medical writing (including translation) is unavoidable, yet the do and do-nots still need to be established. EMWA connects with sister organisations such as The American Medical Writers Association (amwa.org) and International Society for Medical Publication Professionals (ismpp.org) as well as with publishers of scientific journals and Open Pharma (openpharma.blog) to ensure that EMWA maintains a presence in the field and can contribute to external activities.

> Medical writers who embrace AI will have a competitive advantage in the job market as they will be able to produce high-quality work in less time than their peers.

Q7 Do you think medical writers will need to use AI over the next 2 to 3 years?

MD: AI has brought significant changes in various industries, including healthcare. The medical writing field is no exception. AI provides an opportunity to automate certain tasks, reduce errors, and improve efficiency. The use of AI-powered tools will have a significant impact on medical writing, and medical writers who embrace AI will have a competitive advantage in the job market as they will be able to produce high-quality work in less time than their peers.

Q8 Are there specific needs for the different fields of medical communication/writing, such as scientific publications, regulatory, medical devices, etc.? How will the AI Working Group address these differences?

AI Working Group: Each area uses different AI tools for different needs. These include not only writing, editing and translation, but also data and literature analysis, and visual interpretation of scientific content. This field is evolving very quickly and the AI Working Group will initiate and continue discussions within the SIGs, as well as externally, and will debate this very important topic to bring to EMWA members the latest developments in the field. We will introduce the members to people who have an active voice in each field and who can share their learning and experiences.

Q9 How can medical writers prepare for the inevitable arrival of more automation and AI in our profession?

NS: First of all, medical writers have to acknowledge that we are in the midst of a revolution and we have to be open to the changes and adapt to a new way of working. It might yet take some time for these AI tools to become a part of our daily lives, but even now medical writers should engage in conversations with their peers and cultivate a curiosity to know more about the field, since at this time there are very few experts and most of us

are in the learning phase. Understanding the dynamics behind these tools, how they work, and how they can impact our day-to-day working is where we can start. The next important skill to work on could be how to create appropriate prompts because what the AI tool will provide will depend upon our questions. It is something like "Garbage in, garbage out", so to become friends with these tools we have to understand how they work and how we can get the best possible responses from them.

A word of caution at this stage: Medical writers have to ensure the correctness and accuracy of the information provided by these tools since they are known to "hallucinate", that is, provide inappropriate or incorrect answers sometimes.

Finally, medical writers need to be aware of the guidelines and recommendations which are coming up (keep an eye out for news from the AI Working Group) and always be responsible for the content, whether it is created with or without AI.

Q10 What can we learn from translators, who have already been through the transition of AI usage in their profession?

Claire Harmer, our guest translator: Translators have certainly had to embrace AI in order to remain relevant and competitive in the evolving landscape. Translation workflows have undergone immense change, with professionals often being asked to post-edit machine-generated translations rather than translating a text from scratch. Translators have had to become proficient at integrating AI tools such as translation memories and terminology management systems into their workflows, in order to improve productivity.

Some translators have decided to specialise in niche areas of medicine, where their expertise can add value beyond what AI can achieve. Others have focused on areas that require a greater degree of creativity and an understanding of nuance and impact, such as the translation of medical marketing materials and health campaigns.

Members of the AI Working Group

Sarah Tilly values the people with whom she writes in the same way she values the patients about whom she writes, and the customers for whom she writes. She believes that everyone has their own unique contribution to give to our industry, and this includes understanding how we can adapt to and embrace current trends and challenges. Sarah has been medical writing since 2006 in clinical research organisations and medical writing consultancies. She is Founder and Director of Azur Health Science, a small regulatory writing consultancy based in France. She holds a first degree in Biology, a PGCert in International HTA, Pricing and Reimbursement, and is studying for an MBA with a focus in Healthcare Management. She is the current EMWA president-elect.

Slavka Baronikova is Scientific Publications Head at Galapagos NV. She is trained clinical pharmacist with a PhD in pharmacognosy. For over a decade, she worked in the academic world isolating and testing active anti-cancer and anti-HIV compounds from medicinal plants, and teaching university students. In 2003, she moved to the pharmaceutical industry, mainly working in clinical research and then, later on, in the scientific communication field. Slavka has been an EMWA member since 2006, and has served as Conference Director since 2014 and is co-chair of the EMWA MedComms Special Interest Group. She is also an active member of the International Society for Medical Publication Professionals (ISMPP) and Open Pharma initiative.

Q11 How can medical writers reach out to the AI Working Group and for what purpose?

ST: We have established a liaison with each of the EMWA special interest groups (SIGs) so that the AI Working Group remains up-to-date and relevant to all our EMWA members. If you want to get involved, we suggest joining one of the many SIGs, so that you can have your say on ideas, activities, and educational events around the future of AI in our profession. Find out about the SIGs here: https://www.emwa.org/sigs/

> Some translators have decided to specialise in niche areas of medicine, where their expertise can add value beyond what AI can achieve.

Q12 How will the AI Working Group keep EMWA members informed of activities in the field?

AIWG: The AI Working Group will plan together with collaborating SIGs many AI related educational activities, starting with the 2023 EMWA November conference. We will inform our members via the usual EMWA channels – the EMWA website (Latest News, etc.), the monthly newsletter, social media posts, and articles in *Medical Writing*, as well as other channels.

Disclaimers

The opinions expressed in this article are those of the authors and not necessarily shared by EMWA

Disclosures and conflicts of interest

Martin Delahunty is a Director and shareholder of Inspiring STEM Consulting Limited, an independent publishing consultancy. All of his current and past client names are listed at www.inspiringSTEMconsulting.com and he may be subject to non-disclosure agreements.

The other authors declare no conflicts of interest.

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Martin is a former Global Director at Springer Nature with over 30 years experience in science publishing. He is a past Secretary and Board of Trustee Member of the International Society for Medical Publication Professionals and currently, a supporting member of EMWA's Medical Communications Special Interest Group.

Namrata Singh is a paediatrician and a medical writer. She is the founder and director at Turacoz Group about a decade back and works with industry and academic institutes to offer solutions to convey their scientific message to their target audiences. She has special interest in adapting to new technological advancements and mentoring aspiring medical writers. She has been an active EMWA member since 2014 and is currently chair of the Entrepreneurship Special Interest Group.

Claire Harmer works with public health organisations, medical journals, research institutes, and CROs to translate texts from French and Spanish into effective, clear, and compelling English. She also works as an English language editor and a project manager for translations into various other languages.

Diversity in clinical trials: It takes a village

Lorena Kuri, **Cathy Florek**, **Jateh Major**
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Abstract
Clinical trials are becoming more complex and the efforts to optimise drug development are rapidly evolving. This Q&A gives a short overview of the strategies Bristol Myers Squibb implements to incorporate diversity into the clinical trial development process with the intent to enhance equity and inclusion for the diverse patient community that uses the treatments we develop.

Q: Why is diversity in clinical trials important?
A: Diversity in clinical trials is a critical focus area in the pharmaceutical industry. The healthcare ecosystem around the world recognises the urgent need to address serious gaps in care among underserved communities to provide access to medicines to help patients prevail over serious diseases. As evidenced by the numerous webinars and presentations with FDA, diversity in clinical trials is both a social and a scientific imperative.

Recognising these challenges, Bristol Myers Squibb (BMS) aims to remodel multiple aspects of clinical trial design execution strategies, and the efforts to enrol patient participants through the company's diversity in clinical trials programme. The expectation is that doing so will positively impact a broader patient population, more reflective of the real world, and aligned with the epidemiology of the disease studied.

Q: Patient voice is important in enabling clinical trial diversity. How does BMS incorporate patient voice into the clinical trial protocol development process?
A: The BMS Clinical Trial Engagement Strategy Team's work focuses on bringing the patient's unique experiences, perspectives, needs, and priorities into the design and execution of clinical trials. As experts in what it's like to live with their condition, patients are uniquely positioned to help in the drug development process. Each disease affects a person differently based on gender, race, ethnicity, etc. Through our Patient Voice programme, we are able to talk with patients about their lived disease experiences and understand the potential barriers to clinical trial participation. The insights we uncover help us to make recommendations to our protocol development teams that can reduce the burden of trial participation and improve the overall patient experience. We are also able to learn how best to target outreach and engagement at the most favourable inflection points along the patient journey to support clinical trial awareness and participation in diverse populations.

Q: How do these insights obtained through Patient Voice impact the patient experience?
A: The insights from patients through the Patient Voice platform are used to drive change with the expectation of providing an improved experience for both patients and study sites.

Some of these are broadly applicable to a patient's overall clinical trial experience, and some are more specific to the clinical trial experience of a patient with a certain disease. BMS uses the research and learnings obtained from Patient Voice to make recommendations, build strategies, and implement actions to help make our clinical trials less burdensome to patients and sites. As an example, some Patient Advisory Board feedback has had an impact on reducing the site visit schedule and helping to create recruitment messages and materials that are culturally sensitive. Other protocol changes made based on patient feedback were around reduction of invasive biopsy procedures and changes to medication format to reduce the number of times per day patient needed to remember to take their pills.

> As we strengthen the collaboration among groups, we get to learn more about specific populations needs.

Q: What efforts have been made to build trust between underrepresented populations and BMS?
A: This is a multifactorial need, but to mention some strategies, we capture patient and caregiver insights through our diversity and inclusion framework. A disease may have varying severity and outcome based on patient characteristics such as gender, race, ethnicity, etc. BMS works with epidemiologists who serve as experts to help better understand the aggregate disease and patient outcomes.

In order to reduce barriers to enrolling diverse patients into BMS-sponsored studies, BMS is also committed to attracting diverse talent which will provide additional valuable perspective for diverse patient enrolment. In the case of clinical trials, we have created an internal People and Business Resource Groups (PBRG) Advisory Board that functions as an additional internal resource for feedback on patient facing materials and programmes. There are also sustainable relationships with community outreach groups and Patient Advocacy organisations. As we strengthen the

collaboration with the above groups, we get to learn more about specific populations needs.

Q: How has the position of health authorities evolved with respect to clinical trial diversity?
A: The need for greater diversity in clinical trials has been a key message from health authorities around the world for several years with the release of new International Council for Harmonization (ICH) guidelines on multi-regional trials and ethnic factors considered when assessing foreign data. More recently, the FDA has announced project equity with the goal of enhancing access to clinical trials for under-represented populations. Additionally, the FDA had released two guidances on enhancing clinical trial diversity populations (2020) and diversity plans (2022). Certainly, 2020 highlighted this imperative and ignited a more detailed assessment of an approach to enrolling diverse participants in clinical trials.

Q: What specific actions are being taken across BMS to ensure diversity in clinical trials standards meet regulatory expectations?
A: Diversity in clinical trials is a major focus for the company. Some of the key operational strategies include: assessing protocol language to identify ways to minimise barriers to enrolment; embedding study diversity plans as a natural step within the clinical development planning process; and engaging with diverse patient representative groups.

Q: How is BMS engaging with regulatory agencies around diverse clinical trial enrolment?
A: BMS is aligned with the FDA position that diversity in clinical trials is a necessary component of clinical trial execution. In order to ensure that BMS stays active in the conversation we are having study specific interactions with the FDA and engaging in non-asset specific conversations on this topic. Additionally, BMS is receiving feedback on regulatory documents that will further enhance our knowledge on the challenges to diverse enrolment so that we can implement strategies to address them.

Disclaimers

The opinions expressed in this article are the authors' own and not necessarily shared by their employer or EMWA.

Disclosures and conflicts of interest

The authors are employed by Bristol Myers Squibb.

Data availability statement

For inquiries about data and other supplemental information, please contact the corresponding author.

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Lorena Kuri has been leading the Diversity Strategy efforts for R&D at BMS since 2019. Before that, she spent several years in commercial roles in the pharmaceutical industry.

Cathy Florek has been with BMS for over 30 years, spending the majority of her time in R&D. She currently leads the Clinical Trial Engagement Strategy Team within Global Development Operations.

Jateh Major has been working in Regulatory Affairs Strategy for the past 6 years. He started his career at Merck, and joined BMS in 2020. Since then, he has been a key contributor and regulatory lead of the Diversity in Clinical Trials efforts for the company.

News from the EMA

The articles included in this section are a selection from the European Medicines Agency (EMA)'s News and Press Releases archive. More information can be found on the Agency's website: www.ema.europa.eu.

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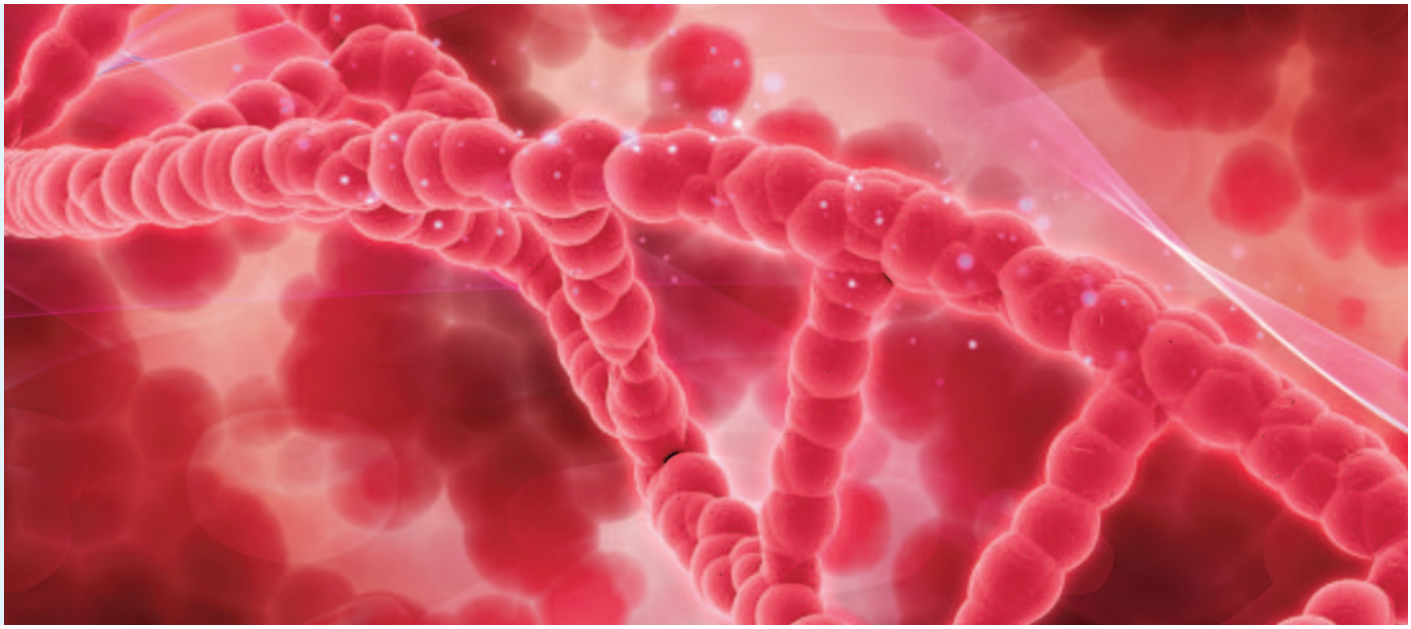


Photo: Freepik

EMA recommends revocation of authorisation for sickle cell disease medicine Adakveo

May 26, 2023

EMA's Committee for Medicinal Products for Human Use (CHMP) has recommended revoking the marketing authorisation for Adakveo (crizanlizumab), a medicine for preventing painful crises (called vaso-occlusive crises) in patients aged 16 years and older with sickle cell disease. The sickle cell disease is a genetic condition in which the red blood cells become rigid and sticky and change from being disc-shaped to being crescent-shaped (like a sickle). These cells can block the blood flow in blood vessels, causing painful crises that affect the chest, abdomen, and other parts of the body.

The active substance in Adakveo, crizanlizumab, is a monoclonal antibody designed to attach to a substance, P-selectin, present on the surface of the cells lining blood vessels. P-selectin helps cells stick to the blood vessels and plays a role in the clogging up of vessels during painful crises in sickle cell disease. By attaching to and blocking the action of P-selectin, the medicine helps prevent painful crises.

The CHMP reviewed results of the STAND study, which compared the effectiveness and safety of Adakveo with placebo (a dummy treatment) in patients who had previously had painful crises leading to a healthcare visit. The study showed that Adakveo did not reduce the number of painful crises leading to a healthcare visit. Patients treated with Adakveo had on average 2.5 painful crises with a subsequent healthcare visit over the first year of treatment, compared with 2.3 crises in the placebo group. In addition, the average number of crises requiring a healthcare visit or treatment at home was 4.7 with Adakveo compared with 3.9 with placebo.

In its review, the CHMP also looked at data from other studies, a managed access programme and real-world data. However, those studies had several limitations, such as the lack of a comparator, and could not be used to show the effect of Adakveo or counterbalance the negative results of the STAND study. In terms of safety, the STAND study did not raise new concerns but showed a higher rate of severe and serious treatment-related side effects for Adakveo compared with placebo. The CHMP therefore concluded that its benefits do not outweigh the risks.

At the time of marketing authorisation, data showed that Adakveo was effective at reducing the number of painful crises in patients with sickle cell disease. However, the data were limited and there was some uncertainty about the size of the medicine's effect. EMA therefore requested the STAND study as a condition for the marketing authorisation of Adakveo, which was granted in October 2020. As the STAND study results do not confirm the benefits previously seen with Adakveo, the CHMP has now concluded that the benefits do not outweigh the risks and recommended the revocation of its authorisation in the EU. The CHMP opinion will now be forwarded to the European Commission, which will issue a final legally binding decision applicable in all EU Member States.

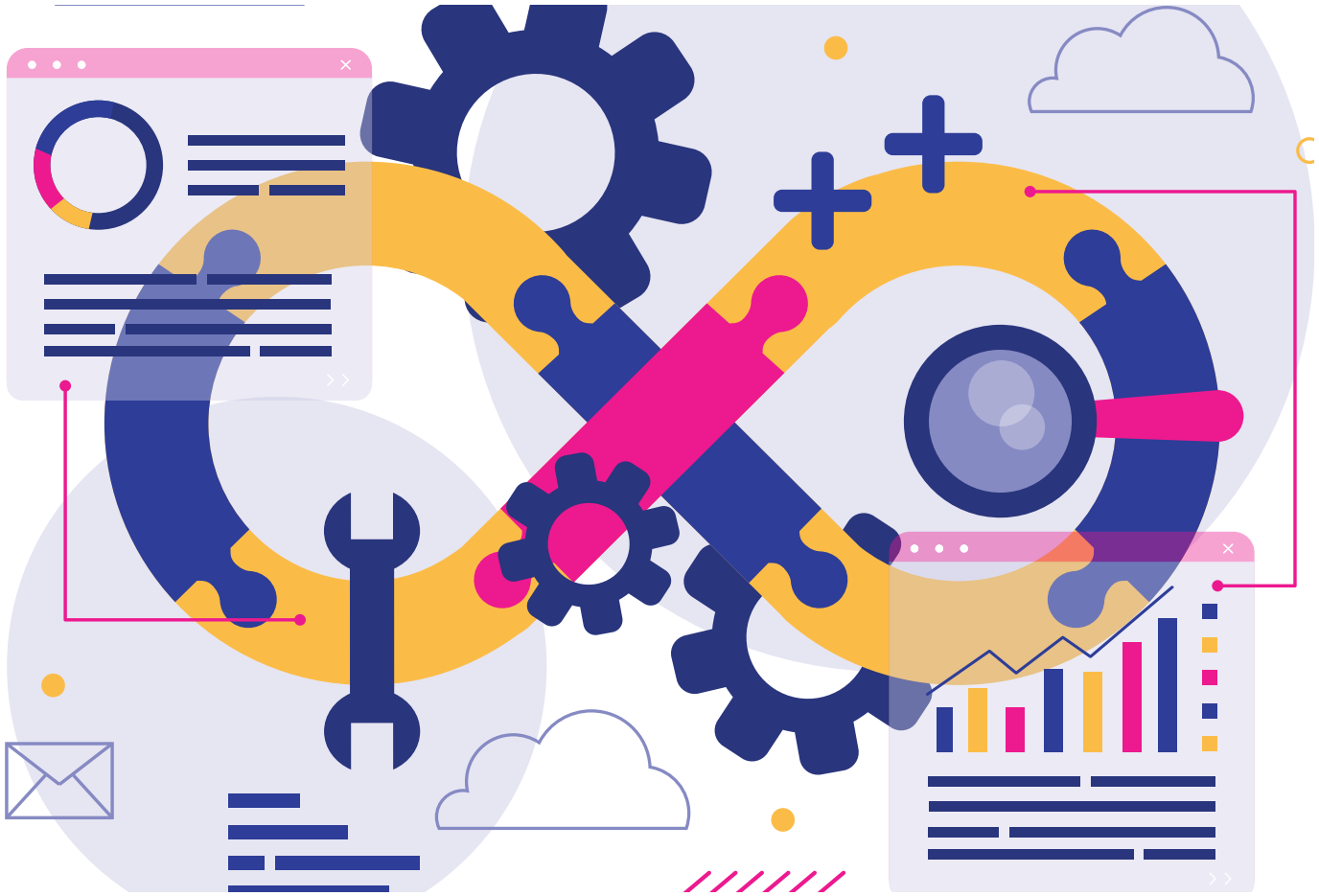


Photo: Freepik

OPEN framework extended to a wider range of medicines

July 20, 2023

EMA has expanded the scope of the OPEN initiative from COVID-19 vaccines and treatments to a wider range of medicines, such as medicines with the potential to address antimicrobial resistance (AMR), respiratory syncytial virus (RSV) infections, or newly diagnosed myelodysplastic syndromes (and other hereditary diseases).

OPEN was established by EMA in December 2020 as a framework to increase international collaboration and share scientific expertise on the evaluation of COVID-19 vaccines and therapeutics, initially as a pilot. All COVID-19 vaccines and therapeutics evaluated since the launch of the pilot were assessed under the OPEN framework. Participating non-EU experts attended and contributed to CHMP and EMA's Emergency Task Force (ETF) evaluations. OPEN allows regulators from Australia, Brazil, Canada, Japan, Switzerland, and the WHO to conduct near-concurrent reviews of certain new medicines and exchange their views and reports on the product assessments. This can help accelerate and align regulatory decisions in several regions in the world, leading to fewer questions for industry and more alignment on the product labelling, while maintaining regulators' independence in their decision making. The extension of the OPEN framework is based on the positive findings and recommendations highlighted in the report on the OPEN pilot.

The collaboration with WHO means that OPEN can also accelerate regulatory decisions and availability of medicines in low- and middle-income countries. Following the success of the pilot, the Agency's Management Board endorsed the expansion of the initiative in March 2022. The new extended scope of OPEN includes marketing authorisation applications for:

- medicines targeting AMR;
- medicines supported through EMA's PRIority MEdicines (PRIME) scheme, but currently not including advanced therapy medicinal products (ATMPs);
- medicines with the potential to address RSV infections or newly diagnosed myelodysplastic syndromes and other hereditary diseases; and
- medicines responding to health threats or public health emergencies.

The first product currently being assessed under the new OPEN framework is an mRNA vaccine against RSV, together with Swissmedic. Discussions are ongoing with OPEN partners on the selection of other products to be included in the OPEN framework. Medicines eligible for assessment under OPEN require CHMP and at least one OPEN partner to agree to conduct parallel assessments.

The dossier content/claimed indication and timing of submissions to both EMA and the OPEN partner(s) should also be aligned. The Agency will engage regularly with stakeholders as more experience is gained. Medicines assessed under OPEN will be clearly labelled in publicly available CHMP agendas and minutes, and on EMA's website. Further information is available in the updated Q&A document. EMA has bilateral agreements with all regulatory authorities involved in OPEN. Standard EMA requirements for EU experts participating in the assessment of medicines (e.g., confidentiality and absence of conflicts of interest) also apply to OPEN experts.

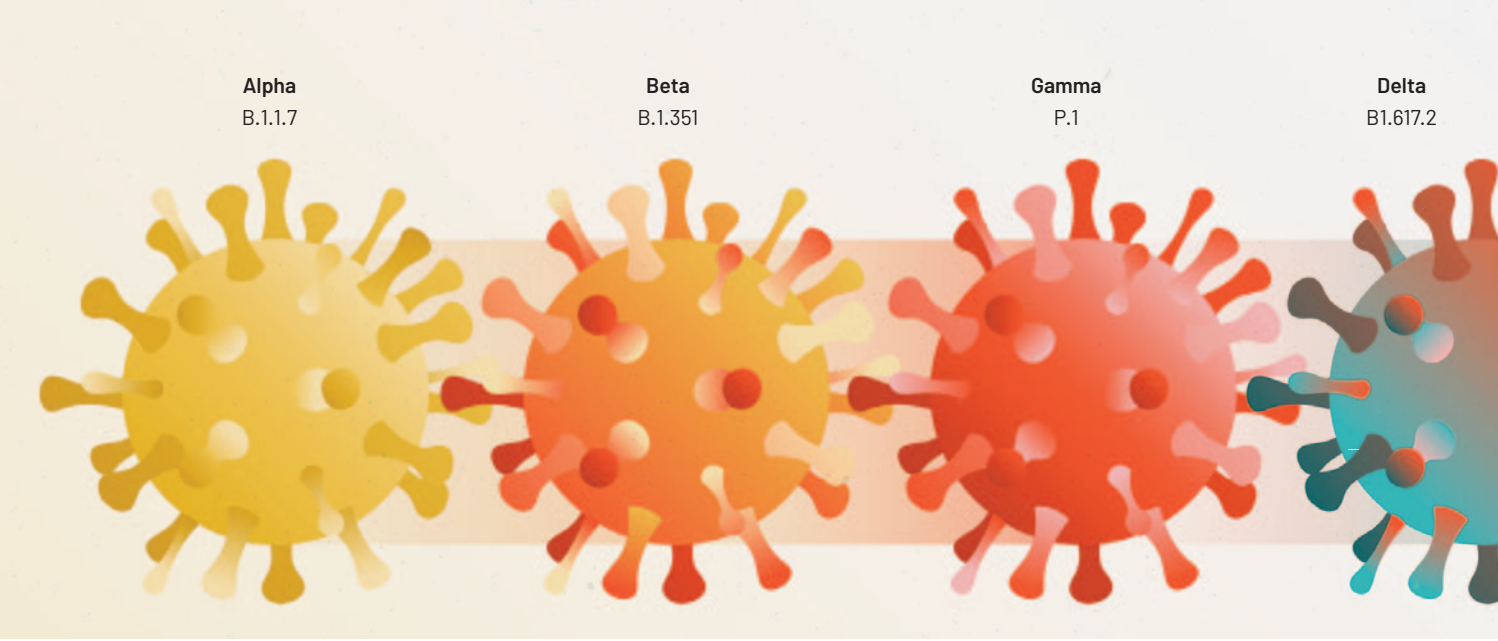
Global regulators agree on way forward to adapt COVID-19 vaccines to emerging variants

May 30, 2023

International regulators have published a report today highlighting the outcomes of their discussions on COVID-19 vaccines and the need for and strategy to update their composition based on the emerging evidence on coronavirus SARS-CoV-2 variants and lessons learned from previous vaccine updates. The workshop, co-chaired by the EMA and the US Food and Drug Administration (FDA), was organised under the umbrella of the International Coalition of Medicines Regulatory Authorities (ICMRA) and took place on May 8, 2023.

Currently authorised vaccines continue to be effective at preventing hospitalisation, severe disease and death due to COVID-19. However, protection against infection wanes over time and as new SARS-CoV-2 variants emerge. Preliminary data show that COVID-19 vaccines adapted to the currently circulating strains improve immunity to recently emerged variants, such as XBB descendent lineages.

Meeting participants discussed the available scientific evidence on epidemiology, seroprevalence (i.e., the number of persons in a population who test positive for a specific disease based on blood serum measurements) and vaccine performance, and key regulatory considerations related to the adaptation of authorised or new COVID-19 vaccines against emerging coronavirus variants. There is a broad agreement that vaccine formulations for the upcoming winter season in the northern hemisphere should include only one virus strain and be based on the XBB family of Omicron subvariants (such as XBB.1.5). International regulators also highlighted that such monovalent vaccines could be used for both booster and primary vaccinations (the latter, for example, only in young children



Phasing out of extraordinary COVID-19 regulatory flexibilities

July 6, 2023

EMA, the European Commission (EC) and the Heads of Medicines Agencies (HMA) are phasing out the extraordinary regulatory flexibilities for medicines put in place during the COVID-19 pandemic to help address regulatory and supply challenges arising from the pandemic. This follows the end of the COVID-19 public health emergency declared by WHO in May 2023.

The extraordinary regulatory flexibilities covered different areas, including marketing authorisation and related regulatory procedures, manufacturing, and importation of active pharmaceutical ingredients and finished products, quality variations, labelling and packaging requirements, and compliance. The EC, HMA, and EMA also agreed during the pandemic on a series of measures to mitigate the impact of disruptions caused by the public health emergency on inspections of manufacturing facilities or other sites relevant for medicinal products in the EU. The extraordinary flexibilities ensured the continued availability of medicines while making sure that good manufacturing (GMP) and distribution practice (GDP) standards were being adhered to.

From now on, the regulatory flexibilities that were introduced jointly by the HMA, EC, and EMA specifically during the COVID-19 pandemic should no longer be granted. For already approved labelling flexibilities, e.g., the English-only labelling for COVID-19 vaccines, their application will be extended until the end of 2023, in order to ensure a smooth phase-out and avoid any supply difficulties or other disruptions due to a sudden change in applicable requirements. After 2023, the regular mechanisms foreseen in the legislation in relation to labelling exemptions should be followed.

Concerning on-site GMP and GDP inspections, these have been restarted after being postponed or carried out remotely during the pandemic; however, a considerable number of postponed inspections still need to be carried out. The validity of GMP and GDP certificates has

below 4 to 5 years of age). They noted that only data on manufacturing and quality of the vaccine and laboratory data would be required for the authorisation or approval of strain changes for the already authorised COVID-19 vaccines, provided that post-authorisation data regarding vaccine quality, effectiveness, immunogenicity, and safety data are collected.

The meeting built on the experience and knowledge gained from a series of ICMRA workshops on COVID-19 vaccine development and virus variants held over the past three years. Participants included representatives of international regulators as well as experts from the World Health Organization (WHO).

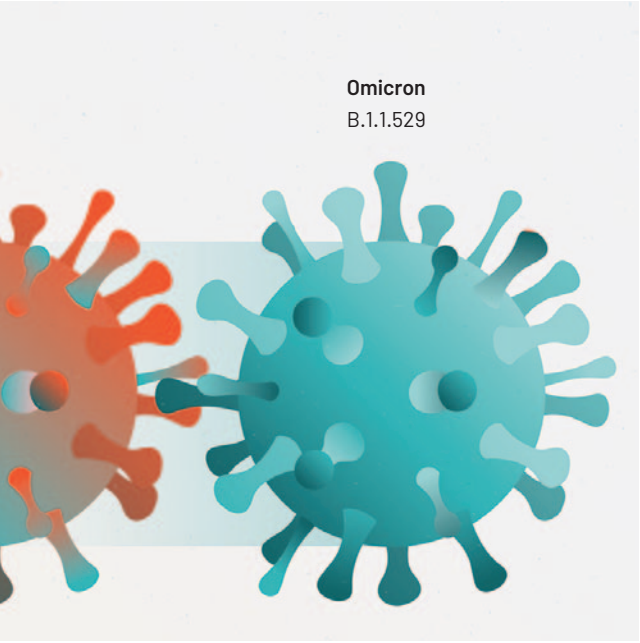


Photo: Freepik

currently been extended until the end of 2023, and the GMDP Inspectors Working Group will issue in the coming months an update on the approach for 2024. This Group has also reviewed experiences with remote working arrangements of Qualified Persons during the pandemic, and will issue guidance on how those specific arrangements can be applied in the future.

Experiences gathered during the application of the COVID-19 regulatory flexibilities are being collected by EMA's Executive Steering Group on Shortages and Safety of Medicinal Products (MSSG). They will consider how lessons learned can inform best practices for tackling medicine shortages in case of new and emerging health challenges in the future.

Reflection paper on the use of artificial intelligence in the lifecycle of medicines

July 19, 2023

EMA has published a draft reflection paper outlining the current thinking on the use of artificial intelligence (AI) to support the safe and effective development, regulation, and use of human and veterinary medicines. This paper, which is now open for public consultation, reflects on principles relevant to the application of AI and machine learning (ML) at any step of a medicines' lifecycle, from drug discovery to the post-authorisation setting.

The reflection paper is part of the joint HMA-EMA Big Data Steering Group (BDSG) initiatives to develop the European Medicines Regulatory Network's capability in data-driven regulation. It has been developed in liaison between the BDSG, EMA's CHMP, and its Committee for Veterinary Medicinal Products (CVMP). The HMA is a network of the heads of the National Competent Authorities (NCA) whose organisations are responsible for the regulation of medicinal products for human and veterinary use in the European Economic Area. The HMA co-operates with the EMA and the European Commission in the operation of the European medicines regulatory network.

AI and ML tools have the potential to effectively support the acquisition, transformation, analysis, and interpretation of data across the medicinal product lifecycle. Their application can include, for example, AI/ML modelling approaches to replace, reduce, and refine the use of animal models during the preclinical development. In clinical trials, AI/ML systems may support the selection of patients based on certain disease characteristics or other clinical parameters; AI/ML tools can also support data recording and analyses which will in turn be submitted to regulators in marketing-authorisation procedures. At the marketing-authorisation stage, AI applications include tools to draft, compile, translate, or review data to be included in the product information of a medicine. In the post-authorisation phase, such tools can effectively support, for example, pharmacovigilance activities including adverse event report management and signal detection.

This range of applications brings with it challenges such as the understanding of the algorithms, notably their design and possible biases, as well as the risks of technical failures and the wider impact these would have on AI uptake in medicine development and health. The reflection paper highlights that a human-centric approach should guide all development and deployment of AI and ML. The use of AI in the medicinal product lifecycle should always occur in compliance with the existing legal requirements, consider ethics, and ensure due respect of fundamental rights. If an AI/ML system is used in the context of medicines' development, evaluation, or monitoring, and is expected to impact on the benefit-risk balance of a medicine, EMA advises developers to seek early regulatory support, e.g., through qualification of innovative development methods (for human medicines) or scientific advice.

All interested stakeholders are invited to comment on the draft reflection paper and to identify opportunities and risks of AI in the field of medicines. The public consultation is open until December 32, 2023, and the topic will be further discussed during a joint HMA/EMA workshop scheduled for November 20-21, 2023. The feedback from stakeholders will be analysed and considered for the finalisation of the reflection paper and future development of guidance as relevant.

First RSV vaccine to protect infants up to 6 months of age and older adults

July 21, 2023

EMA has recommended granting a marketing authorisation in the European Union (EU) for Abrysvo, a vaccine to protect against disease caused by the respiratory syncytial virus (RSV). Abrysvo is the first RSV vaccine indicated for passive immunisation of infants from birth through 6 months of age following administration of the vaccine to the mother during pregnancy. This vaccine is also indicated for active immunisation of adults aged 60 years and older.

RSV is a common respiratory virus that usually causes mild, cold-like symptoms but it can cause serious consequences for children and older adults. In fact, in children RSV is a leading cause of paediatric hospitalisation in Europe. It may cause bronchiolitis and pneumonia and can lead to fatal respiratory distress. RSV infection can also be serious for adults aged 50 years and older as it can cause acute respiratory infection, influenza-like illness, or community-acquired pneumonia.

Abrysvo is a bivalent vaccine composed of two recombinant RSV fusion surface glycoproteins selected to optimise protection against RSV A and B strains. These proteins are essential for RSV to infect the body and are also the main targets of the antibodies generated to fight the infection.

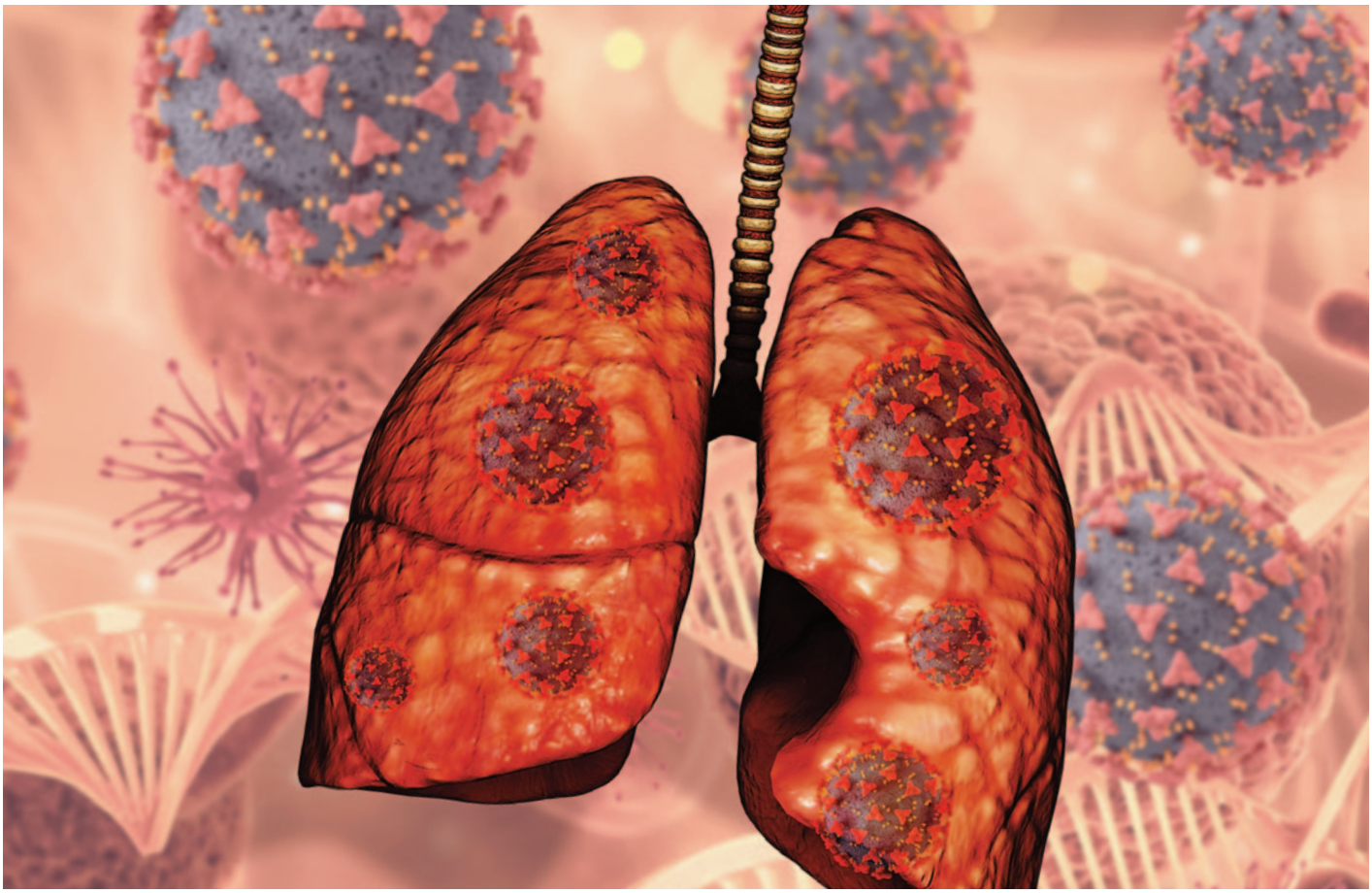
Abrysvo was evaluated under EMA's accelerated assessment mechanism because prevention of RSV disease is considered to be of major public health interest. When a person is given the vaccine, their immune system generates specific antibodies and T cells (immune system cells) that help prevent RSV infection. In case of pregnant individuals, the neutralising antibodies cross the placenta, providing infants with protection up to 6 months after birth.

The opinion by EMA's CHMP is based on data from two randomised, placebo-controlled, pivotal studies. In one study, 3,695 women at 24-36 weeks of pregnancy were administered Abrysvo while 3,697 received a placebo (dummy injection). The assessment showed that the vaccine was effective in reducing both severe medically attended lower respiratory tract illness and medically attended lower respiratory tract illness occurring within 180 days after birth.

In the other study, 18,488 adults aged 60 years and older were administered the vaccine, while 18,479 received a placebo. The results of the study demonstrated efficacy for Abrysvo in the reduction of RSV-associated lower respiratory tract illness with 2 (or more) symptoms and with 3 (or more) symptoms.

The most common side effects reported in individuals between 24 and 36 weeks of pregnancy were vaccination site pain, headache, and muscle pain. In individuals 60 years of age and older the most frequently reported side effect was vaccination site pain.

The opinion adopted by the CHMP is an intermediary step on Abrysvo's path to patient access. The opinion will now be sent to the European Commission for the adoption of a decision on an EU-wide marketing authorisation. Once a marketing authorisation has been granted, decisions about price and reimbursement will take place at the level of each Member State, taking into account the potential role/use of this medicine in the context of the national health system of that country.



Don't miss!

The June 2024 edition

Soft Skills for Medical Writers

Medical writing is a highly specialised field that requires a unique combination of technical knowledge, writing skills, and soft skills to produce high-quality work. While technical knowledge and writing skills are undoubtedly important, it is how one interacts with people that can truly set medical writers apart and enable them to succeed in their careers. This issue will focus on how soft skills are used within the different areas of the medical writing industry, and we hope it will provide valuable insights and inspiration for medical writers at all stages of their careers.

Guest Editors: Clare Chang and Nicole Bezuidenhout
The deadline for feature articles is March 1, 2024.

Digital Communication

Editorial

Collaboration has always been a cornerstone of medical writing. However, how we collaborate has undoubtedly changed in the digital age. Sophisticated online communication and collaboration tools make it much easier to connect with colleagues around the world to work together on multidisciplinary, international projects. By now, we are all quite familiar with cloud-based applications like those from Google Suite and Microsoft 365.

Their tremendous contribution to improving productivity and efficiency in our project teams is similarly well-recognised, especially when it comes to co-authoring documents. With the recent boost in the development of AI technology and applications suitable for medical writing, we are excited to learn more about how AI will once again reform how we author, communicate, and collaborate online. My colleagues from TFS HealthScience shed light on a next-generation AI tool from Microsoft that could take our collaboration and authoring activities to the next level. I hope you enjoy learning about this new technology as much as I did.

Nicole

SECTION EDITOR

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Embracing artificial intelligence in medical writing: A new era of efficiency and collaboration

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Artificial intelligence (AI) tools have already shown great promise in improving the workflows of key tasks and processes within medical writing,[1-4] freeing up time for us humans to focus on those unique abilities AI cannot replace…yet. At the top of the list are critical thinking, analytical skills, emotional intelligence, and creativity. More than that, we can harness those abilities to collaborate in multidisciplinary, international teams to create innovative and apt solutions – an integral part of our daily work as medical writers, particularly in joint tasks such as co-authoring. Indeed, digital collaboration tools for project teams are abundant (e.g., Google Suites, Asana, and Microsoft Teams) and have transformed the way we work,[5] especially now that remote work has become the norm. Nevertheless, collaborative technology using AI appears to be lagging slightly behind in the new wave of AI tools suitable for medical writing. With the application of emerging technologies and AI on the rise, the potential for automating the collaborative medical writing experience looks promising.

What is artificial intelligence?

AI is a general term describing computer systems with the ability to model human intelligence. It is a broad field that encompasses many different subfields, including machine learning and natural language processing, all of which are now widely recognised terms that have generated much interest in recent years. The idea of creating intelligence is, however, not new; it has fascinated people for centuries and is mentioned in Greek mythology and the famous novel about Frankenstein's monster, originally from 1818.[6–8]

Put simply, AI is the creation of a system that uses algorithms to perform tasks that would normally require human intelligence, such as visual and speech recognition, decision-making, and language processing.[9] In certain cases, it even outperforms humans, including the pace at which humans can operate and process information. AI's strength is its ability to collect big data, analyse them, identify patterns, learn from them, and extract an output without any human intervention. Its weakness (or one thereof) is its ineptitude in performing uniquely human abilities,[10] which are essential in medical writing.

The progress of more advanced AI technologies alongside increased computational power has fuelled explosive development within the field. With the release of ChatGPT by OpenAI in November 2022, the term "large language model (LLM)" has become widely used when talking about AI. As a generative pre-trained transformer (GPT), ChatGPT has been trained on a vast amount of text data so that when provided with text, it uses algorithms and statistical models to analyse the words and their relationships with one another. The model then predicts what comes next based on its learnings from the data on which it was trained.

> The total number of articles containing the term "artificial intelligence" is already much higher than several other hot topics in recent years.

ChatGPT, quite impressively, reached over one million users in just five days and 100 million monthly active users in two months after its launch, making it the fastest-growing consumer application in history.[11,12]

AI is steadily making its way into many areas and fields, as illustrated by the number of papers published in PubMed with the term "artificial intelligence" (Figure 1). Though the first paper was published as early as 1951, development in the field has been very rapid in the last five years, with approximately 200,000 articles (and counting) spanning the field of medical research published today. Interestingly, the total number of articles containing the term "artificial intelligence" is already much higher

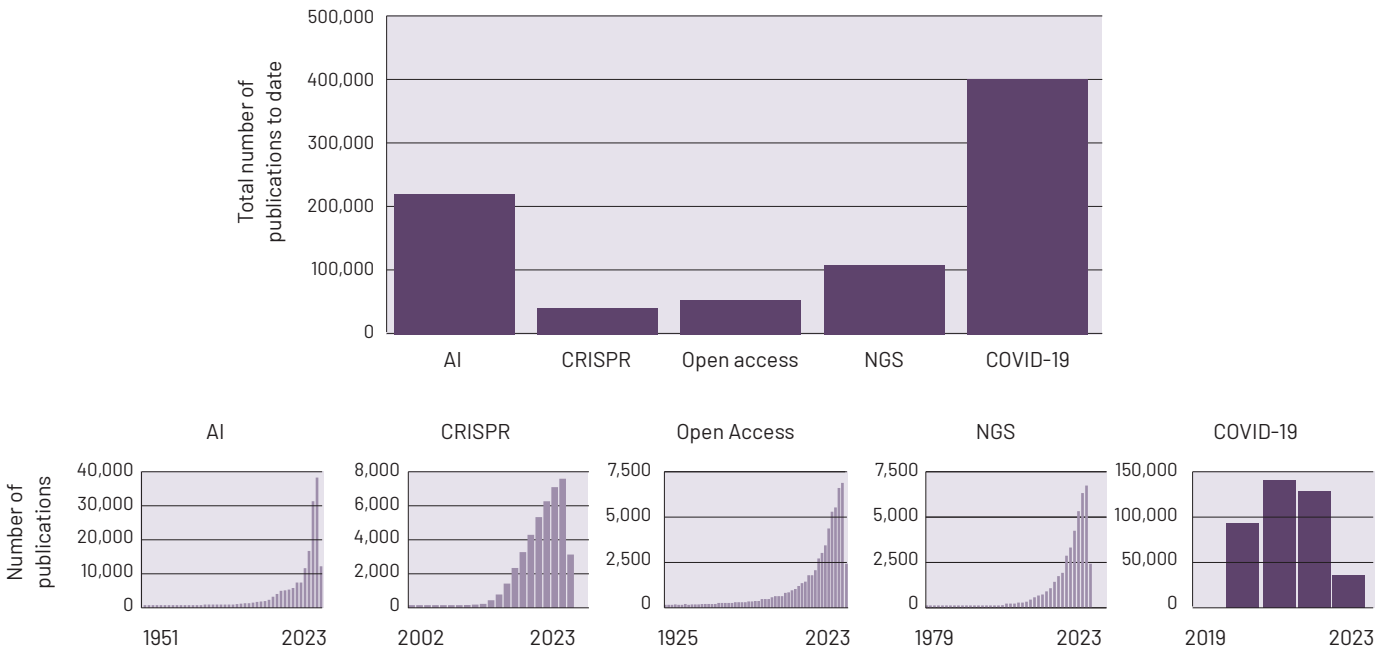

Figure 1. A comparison of the number of publications on PubMed among different "hot topics" in the medical/scientific field and artificial intelligence

Abbreviations: AI, artificial intelligence; CRISPR, clustered regularly interspaced short palindromic repeats; NGS, next-generation sequencing; COVID-19, coronavirus disease 2019.

than several other hot topics in recent years, including open access, clustered regularly interspaced short palindromic repeats (CRISPR), and next-generation sequencing (NGS), none of which come close to the search results for coronavirus disease 2019 (COVID-19) (Figure 1).

What can AI do for medical writers?

Given the complexity and variety of tasks involved in medical writing, it is highly advantageous that AI can assist medical writers in a number of ways (Figure 2).[1–4] However, AI support for tasks like collaboration is not available on quite the same level yet.

Tracking progress, managing deadlines, and communicating with colleagues form a significant part of a medical writer's repertoire. These activities not only make it easier to work together on large-scale projects, but doing so effectively is also critical to the success of such projects. Digital communication tools and channels, in particular cloud-based applications (apps) such as Microsoft 365 SharePoint, OneDrive, and Teams, are standard in our industry and have proven exceptionally useful in facilitating these activities.[13] Similarly, co-authoring or collaborative authoring of documents is powered by cloud-based apps to improve productivity and efficiency, as the demand for a quick turnaround of high-quality documents continues to grow, to support the rapid pace at which new therapies are being developed. It is, therefore, no surprise that AI technology is being integrated into cloud-based apps to optimise and personalise the digital communication and collaboration experience.

Collaborative authoring of documents is powered by cloud-based apps to improve productivity and efficiency, as the demand for a quick turnaround of high-quality documents continues to grow.

A look into Microsoft 365 Copilot

Microsoft provides some of the most popular authoring, communication, and collaboration apps – most of which we, as medical writers, use daily (Figure 3). So, one could say it was inevitable that this tech giant would develop AI technology suitable for enhancing the medical writing experience. In March 2023, Microsoft announced its next-generation AI tool, Microsoft 365 Copilot.[14] Though not yet available on the market, it has the potential to take the use of their tools/apps and our co-authoring and productivity to the next level.

This AI assistant is powered by the advanced LLM GPT-4 and works in tandem with Microsoft Graph – an application programming interface that gives developers access to a broad spectrum of Microsoft 365 services. With this unique combination, Copilot can enhance the user experience for Microsoft 365 apps, making them more intuitive and user-friendly. One could think of it as having a ChatGPT built into – what is for many medical writers – our normal digital work environment with the apps we use every day. However, according to Microsoft, Copilot is even better than that.[15,16]

The typical Microsoft 365 user tends to use only a limited number of available features and functions across the various apps – a limitation brought about by the demand for users to be technologically savvy and the time it takes to develop the necessary know-how. The implementation of Copilot aims to improve accessibility to a wider range of functionalities by providing the possibility to write prompts to guide Copilot's task performance. Since Copilot performs tasks based on simple text input, users will no longer need advanced knowledge or skills

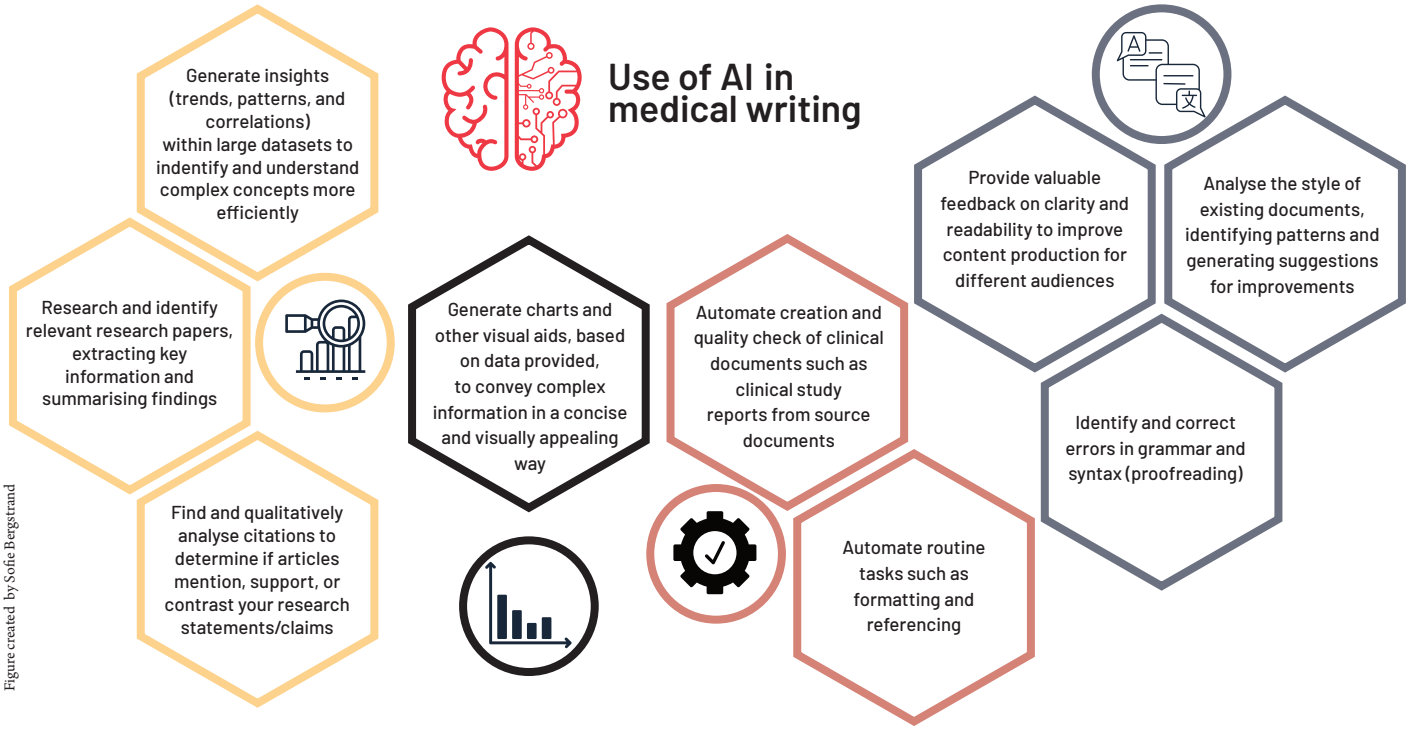

Figure 2. A selection of AI features suitable for medical writing

to use the Microsoft 365 apps to their full potential. This could facilitate a smoother onboarding experience for novice users and provide speed and even more functionality to advanced users.

For medical writing professionals, the features offered by Copilot could be very useful across several popular apps (Figure 3).

Word

With the integration of Copilot in Microsoft Word, users can instruct Copilot to generate a first draft or a document structure complete with headings and subheadings. This draft can be sourced from information available on the internet, used to train GPT-4, or from local documents. For instance, to generate an abstract for a review article, users can simply request Copilot to "write a 300-word abstract summarising document X," and within seconds, a draft will be produced, providing a starting point for the writing process. Similarly, Copilot can be asked to "write a 150-word paragraph about topic X" after which it will provide text based on the data used to train the model.

> Since Copilot performs tasks based on simple text input, users will no longer need advanced knowledge or skills to use the Microsoft 365 apps to their full potential.

Excel and PowerPoint

The use of Copilot in Microsoft Excel and Microsoft PowerPoint exemplifies well the easy unlocking of features through which users can, for example, prompt Copilot to "present the data in sheet X in a pie chart using different shades of blue" or "present the information in document X in a PowerPoint presentation". Even if these prompts do not generate perfect results, users can modify their prompts, try again, and quickly end up with something that can be edited, instead of starting from scratch and doing everything manually.

SharePoint, OneDrive, and Teams

The Microsoft apps OneDrive, SharePoint, Teams, and to a lesser extent, Outlook, offer many useful solutions for document sharing, meeting, and chat functionality. Adding Copilot on top of these will enable functions such as:

- Summarising long email threads and quickly drafting suggested replies
- Automatically producing meeting notes after Teams calls with summaries of key discussion points
- Easily drafting project updates from meeting notes and email conversations

Copilot is currently being tested by selected business clients and in an invitation-only paid preview version.[17] In an article by Microsoft in May 2023, the corporation announced that they have broadened access to Copilot from 20 to 600 enterprises worldwide and added several new capabilities, including Copilot in Outlook, Copilot in OneNote, and Copilot in Viva Learning.[18] Additionally, they have released new data, presenting their findings from a survey of 31,000 people in 31 countries.[19] The data highlight the exponential pace and volume with which work has increased, and the eagerness from business leaders and employees for AI to help lift the burden.[19] It will be exciting to see how well it works and how easily it can be integrated with our workflows.

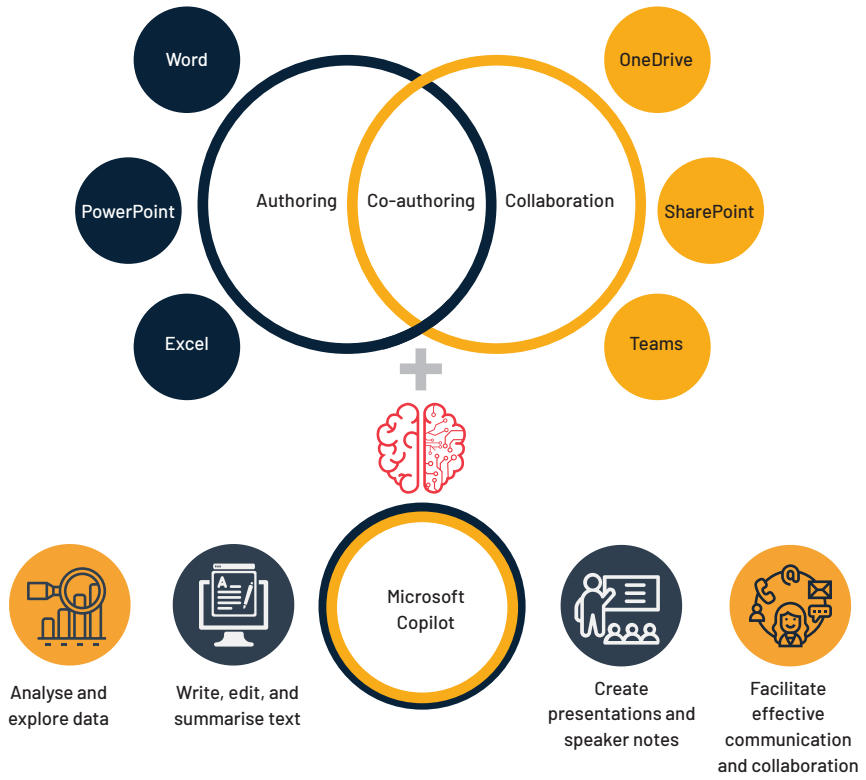

Figure created by Sofie Bergstrand

Figure 3. How Microsoft Copilot can take co-authoring to the next level

Challenges with using AI tools in medical writing

With the possibility of integrating AI technology with our everyday digital tools, it is important to consider the long list of challenges that might arise with their use, of which privacy, confidentiality, and accuracy are at the top.

Legislation and regulation, especially in highly regulated industries like healthcare, pharma/biotech, and by association, medical writing, are major concerns. Authorities such as the EMA, the FDA, and the Medicines and Healthcare products Regulatory Agency (MHRA), are all keeping a close eye on developments within the AI field.[20-22] The liability and accountability of AI-generated text and their platforms are still uncertain, and compliance with regulations and standards must be ensured. Confidentiality is a particularly sensitive topic since many of the AI services available use input data to keep training the model, which becomes problematic when working with confidential material.

As LLMs generate text based on already existing text without providing sources, plagiarism comes into play as well. These very valid concerns have already led to reactions within the publications community.[23] For instance, ChatGPT has been banned as a co-author of scientific papers, and many publishers are requesting that authors clearly state if and how they have used AI tools in their writing.[24] ChatGPT was also banned by Italy's Data Protection Authority in Spring 2023 when the agency complained about the lack of a legal basis to justify the collection and storage of data.[25] As addressed by the WHO, it is also important to keep ethical considerations, such as patient safety, inclusivity, and equity, in mind when developing and using these tools.[26] It is clear that this rapid technological development leads to difficulties in establishing laws and regulations to accompany the timely use of AI tools and services in a "safe" way.[27]

Another important, inherent challenge is quality control. The accuracy and reliability of AI-generated text depends on the quality and quantity of data used to train the model. If the model is not trained on sufficient, relevant, and diverse data, it may generate inaccurate or misleading information.[28] This concept of answering convincingly but inaccurately is called hallucinating;[29] and was exemplified in a study[30] which showed that four out of five ChatGPT-generated articles were found to be significantly inaccurate. All of them were, however, written with convincing and coherent language, making it difficult to spot errors for non-expert readers.

In contrast, another study[31] showed that ChatGPT was able to answer questions within a wide range of medical fields accurately. This shows that LLMs can generate accurate content, but there is also a high risk of inaccuracies making their way into the text. It should be noted that due to the underlying technology, LLMs are language models, not knowledge models.

Favourably, Microsoft, in its development of Copilot, has taken care to address some of the above concerns. According to their blog, they "are guided by their AI principles and Responsible AI Standard and decades of research on AI, grounding, and privacy-preserving machine learning".[32] Their Responsible AI Act[33] and Microsoft Privacy Statement[34] are additional guides to developing trustworthy AI technologies for their users. As an example, they state that their AI tools will be run locally on the user's device, meaning that no data contained within the documents of a user can be leaked to other users.

Unlike Copilot, ChatGPT is open to the public free of charge because it is in its research and feedback-collection phase. In an article by ChatGPT,[35] the chatbot argues that stringent oversight and regulation of LLMs might "stifle innovation and prevent the technology from reaching its full potential". However, it recognises

the importance of having safeguards in place "to prevent the technology from being used for nefarious purposes," and suggests that a regulatory body that would work closely with the developers and users of the technology should be established specifically to oversee the use of LLMs and ensure responsible use.[35]

OpenAI is also taking steps towards addressing these concerns and has implemented an option for users to prevent their input data from being used to further train the model. A ChatGPT Business version is also planned, which will be a paid subscription allowing users more control over their data.[36] Regarding accuracy and hallucination challenges, for now, it will be up to us users to keep this phenomenon in mind and check that the content generated is factual. However, it is likely that this will also be improved with further technological developments.

Future perspectives

It is still early days, but AI really does have the potential to revolutionise the way medical writers work. As a supporting tool, AI can help to optimise our productivity and efficiency, whilst we channel our uniquely human insights and expertise to collaborate and generate high-quality content. Nonetheless, our ability to adapt to, collaborate with, and incorporate AI in our medical writing practices will play a significant role in maximising its potential benefits. Integrating AI technology into apps with which we are already familiar and trust will aid in this transition. Ongoing research and development are further needed to ensure the accuracy, fairness, and reliability of AI-generated medical writing, as well as regulatory and legal frameworks to govern its use. With the responsible use of AI, we are heading towards an exciting future in which our role as medical writers will evolve alongside the evolution of AI technology.

Disclaimers

The opinions expressed in this article are the authors' own and not necessarily shared by their employer or EMWA.

Disclosures and conflicts of interest

The authors declare no conflicts of interest.

Our ability to adapt to, collaborate with, and incorporate AI in our medical writing practices will play a significant role in maximising its potential benefits.

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Medical Communications and Writing for Patients

Editorial

Dear all,

In this edition of *Medical Writing*, we have a report from the inaugural "Meet & Share" session from the Communicating with the Public Special Interest Group (CwP SIG). EMWA's SIGs host these sessions throughout the year, encouraging open and honest discussion between medical writers on a variety of topics (identified and advertised ahead of the session). EMWA is an incredible community with a lot of very experienced and talented medical writers who never cease to amaze me with their generosity of time and advice, so I strongly encourage you to look out for the Meet & Share sessions and get involved!

For its first meeting, the CwP SIG held an open forum to introduce the new SIG, explain what writing for the public means, offer examples of the areas medical writers can explore and be involved in, and then answer any questions that the attendees might have. The objective of the session was to formally introduce the SIG, to share its objectives, and to get input from the attendees to help refine our aims. The key topics discussed at the session are summarised in the excellent report from Sampoorna Rappaz, a member of the SIG.

I hope that you enjoy Sampoorna's article as much as I did, and in the meantime, stay safe and sane – enjoy the sunshine (if you have any!), and see you in the December issue!

Bestest,

Lisa

SECTION EDITOR

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Introducing a new EMWA Special Interest Group: Communicating with the Public

A report of the group's first Meet and Share

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The Communicating with the Public Special Interest Group (CwP SIG) held its first Meet and Share session as an open interactive forum on October 25, 2022. The session consisted of presentations by SIG Chair Lisa Chamberlain James and panellists and SIG volunteers Sara Ferrão, Adeline Rosenberg, and myself, followed by a thought-provoking discussion with an audience of about 30 attendees. Lisa introduced the SIG and was the session moderator. The panellists gave a brief overview of the types of public-facing documents, spread across the main specialisations within medical writing, that a professional medical communicator could be expected to develop. The objective of the session was to formally introduce the SIG, to share what we want to do, and to get input from the audience to help refine our aims. The key topics discussed at the session are summarised below.

CwP SIG's main goals

The main goals of the CwP SIG are:

- To educate and inform EMWA members about the crucial and expanding field of medical writing that is "communicating with the public". It requires a specialised skill set and a more nuanced understanding of the audience than that required for other types of medical writing.
- To engage with regulatory agencies to highlight the importance and value of trained medical communicators when developing public-facing materials.
- To interact with patient advocacy groups and specialists to highlight the added value, in terms of scientific and communication know-how, that medical communicators can bring.
- To involve industry colleagues from other departments (for example, patient centricity, public relations) to create awareness about plain language writing and the advantages of engaging a trained medical communicator for their deliverables.

Communicating in plain language is a widely useful skill

Apart from developing clinical study-related documents solely meant for regulators, regulatory writers also need to be able to communicate complex details about the clinical study to study participants, who are most likely to be non-specialists and thus would need text written in plain language and simple graphs. Some of the regulatory documents that would require plain language writing skills include the information consent form, the lay summary of clinical study results, the product information leaflet (or package insert), and the summary of safety and clinical performance (for a medical device). These documents must be prepared following the guidelines and regulations stipulated by regulatory agencies and ethics committees. The Declaration of Helsinki mandates that clinical study results must be made accessible to the public,[1] but accessibility implies more than being just made available on an online portal; it implies making results understandable and usable. Effective plain language writing in regulatory documentation can help improve patient recruitment, engagement, and understanding.

In scientific communication, there are two major kinds of plain language documents that can be developed in association with a primary manuscript. One is a brief jargon-free summary

of a peer-reviewed publication called publication-associated plain language summary (PLS). It is embedded either within the main manuscript or in the supplementary materials. Concise, text-only PLS can be indexed on PubMed. The other is a standalone, secondary publication called the plain language summary of publication (PLSP), which is often developed for a patient audience (and can include the patient perspective and patient-authors). Currently, PLSPs are published by Future Science Group journals. Visual communication deliverables associated with a manuscript, such as slide decks, graphical abstracts, and video abstracts, would also be more effective if presented in a simplified and clear format.

Medical journalism, also called health journalism, involves communicating medical news, research, and scientific advances to the public. While medical writers engaged by clients to craft news reports or press releases cannot call themselves journalists (as journalists must be truly objective and without a shadow of a conflict of interest in their reporting), they can become independent science journalists or writers by learning journalistic writing techniques. These medical writers, like traditional medical journalists, can then write for newspapers, consumer publications, e-zines, radio, and television. Rigorous medical writing with a journalistic style would improve the quality of the medical and health content on the internet, social media outlets, and mass media. Journalistic writing has many uses within the regulatory writing and medical communications landscapes: crafting clinical study backgrounders, Q&A, study newsletters, spokesperson bios, slide decks on study, press releases, website content, reports (like this one!), blogposts, newsletters, social media posts, feature articles, profiles and interviews, infographics, and a myriad of patient-facing material (print and online).

Medical editors specialising in plain-language editing and fact-checkers with training in how news organisations fact-check content also play a crucial role in ensuring that the information being communicated to the public is trustworthy, i.e., the content is relayed truthfully and the sources are reliable and competent. Therefore, medical editing (that focuses on audience, purpose, coherence, and clarity) and fact-checking (that focuses on accuracy, precision, compliance, consistency, and completeness) are the final two critical pieces that solve the "communicating with the public" puzzle to produce a balanced, understandable, and useful document.

Role of the medical communicator

Following are some of the actions a medical communicator must take when developing a document meant for the public:

- Understand, use, and advocate for plain language writing
- Provide assurance of the credibility, quality, and compliance of plain language documents
- Manage expectations about differences between scientific writing and plain language writing
- Understand and implement health literacy principles
- Implement workflows that make fact-checking easy and efficient

Challenges faced when writing for the public

The problems encountered when assessing and developing deliverables for the public were the major focus of the discussion that followed the presentations. Some of the general issues raised were: ethics, appropriateness, and usability of patient and public involvement (PPI) in healthcare research; lack of formal assessment of readability of lay language summaries; and "spinning" and the wrongly implemented notion of "fair balance" in medical journalism. The specific challenges when it comes to writing for the public include: precision in cross-cultural translation of lay language summaries; determining the readability of graphs; misalignment between the language and the purpose of the document; getting different stakeholders to agree on the benchmarks for a plain language document; and eliminating blind spots innate to medical writers who have been writing for specialist audiences.

Communicating effectively with the public requires the writer to be empathic; this is a difficult skill to master and a tough concept to teach when working with teams who haven't done this before. Medical communicators would need to move beyond readability, ensure that patients understand the text on first read, and write in a way that allows patients to feel the writer's "voice". The session ended with all agreeing that writers can do more than share medical information: they can send their readers verbal hugs and there's nothing wrong with that at all!

The CwP SIG thanks all the attendees for their insightful contributions to the discussion. The session was recorded and will be available on the EMWA website.

Disclosures and conflicts of interest

The author declares no conflicts of interest.

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Good Writing Practice

Syntactic punctuation distraction

Comma: Over-usage Part 2

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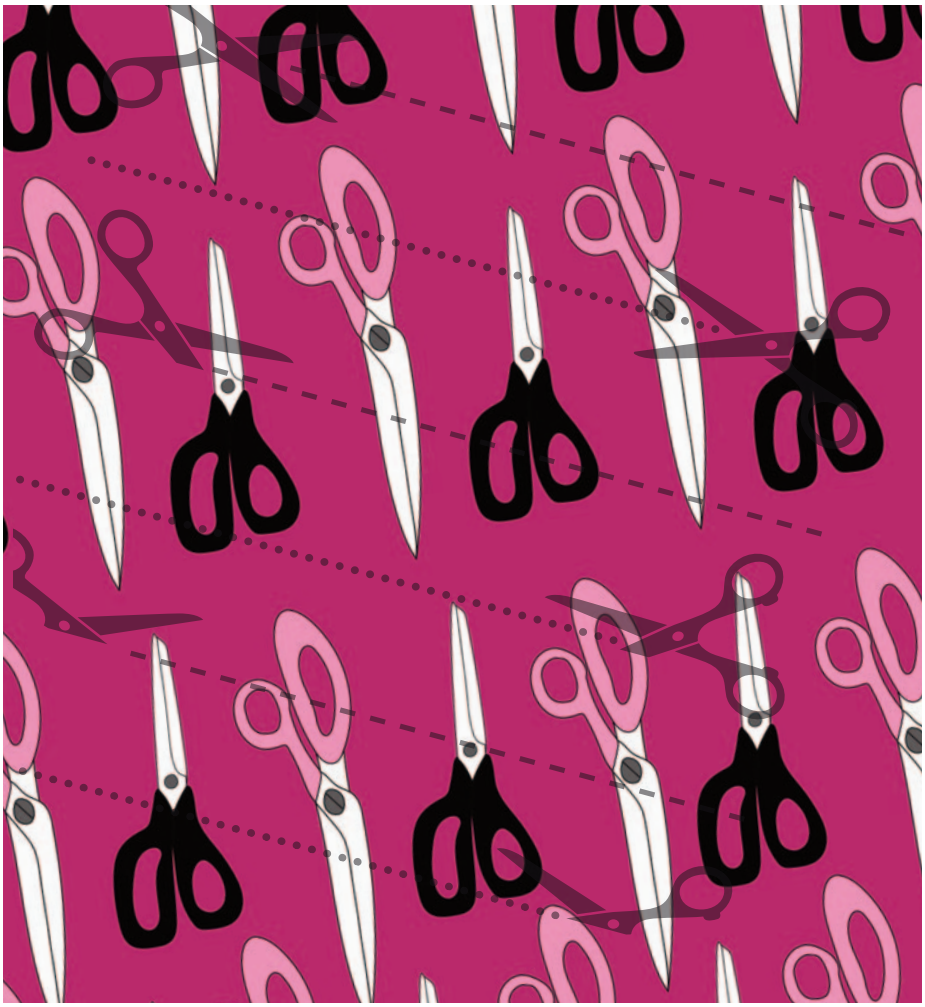

Introduction

Coordinated noncore sentence constituents are likely to be disrupted by unnecessary comma punctuation.

Between coordinated adjectives

Example

(Introduction section: research problem background)

The soluble, truncated form of HA was generated by substitution of codon L (20) for the first trans membrane residue (T514) containing the stop codon TGA.

Revision

The soluble truncated form of HA was generated by substitution of codon L (20) for the first trans membrane residue (T514) containing the stop codon TGA.

Notes

The comma-separation is considered acceptable because the meanings are coordinatable (i.e., *soluble* and *truncated* each modifies *form*) –not cumulative (*soluble* modifies *truncated form*). However, soluble is emphasised by its comma-marked segregation.

Soluble and *truncated* are adjectives of form, so their positions are inter-changeable, and the adjectives are coordinatable by *and*.

Another consideration is whether the sequence *soluble truncated* does adhere to placement of adjectivals before a noun, whereby the innateness of the noun increases with proximity; thus, *truncated* is more innately descriptive of form than is *soluble*, and soluble may even be a consequence of *truncated*.

Another type of distraction is a slight misreading possibility that two forms (*soluble* and *truncated*) exist; however, the singular word *form* and verb *was* indicate otherwise. Overall, usage of either the comma or the *and* is distracting. Both may be eliminated.

Between parallel noun clauses

Example

(Introduction section: hypothesis)

It is possible that these two types of tumours originate from common pax3- and pax-7-expressing cells, and that subsequent genetic alterations drive the cells into different outcomes.

Revision

It is possible (1) that these two types of tumours originate from common pax3- and pax-7-expressing cells and (2) that subsequent genetic alterations drive the cells into different outcomes.

Notes

The comma between the two dependent noun clauses is disruptive by segregation, the disruption indicating a contrast. However, numbering the coordinating noun clauses coheres these clauses, their parallelism, and their relation.

Regulatory Public Disclosure

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Editorial

So far, activity in 2023 in the EU regulatory public disclosure (RPD) environment has been well-paced. By that, I mean that the regional and country agencies and sponsors are becoming more familiar with the Clinical Trial Regulation (CTR) and the Clinical Trials Information System (CTIS) space, and are knowledge- and information-sharing effectively enough to save stakeholders valuable time. The EMA information sessions and posted documentation are key resources that help sponsors with their clinical trial applications (CTAs) uploaded to CTIS. What we have not yet seen are the results emerging from the "back end" of CTIS, as studies conducted under the CTR remain active. As these studies begin to approach their end, this will surely herald another period of intense activity and learning for the community.

Recently, we have received notification that clinical data publication (CDP) for non-COVID indication studies will restart in Quarter 4 of 2023, so we will need to be prepared for both CDP relaunch under Policy 0070, as well as studies conducted under the CTR reporting through CTIS – which should be interesting – there will be differences. The Policy 0070 relaunch – or what we currently know of it – is nicely summarised below by Alison McIntosh. The public consultation to "Review transparency rules for CTIS" (https://www.ema.europa.eu/ en/news/review-transparency-rules-eu-clinical-trials-information-system-ctis) over the period May 3 to June 28, 2023, means that we can expect updates – and the outcome of an Accelerating Clinical Trials in the EU (ACT EU) public consultation (May to end June 2023) will drive the changes. We now have the July 10, 2023, "Guidance document on how to approach the protection of personal data (PD) and commercially confidential information (CCI) whilst using CTIS version 1.1" comprising chapters on personal data, commercially confidential information, and good clinical practice (GCP) inspection reports. All of this tells us that the authorities continue to "work it out", often with input from other stakeholders and end-users – and that none of this is simple! It is also wonderful to see inter-agency cooperation and dialogue ongoing through development of public disclosure-related guidances, with Health Canada and EMA working together on some initiatives.

The EU and Canada are not the only jurisdictions with a lively public disclosure landscape. Zuo Yen Lee, the CORE Reference Team's disclosure expert for Asia, shares relevant information for four key countries in Asia to help you navigate the authorities' requirements (p. 96).

So as a community at the sharp end preparing texts for public disclosure, hold your nerve and continue to keep yourself well-informed. The CORE Reference Special Project can support you with your learning (see box below).

Finally, you may be aware that EMWA's Regulatory Public Disclosure Special Interest Group (SIG) has been retired, and a broader-based SIG, the Regulatory SIG, is now up and running. The CORE Reference Team is to be a key contributor of RPD content for the new Regulatory SIG, and so our team hope to meet many of you at the SIG meetings.

Sam Hamilton
Chair, The CORE Reference Project

Clinical Data Publication (Policy 0070) relaunch

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In preparation for the relaunch of EMA Clinical Data Publication (Policy 0070), a webinar was held on May 16, 2023, and a video recording of the meeting can be viewed online (https://www.ema.europa.eu/en/events/clinical-data-publication-policy-0070-re-launch-ema-webinar).

EMA Policy 0070 relaunch applies to new active substances from September 2023 onwards and includes negative and withdrawn products. Invitation letters will be sent if your product is in scope. Notably, COVID-19 and other public health emergency clinical data publication continues. EMA has confirmed that pre-submission meetings specific to a product can be offered and encourages sponsors to make use of such meetings.

EMA recommends that Sponsors prepare their Policy 0070 packages early and prior to Opinion. A new Q&A document relevant to the 2023 relaunch of Policy 0070 has been developed by EMA to address a number of practical questions concerning procedural matters including timelines, commercially confidential information, and the anonymisation process.

In this Part 1 of the relaunch, there are no plans to request clinical data for products authorised during the suspension of Policy 0070. Step 2 of the Policy 0070 relaunch will look at the backlog of studies and may require some to be published, e.g., publication upon request for particular products.

Sponsors should review documents to make sure any proposed Commercially Confidential

Information (CCI) is not already in the public domain. Given the EMA's COVID-19 experience of CCI, they are not expecting to see CCI in clinical documents for Policy 0070.

A new Anonymisation Report (AnR) template with structured fields has been developed jointly with Health Canada (HC) to allow "one report for joint EMA/HC packages". The use of structured fields in the AnR template is to provide content predictability, consistency, and efficient writing.

A full quality control check prior to submission is to be completed by the Sponsor to confirm all necessary documentation is submitted. Based on EMA experience with COVID-19 clinical data publication, an updated cover letter includes a checklist to ensure validation success.

CORE Reference Special Project – Continual Professional Development

The EMWA Webinar titled "CORE Reference – Value for the Global Regulatory MW Community" was held on June 21, 2023. Topics included:

- Website (www.core-reference.org) and resources
- Practical utility of CORE Reference, including PDF open-book demonstration
- Transparency and disclosure in Asia
- EMA Policy 0070 relaunch 2023
- Q&A

The webinar recording, transcript of the chat, and PDF of the slides are available here: https://emwa.org/education/public-webinars/. Please share these resources widely in your professional communities.

Receive Continual Professional Development resources direct to your inbox (sign up at: https://www.core-reference.org/subscribe), or periodically check the News Summary page of the existing website (https://www.core-reference.org/news-summaries/) where information gathered on matters concerning RPD and clinical study reporting is archived monthly. A recent selection of the most relevant information in the world of RPD is in Table 1.

Table 1. Selected regulatory information shared via CORE reference (March 2023 – July 2023)

Disseminated information	Brief description	Link
March 2023 highlights		
CTIS training materials – Latest updates	EMA guidance document to help users to easily identify which are the latest updated materials on the EMA website and which materials have been developed since the last time users have consulted them.	https://www.ema.europa.eu/en/documents/other/ctis-training-materials-latest-updates_en.pdf
Clinical Trials Coordination Group (CTCG)	Q&A document to support sponsors submitting or transitioning their complex trials to CTIS.	https://www.hma.eu/fileadmin/dateien/HMA_joint/00-_About_HMA/03-Working_Groups/CTCG/2023_03_CTCG_QA_complex_clinical_trials_and_CTIS_v1.0.pdf
New UK law will require all drug clinical trials to rapidly report results: TranspariMED article	The UK government will introduce a legal requirement to make public the results of all drug clinical trials within 12 months of trial completion. The new law will also make it mandatory to pre-register trials and to share their outcomes with participants.	https://www.transparimed.org/single-post/uk-clinical-trial-law
Electronic systems, electronic records, and electronic signatures in clinical investigations: Q&A. FDA draft guidance	Provides information for sponsors, clinical investigators, institutional review boards, contract research organisations, and other interested parties on the use of electronic systems, electronic records, and electronic signatures in clinical investigations of foods, medical products, tobacco products, and new animal drugs under FDA regulations and revises the draft guidance for industry issued in June 2017 entitled *Use of electronic records and electronic signatures in clinical Investigations under 21 CFR Part 11 — questions and answers* and, when finalised, will supersede the guidance for industry entitled Computerised systems used in clinical investigations (May 2007).	https://www.fda.gov/regulatory-information/search-fda-guidance-documents/electronic-systems-electronic-records-and-electronic-signatures-clinical-investigations-questions?utm_medium=email&utm_source=govdelivery
Registration of clinical trials and public disclosure of results: Health Canada draft guidance	To provide guidance to sponsors of Health Canada-authorised clinical trials to support the registration and public disclosure of results (reporting of results) using international registries. Additionally, this document describes the clinical trial information that Health Canada is publishing on the Health Canada Clinical Trials Portal.	https://www.canada.ca/en/health-canada/programs/consultation-registration-clinical-trials-public-disclosure-results-new-guidance-public-search-portal/overview.html
April 2023 Highlights		
EU CTR Implementation: PHUSE blog post	Summary of Year 1 of the regulation from a sponsor perspective, with a focus on transparency aspects.	https://phuse.s3.eu-central-1.amazonaws.com/Deliverables/Data+Transparency/EU+CTR+Blog+Update_Year+1.pdf
CTIS - Sponsor Handbook, v. 3.02	This version includes newly added information about multi-factor authorisation in CTIS, as well as links to CTIS bitesize talks.	https://www.ema.europa.eu/en/documents/other/clinical-trial-information-system-ctis-sponsor-handbook_en.pdf
Diversity Plans: FDA Draft Guidance	The FDA recommends that sponsors develop and submit a diversity plan to help ensure the adequate participation of relevant and underrepresented populations and analyses of data collected from clinically relevant populations.	https://www.federalregister.gov/documents/2022/04/14/2022-07978/diversity-plans-to-improve-enrollment-of-participants-from-underrepresented-racial-and-ethnic
Considerations on evidence from single-arm trials: EMA reflection paper	The paper discusses key concepts for single-arm clinical trials that are submitted as pivotal evidence in support of marketing authorisation applications for medicines in the EU. Stakeholders are invited to send their comments via an online form by midnight (CET) on September 30, 2023.	https://www.ema.europa.eu/en/documents/scientific-guideline/reflection-paper-establishing-efficacy-based-single-arm-trials-submitted-pivotal-evidence-marketing_en.pdf

Disseminated information	Brief description	Link
Software and Artificial Intelligence (AI) as a Medical Device (SaMD and AIaMD, respectively): MHRA guidance	This guidance provides access to important Software Group outputs that might be of assistance. Software Group are responsible for taking all reasonable steps to assure the safety of SaMD and ensure the UK public have access to technology that meets a clinical need. They work across the MHRA to achieve this aim for SaMD and AIaMD.	https://www.gov.uk/government/publications/software-and-artificial-intelligence-ai-as-a-medical-device/software-and-artificial-intelligence-ai-as-a-medical-device
May 2023 highlights		
ICH Harmonised Guideline, GCP E6(R3)	This version of E6 includes an updated version of the already-released GCP principles and the protocol content has moved from Section 6 in E6(R2) to Appendix B in E6(R3).	https://database.ich.org/sites/default/files/ICH_E6%28R3%29_DraftGuideline_2023_0519.pdf
MHRA Inspectorate Blog: ICH E6(R3) GCP guidance - Step 2 Public Consultation	MHRA wishes to consult directly with UK stakeholders to compile and coordinate their comments to the ICH Expert Working Group.	https://mhrainspectorate.blog.gov.uk/2023/05/02/ich-e6r3-good-clinical-practice-guidance-step-2-public-consultation/
FDA discussion paper: Artificial Intelligence and Machine Learning (AI/ML) for drug development	This paper aims to communicate with a range of stakeholders and to explore relevant considerations for the use of AI/ML in the development of drugs and biological products.	https://www.fda.gov/science-research/science-and-research-special-topics/artificial-intelligence-and-machine-learning-aiml-drug-development?utm_medium=email&utm_source=govdelivery
Discussions for the next revision of the Declaration of Helsinki (DoH): Meetings for the WMA and IFAPP (The Global Newsletter on Pharmaceutical Medicine)	The WMA is committed to reviewing the DoH every 10 years and 2023 is the 10th year since the previous update (2013, Brazil). Discussions are ongoing with the aim to adopt the revised version at the General Assembly in Helsinki, Finland in October 2024. You can read more in the 34th issue of the IFAPP Newsletter starting on page 8.	https://ifapp.org/static/uploads/2023/05/IFAPP-TODAY-34-2023.pdf
EC guidance on the content and structure of the summary of the clinical investigation report	"This guidance aims to ensure that the summary of the clinical investigation report presents information about the design, conduct, analysis, and results of the clinical investigation in terms and in a format that are easily understandable to the intended user of the medical device." There is an equivalent requirement under the EU CTR – the Lay Summary of Clinical Study Results.	https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52023XC0508(01)
June 2023 highlights		
An overview of comments from the public consultation on the ICH M11 guideline, template, and technical specifications have been published.	These comments will be sent to the ICH M11 Expert Working Group for consideration in the context of Step 3 of the ICH process.	https://www.ema.europa.eu/en/documents/comments/overview-comments-received-ich-m11-guideline-clinical-study-protocol-template-technical_en.pdf, https://www.ema.europa.eu/en/documents/comments/overview-comments-received-ich-m11-template-step-2b_en.pdf, and https://www.ema.europa.eu/en/documents/comments/overview-comments-received-ich-m11-technical-specification-step-2b_en.pdf
Reminder to re-subscribe to receive the Clinical Trials Highlights Newsletter.	Issues from mid-July 2023 will only be circulated to re-subscribers.	https://ec.europa.eu/newsroom/ema/user-subscriptions/3201/create

Disseminated information	Brief description	Link
June 2023 highlights - continued		
EMA Virtual CTIS: Information Day on Oct 17, 2023, from 13:30- 17:30 Amsterdam time (CET)	The purpose of this information day is "to support sponsors of clinical trials in preparing and proceeding with the transition to meet the deadline of January 30, 2025". Commercial and non-commercial sponsors with experience in transitioning trials as well as representatives from EMA and EU/EEA member states will share insights and best practices. The registration for the event is through DIA Europe and it is a paid event. Ample time is foreseen for Q&A. Participants are invited to submit related questions by October 3, 2023 to emaevents@diaglobal.org	https://www.ema.europa.eu/en/events/clinical-trials-information-system-ctis-information-day
Modernised ClinicalTrials.gov	The modernised ClinicalTrials.gov is now available. To allow users time to adapt to the modernised website, the classic ClinicalTrials.gov website will remain available until it's retired in 2024.	https://www.clinicaltrials.gov/?utm_medium=email&utm_source=govdelivery and https://classic.clinicaltrials.gov/
July 2023 highlights		
ICH E6(R3) exploratory video	ICH has published a 9-minute video that provides the rationale for the update of GCP, and the foundational elements that the update aims to achieve.	database.ich.org/sites/default/files/ICH_E6%28R3%29_Guideline_GCP_Video_2023_0601.mp4
EMA CTIS webinar	The slide presentation from the "Clinical Trials Information System Webinar: Second Year of Transition" is available to view including Sponsor experiences and perspective on transitional trials.	https://www.ema.europa.eu/en/events/clinical-trials-information-system-webinar-second-year-transition#documents-section
Guidance document on how to approach the protection of personal data and commercially confidential information (CCI) while using the Clinical Trials Information System (CTIS). Version 1.1	A further update to the guidance which now includes Chapter 4 on CCI (Management of CCI in clinical trial information submitted to CTIS) and Chapter 5 (GCP inspection reports). Accompanying the guidance update there has been an update to Annex I (Acronyms) and Annex II is a template that applies to GCP inspections carried out to category 1 trials where the publication of clinical trial information is delayed by deferral.	https://www.ema.europa.eu/en/documents/other/guidance-document-how-approach-protection-personal-data-commercially-confidential-information-while_.pdf and https://www.ema.europa.eu/en/documents/template-form/annex-ii-guidance-document-how-approach-protection-personal-data-commercially-confidential_ir.pdf

Abbreviations: CFR, Code of Federal Regulations; CTIS, Clinical Trials Information System; EC, European Commission; GCP, Good Clinical Practice; ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use; MHRA, Medicines and Healthcare products Regulatory Agency; WMA, World Medical Association.

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Table 1 provides a selection of key information disseminated by the CORE Reference Project Team between March and July 2023. Thanks to Vivien Fagan (Vivien.Fagan@iqivia.com) for summarising.

Current clinical trial disclosure landscape in Asia

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The transparency and disclosure landscape in Asia has been rapidly evolving during the past decade. With respect to clinical trial registries, China launched its national registry, ChinaDrugTrials.org.cn, in 2013; South Korea introduced the new clinical trial disclosure platform through its Ministry of Food and Drug Safety (MFDS) in 2019; whilst Japan unified its three existing primary registries into a single clinical trial registry – Japan Registry of Clinical Trials (jRCT) – in 2020.

In Table 1, we provide an overview of the national clinical trial registries and the trial results disclosure practices for 4 Asian countries – China, Japan, South Korea, and Taiwan.

First, registration of all interventional clinical trials, with certain exceptions, in the national registries are required before subject enrollment in all four countries. Clinical trials can also be registered in a variety of other trial registries which may have been used long before these national registries, and which now serve as voluntary registries. Most of these voluntary registries are operated in both the local language and English, and are registered as a primary registry in the WHO International Clinical Trials Registry Platform (ICTRP) Network. Except for Taiwan, the clinical trial results should be posted on the registries within 1 year following study completion. The definition of "study completion" should normally be in the protocols of individual trials. We typically define the term as the date of the "last subject last visit" in the trial, but for trials with exceptionally long follow-up periods, it may be defined as the last visit of the treatment.

In China, trial results are posted on the ChinaDrugTrials.org.cn as a separate summary or overview document which, per the Center for Drug Evaluation (CDE) guidance, should at least contain the content of the clinical study report (CSR) synopsis as described in the ICH E3 guideline. The results summary is, however, not accessible to the public. In Japan and South Korea, on the other hand, trial results are posted within their registries in brief synoptic summaries, which mostly include the primary and key secondary endpoints, and these are accessible to the public.

For drugs that are granted marketing authorisation, the CDE in China also publishes the trial results in the format of CDE review reports and drug instruction manuals on the CDE website, whereas the Pharmaceuticals and Medical Devices Agency (PMDA) in Japan publishes certain sections of Modules 1 and 2 of the Common Technical Document, PMDA review reports, and data summaries of the drugs on the PMDA website. In all four countries, the disclosure of CSRs is not required by the regulation. Of note, all these countries follow the ICH E3 guideline for developing the CSRs, mostly with their own specific additional requirements.

Specifically for China, more background information on the existing voluntary clinical trial registries, the development of its current national registry, and regulations pertaining to drug registration in the country is presented in the Regulatory Matters section in this issue of *Medical Writing* on p. 98.

Table 1. Current clinical trial disclosure landscape in Asia – Trial registration and results disclosure

	 China	 Japan	 South Korea	 Taiwan
National clinical trial registry (mandatory)	Drug Clinical Trial Registration and Information Disclosure Platform http://www.chinadrugtrials.org.cn/index.html	Japan Registry of Clinical Trials (jRCT) https://jrct.niph.go.jp//	Ministry of Food and Drug Safety (MFDS) Registry https://nedrug.mfds.go.kr/searchClinic	Taiwan Clinical Trial Registry (TCTR) https://www1.cde.org.tw/ct_taiwan/
Type of trial	Interventional (including BE, PK, Phase 1-4) (Not required: Observational)	Interventional (Phase 1-4), Observational (Not required: BE)	Interventional (Phase 0-4) (Not required: Observational)	Interventional (Phase 1-4), Observational
Trial registration timeline	Before subject enrolment	Before subject enrolment	After the study obtains MFDS approval; before subject enrollment	After the study obtains TFDA/CDE approval; before subject enrollment
Results posting required	Yes	Yes	Yes	No

	China	Japan	South Korea	Taiwan
Results posting timeline	Within 12 months of study completion or before marketing authorisation (for trials supporting an NDA), whichever occurs first	Within 1 year of study completion	Within 1 year of "last subject last visit"	–
Public accessibility to posted results	No	Yes	Yes	–
Format of posted results	Uploaded as a separate summary or overview document. Per China CDE guidance, the results summary/ overview should at least consist of the content of the CSR Synopsis as described in the ICH E3.	Posted within the registry as brief synoptic summaries or summary in text boxes; limited trial results, mostly only include primary and key secondary endpoints. Posted as links to publications.	Posted within the registry as brief synoptic summaries or summary in text boxes; limited trial results, mostly only include primary and key secondary endpoints.	–
Language	Mandarin (Simplified)	Japanese, English	Korean	Mandarin (Traditional)
Other optional/ Voluntary registry	• Chinese Clinical Trial Registry (ChiCTR) • Centre for Clinical Research and Biostatistics – Clinical Trials Registry (CCRBCTR) • Acupuncture-Moxibustion Clinical Trial Registry (AMCTR) • International Traditional Medicine Clinical Trial Registry (ITMCTR)	–	Clinical Research Information Service (CRIS) (which may contain more comprehensive information than the MFDS registry)	ClinicalTrials.gov (many studies conducted in Taiwan are also registered on this registry where trial data may be provided via links to publications)
Other means of results disclosure (Type of document)	For approved drugs: CDE website (CDE review reports, drug instruction manual)	For approved drugs: PMDA website (Some sections of CTD Modules 1 and 2, PMDA review reports, summaries of data)	Not known	For approved drugs: TFDA website (Package insert)
CSR structure/Format	ICH E3 Specific requirements for the title page and appendices.	ICH E3 Separate comparison of Japanese vs. non-Japanese data is required (for Module 5.3.7).	ICH E3	ICH E3 For multinational trials, Taiwan safety and efficacy data summary should be included in the appendix.
CSR Disclosure	No	No	No	No

Abbreviations: BE, bioequivalence; CDE, Center for Drug Evaluation; CSR, clinical study report; CTD, Common Technical Document; MFDS, Ministry of Food and Drug Safety (Republic of Korea); NDA, new drug application; PK, pharmacokinetic; PMDA, Pharmaceuticals and Medical Devices Agency (Japan); TFDA, Taiwan Food and Drug Administration.

Note: The information in Table 2 is correct as of April 2023.

Regulatory Matters

SECTION EDITORS

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Editorial

On June 21, 2023, EMWA's Clarity and Openness in Reporting: E3 (CORE) Reference Project team presented a webinar which featured an overview of the current clinical trial disclosure landscape in Asia. The comprehensive overview table, along with a brief description, are also presented in the Regulatory Public Disclosure section in this issue of *Medical Writing* on p. 91.

Over the past two decades, we have seen rapid evolution of drug regulations in China, including the re-organisation of their drug regulatory authority from the State Drug Administration (SDA) which was inaugurated in 1998, to China Food and Drug Administration (CFDA) in 2013, to the current National Medical Products Administration (NMPA) since 2018. Then, China joined the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH)in 2020. Significant changes in drug regulations are being introduced constantly to accelerate drug review and approval while staying in alignment with international guidelines.

In this article, I provide further background on the existing clinical trial registries, the development of the current national registry, and regulations pertaining to drug registration in China. This complementary background information provides extended reading on the concise content for China in the overview table mentioned above. I hope you find it useful and enjoy reading it!

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Current clinical trial disclosure landscape in China

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Existing clinical trial registries in China

In China, before the launch of the current national clinical trial registry in 2013, i.e., ChinaDrugTrials.org.cn (http://www.chinadrugtrials.org.cn/index.html), two common trial registries already existed and have been in use until the present day. In addition, two new registries for traditional medicines were established after 2013. These registries and their brief descriptions are presented in Table 1.

> Sponsors should register the clinical trial protocol and trial information ... and include the trial results following the completion of the trial.

Development of the new National Clinical Trial Registry

- **November 2012** – The Centre for Drug Evaluation (CDE) in China launched a trial run of the new Clinical Trial Registration and Information Disclosure Platform for Drugs via the CDE website.
- **September 2013** – The then China Food and Drug Administration (CFDA) released Notification No. 28 on the Clinical Trial Information Platform for Drugs,[1] requiring all clinical trials conducted in China (including bioequivalence, pharmacokinetic, Phase 1 to 4) to be registered and trial information be disclosed on the abovementioned platform on the CDE website. Pre-registration to obtain the trial's unique identifier must be completed within 1 month after obtaining an approval of the trial. The rest of the registration must be completed before the first subject enrolment. Trial registration is to be seen as a pre-requisite for the subsequent communication and consultation with the regulatory authority during the clinical trial.
- **October 2013** – The CDE released further information following Notification No.28, announcing the effort of completing a new clinical trial disclosure platform.
- **November 2013** – An independent registration platform called ChinaDrugTrials.org.cn was first launched. The trial run of the original platform on the CDE website was terminated.
- **December 2015** – The then-CFDA released Notification No. 257 on the Management of Bioequivalence Trials of Chemical Drugs,[2] which indicated the integration of the Registry for Generic Drugs and Bioequivalence Clinical Trials into the ChinaDrugTrials.org.cn platform.
- **2020** – In conjunction with the enforcement of the Drug Administration Law in 2019 and the Drug Registration Regulation in 2020, the original ChinaDrugTrials.org.cn platform was upgraded and officially merged with the Registry for Generic Drugs and Bioequivalence Clinical Trials.

Drug Registration Regulation in China

The Drug Registration Regulation[3] was enforced in July 2020. According to the regulations:

- **Article 28** – Sponsors should submit a safety update report every year during the clinical investigation of the drug. [...] Any suspected unexpected adverse reaction and other underlying important safety issues must be reported to the CDE promptly as required. The trial protocol, subject informed consent, or the investigator's brochure should be updated as necessary based on the severity of the safety risks. A trial may be suspended or terminated if deemed appropriate.
- **Article 33** – Sponsors should register the clinical trial protocol and other trial information on the registration and information disclosure platform before starting a trial. During the trial, sponsors should continue to update the registration information and to include the trial results following the completion of the trial. The sponsors are

responsible for the authenticity of the trial information.

- **Article 116** – Sponsors who violate Article 28 and Article 33, or any of the following events will be warned and ordered to take corrective action; failure of corrective action within the given time window may result in a penalty of 10,000 to 30,000 Chinese Yuan. The events that require corrective actions include:
  1. Failure to register the clinical trial on a registration and information disclosure platform;
  2. Failure of timely submission of safety reports;
  3. Failure to provide trial results after the completion of the trial.

In response to the new regulation, the CDE issued a draft guidance on the Management of Clinical Trial Registration and Information

Table 1. Clinical trial registries in China

Clinical trial registry description
Chinese Clinical Trial Registry (ChiCTR) • https://www.chictr.org.cn/ • Established in 2005 • Accepts registration of clinical trials in China and globally • Operated in Mandarin and English • Primary registry of the WHO International Clinical Trials Registry Platform (ICTRP) since 2007 • Served as the primary registry for clinical trials in China before the launch of ChinaDrugTrials.org.cn. Thereafter, the role of the ChiCTR became unclear in relation to the regulation.
Centre for Clinical Research and Biostatistics – Clinical Trials Registry (CCRBCTR) • https://www2.ccrb.cuhk.edu.hk/ • Partner registry of ChiCTR since 2009 • Accepts registration of clinical trials globally • Operated in English only (only the study title is bilingual in Mandarin and English) • Compliant with WHO ICTRP trial registration requirements
Acupuncture-Moxibustion Clinical Trial Registry (AMCTR) • Partner registry of the WHO ICTRP[4] • Established in 2014 and became a partner registry of ChiCTR since 2016 • Accepts registration of clinical trials using acupuncture-moxibustion as interventions • Compliant with WHO ICTRP trial registration requirements
International Traditional Medicine Clinical Trial Registry (ITMCTR) • Primary registry of the WHO ICTRP since March 2023[5] • Operated in Mandarin and English • Accepts registration of clinical trials conducted in China or globally since 2019 • For trials in the field of traditional medicine, including but not limited to Chinese medicine, acupuncture, tuina massage, herbal medicine, ayurveda, homeopathy, and complementary and alternative medicine

Disclosure,[6] which came into effect on July 1, 2020. The draft guidance specifies the following important registration and disclosure policies:

- **Article 6** – All clinical trials that obtain approval from the National Medical Products Association (NMPA) and are conducted in China, including bioequivalence and Phase 4 or post-marketing surveillance studies, are required to be registered on the registration and information disclosure platform.
- **Article 14** – [...] Trial registration should be completed before subject enrolment.
- **Article 15** – [...] Following trial completion, the trial results should be posted on the platform within 12 months of trial completion; for trials supporting a New Drug Application (NDA), sponsors are recommended to post the trials' results before NDA submission, whichever occurs first. The trial results should at least consist of the content of the clinical study report synopsis as described in the ICH E3 guideline.

As a note, results of clinical trials completed before July 1, 2020, without an NDA submission, should still be posted on the platform within 12 months of trial completion or before the NDA submission. Nevertheless, if an NDA is already submitted, trial results posting is at the discretion of the sponsors.[7]

Afterthought

From a quick glance at the completed trials dated between 2020 and 2022 in the ChinaDrugTrials.org.cn registry, not all registered trials have included the trial results. Imposing a penalty for failure to provide trial results as stated in the regulation is only the first step. Effective and consistent oversight in trial registration and result posting must not be overlooked in the effort towards improving transparency of clinical trial information.

There potentially are issues of redundancy, inadequate maintenance, and missing information as we have seen with many other major clinical trial registries worldwide.

As of June 25, 2023, more than 70,000 clinical trials were registered on the older ChiCTR whilst just shy of 21,000 clinical trials are found on ChinaDrugTrials.org.cn. How many clinical trials are registered on both platforms and maintained equally, how many are registered on only one and not the other? There potentially are issues of redundancy, inadequate maintenance, and missing information[8] as we have seen with many other major clinical trial registries worldwide. It is suggested that data exchange between ChiCTR and ChinaDrugTrials.org.cn and mutual recognition of the two platforms should be considered to improve transparency and sharing of clinical trial information.[9]

Disclosures and conflicts of interest

The author declares no conflicts of interest.

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Getting Your Foot in the Door

SECTION EDITOR

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Editorial

"Preparation is half of victory" – as 16th century Spanish novelist Miguale de Cervantes said so well; it is the key to success in any field, even when attending an EMWA conference!

Why, you ask? Anna Isermann and Louisa Ludwig-Begall can definitely answer that question. They have written a short, inspiring guide based on their first hands-on experience. Here, they have summarised key points on how to prepare for EMWA's conferences. The authors attended their first one in Prague last May, and have laid out a roadmap for first-time (and even second-time) attendees to get the most they can from the conference. And by the way, the next virtual EMWA conference starts on November 9, 2023, while the next in-person-conference, in Valencia, Spain, takes place May 7-10, 2024. So start your preparation!

Ivana

The hitchhiker's guide to the EMWA conference: Reflections and recommendations from first-time delegates

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Introduction

"The story so far: In the beginning, the Universe was created. This has made a lot of people very angry and been widely regarded as a bad move."[1]

Douglas Adams, *The Ultimate Hitchhiker's Guide to the Galaxy*

In 1992, EMWA was created.[2] This has made a lot of people very happy and been widely regarded as a good move. In May 2023, two newbies, as yet unknown to one another, set out to join the five-day 55th EMWA conference in Prague, Czech Republic. Here, we share our impressions of this journey. This article is a personal reflection on the valuable insights gained, and the vibrant community spirit experienced, at our inaugural EMWA conference. It is also intended to serve as an informative guide for prospective, first-time delegates.

Before the conference

Every journey has a prelude: a time of planning, provisioning, and packing. Pre-conference prep certainly helped us get the most out of our first EMWA conference, so let's share some to-dos:

Personalise your programme

EMWA conferences offer an array of seminars, plenary sessions, symposia, and EMWA Professional Development Programme (EPDP) workshops.[3] They cover every aspect of medical writing and cater to both "old hands" and newcomers. When booking the conference, one is faced with the question of what and how much to select from this tantalising menu (the fact that there is an additional fee for each EPDP workshop may not be a negligible consideration).

To work towards gaining credits for an EMWA professional certificate (a valuable asset for your career!), we would recommend choosing at least one EPDP workshop to accompany the rest of your programme selection. However, do take care not to "overindulge" and remember to budget some time before and after the conference, as to gain EPDP credits, additional two- or three-hour pre- and post-workshop assignments must be completed. EMWA recommends registering for a maximum of four EPDP credit workshops per conference. Having spoken to slightly harried delegates who tried to attend four or more, this seems like a limit one should stick to!

> "We're a serious organisation with not-so-serious members." A fact that, to our delight, was proven time and again from that moment on.

Link and liaise

Apart from one's personalised programme, another important aspect to focus on during the conference is networking with other medical writers and getting to know the EMWA community. Who is to say this has to wait until the conference commences? Reach out to fellow medical writers in your area on LinkedIn. Ask them if they are also attending the EMWA conference. We were actually on the same outbound flight and did not know it. Had we but known, the wait at the airport would have been so much more fun and the pre-conference jitters (and taxi fees) would have been a lot less!

Ramp up the reading

Most aspiring medical writers have probably googled "How to become a medical writer". Information-seekers need look no further than EMWA's hot-off-the-press "Career Guide for New Medical Writers".[4] The newest edition, created by EMWA's aptly named "Getting into Medical Writing" Working Group, was released in May this year (available at https://emwa.org/ about-us/getting-into-medical-writing/career-guide-for-new-medical-writers/). This free career guide is worth reading at any time but is to be particularly recommended before the conference. It gives great insights into the vast landscape of

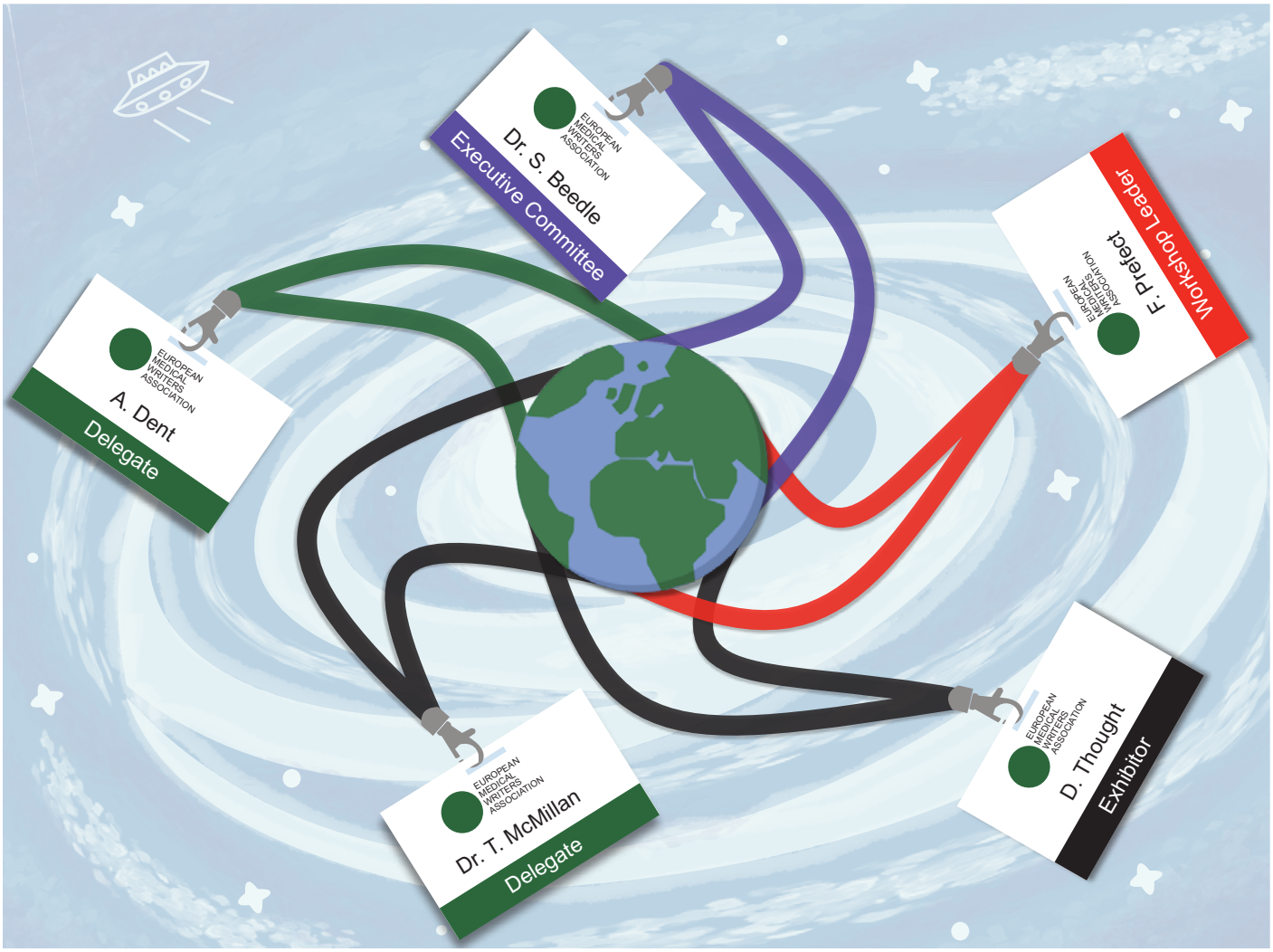


Illustration by Anna Isermann

Figure 1. Decoding the lanyard lingo

medical writing – useful knowledge indeed to help tailor your workshop choices to your preferred field. The guide will send you on an information-seeking mission across the entire conference. Countless unsuspecting EMWA members were accosted with "So, are you in regulatory writing or medical communications?" followed by an eager "And what is it you like so much about it?". Each answer was delivered with infectious enthusiasm and drove us to delve even deeper!

Clear your calendar

EMWA conferences provide a wealth of knowledge, new impressions, and fascinating insights. Both of us had cleared our schedules for the conference and were glad we did so. While unexpected work still cropped up (doesn't it always?) in the form of prospective client calls and urgent project edits, we managed to stick to the plan overall. If feasible, we recommend scheduling as little work as possible during conference days. Between studying and socialising, you will soak up so much information that you will have little time or inclination (or indeed energy) for anything else.

Grab your garb

Coming from academia (as is probably the case for many EMWA conference first-timers), we were well-versed in the world of conferences and knew that the dress codes for such occasions can vary widely indeed. What, we both wondered, would a bunch of medical writers be wearing? Our sartorial solution: Agonise for ages, pack every possible item in one's wardrobe (from track to pantsuit), and lug an enormous bag around the conference city (in our case, Prague). Not ideal. So, let's clear this up for future newbies: You can't go wrong with business casual (also, everyone will just be happy to meet you, whatever your go-to style may be).

Embrace the experience

Entering into a new association and a new environment can be daunting. For us, any pre-conference anxiety was immediately extinguished at the Opening Session: Conference Organiser Slavka Baronikova put us at our ease and perfectly captured the EMWA spirit when she said "We're a serious organisation with not-so-serious members." It was a fact that, to our delight, was proven time and again from that moment on.

During the conference

Lanyard language

Waiting for the opening session to begin, we quickly clocked the different lanyard and name tag colours that everyone had received upon in-person registration. Each colour stands for a different type of delegate (see Figure 1) and first-time attendees are awarded a green lanyard. The

purpose of this colour code is not to exclude but to include; it is intended to act as a bi-directional conversational prompt, letting seasoned members know to involve newcomers in the community and signalling to newcomers whom to approach. So, wear your lanyard colour with pride and let it lead you into interesting discussions!

Programme points

Following on from early-morning yoga (we solemnly swear to join the ranks of the downward-facing writers next year!), the conference programme was packed each day. Determined not to miss a thing, we kicked off each full day (Wednesday to Friday) at 7:45 a.m. and attended as many of the (free) parallel sessions as possible. While we each customised our programme according to individual taste, the "Introduction to Medical Writing" and "Getting into Medical Writing" sessions were a must for us both!

Encountering exhibitors

The programme was generously interspersed with coffee and lunch breaks. These hitchhikers found, however, that indeed "Time is an illusion. Lunchtime doubly so."[5] We dived into prandial patter with gusto and never noticed the time fly by! Never had either of us met such a welcoming crowd (perhaps unsurprisingly, professional communicators like to communicate!).

Coffee breaks or individual gaps in the programme were an excellent time to talk to the exhibitors at the company booths. We would both highly recommend engaging with the company representatives. They are a mine of information and can often give you invaluable insights and perspectives into the industry (as well as free pens, of course). You never know who you might meet; you could find yourself chatting with a medical writer, a recruiter, a manager, or even the CEO themselves. We found that having phones at the ready was particularly useful on these occasions, both to directly connect on LinkedIn and to scan displayed QR-codes (having a couple of business cards at hand was also a useful, if not essential, option).

> One EMWA member told us "Go drinking and close down the bar with the other delegates!"

Laughter and libations

EMWA conference evenings were enlivened by a networking reception, a conference dinner, and two guided walking tours through beautiful Prague. For many of us, these events ran rather late since we took some expert advice to heart: "Go drinking and close down the bar with other delegates!" said long-time EMWA member Lisa Chamberlain James (who also happens to be a section editor of this very journal).

Thus, social strolls seamlessly segued into drinks at the pub(s) and many happy hours were spent talking all things medical writing with fellow enthusiasts. This is a brief that is easy to follow and is to be heartily recommended to all future first-time delegates!

Conference chronicles

> "Write, write, write!" There may soon be two new entries for next year's Geoff Hall Scholarship and, hopefully, our readers will be enjoying the fruits of another of our writing endeavours!

An EMWA conference is an extraordinarily intense and immersive experience. We attended so many programme sessions, gained such a plethora of insights into medical writing, and met so many new people, that both our heads were spinning at the end of each long day. Neither of us slept much because of the intense socialising. Even late at night, we both took the time to jot down some notes (delegates' names, salient information, sage advice). Now, caught up on sleep, but also back to "business as usual", we're both glad to have these conference logs to refer back to!

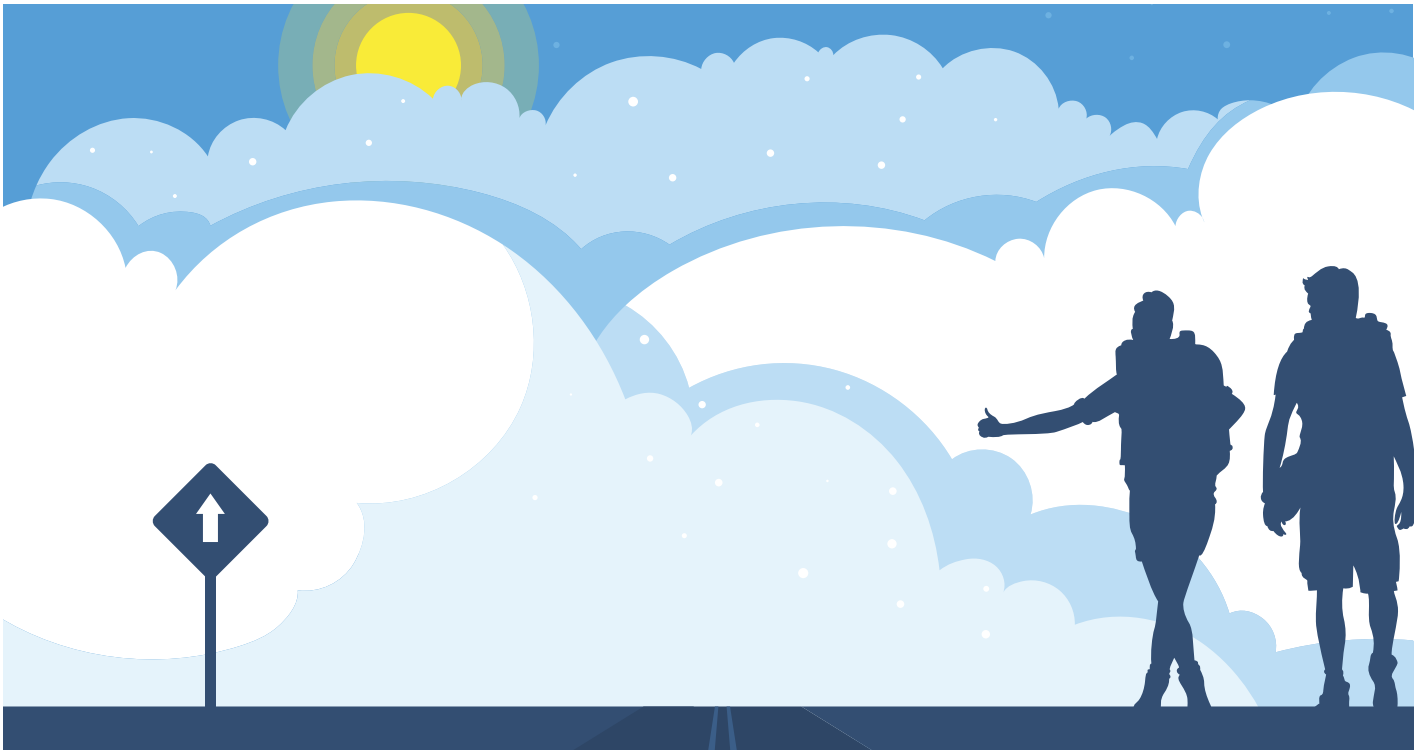
After the conference

Write, write, write

Since the conference, we have been ticking boxes on a new to-do list (Figure 2). We've been busy with post-workshop assignments, have each got involved with different EMWA SIGs, and have continued to connect on LinkedIn with other delegates – it's great to see our network grow! Staying in touch with the EMWA community has kept the conference momentum and motivation going. There is still so much to see and learn, so many seminars, webinars, lunchtime talks, and informative posts from and for medical writers!

We both also have been diligently following

Figure 2. EMWA conference checklist



EMWA member Diarmuid De Faoite's excellent advice to "Write, write, write!" There may soon be two new entries for next year's Geoff Hall Scholarship and, hopefully, the readers of this guide have enjoyed the fruits of this joint writing endeavour!

Conclusion

So, can we provide the answer to the Ultimate Question of Life, the Universe, and Everything? No, but we can, without aeons of calculations, recommend that you visit an EMWA conference!

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Disclaimers

The opinions expressed in this article are the authors' own and not necessarily shared by their employers or EMWA.

Disclosures and conflicts of interest

The authors declare no conflicts of interest.

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The Crofter: Sustainable Communications

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Editorial

Greetings from the croft. I've been trying out some carbon footprint calculators and there was something about seeing how flying "affected my numbers" that reinforced my decision to limit my travel within Europe to train/boat/car, and be very selective as to future air travel. According to the United Nations Framework Convention on Climate Change Lifestyle Calculator,[1] my carbon footprint was 6.60 tonnes CO_2e and family-related inter-continental travel accounted for a quarter of this. When I used the UN carbon footprint calculator[2] to estimate the footprint of my family of four, air travel accounted for more than half. (My next step is looking into the various carbon offset options as I can't avoid air travel when visiting family and friends in Canada. But more on offset options at another time.)

Getting back to reinforcement, I appreciate this issue's contribution by Egid van Bree, MD, who was also a speaker during our Expert Seminar Series on Sustainability in November 2022. In his article, Dr van Bree expands on the complementary concept of the handprint, in which actions that increase our handprint increase the health of our planet. I found it motivating to see how we can increase our handprint on different levels and how medical and scientific writers are well-equipped to have impact. This issue of the Crofter also includes a follow-up interview with Dr van Bree to learn more about his volunteer work with the Dutch Green Health Alliance, which is a thriving non-for-profit network that aims to make the healthcare system in the Netherlands sustainable through sharing knowledge and advocacy. Coincidently, since he currently works in Leiden, which is a short bike ride away from where I live, we were able to meet and talk over lunch – a fun bonus in the process!

And now speaking of food, please check out this issue's recipe. It's quick to prepare so it's a great workday dinner idea and can help convince people that tofu can be tasty ☺.

Best, **Kimi**

1. Lifestyle Calculator [cited 2023 July 3]. Available from: https://lifestylecalculator.doconomy.com/unfccc/
2. UN Carbon Footprint Calculator [cited 2023 July 3]. Available from: https://offset.climateneutralnow.org/footprintcalc

Why environmental sustainability requires us to focus on our handprint – and write about it

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Environmental sustainability has gained increasing attention in the healthcare sector – and likewise, in medical journals. Historically, September 2021 marked an interesting event as over 200 medical journals conjointly published a call for emergency action to limit global temperature increase.[1] Much has continued to happen since then, with major medical journals frequently publishing on the health effects of environmental change and growth of dedicated daughter journals such as the *Lancet Planetary Health*. Why has this interest been growing so rapidly and how might medical writers positively shape its development?

Threatening our health

Human-induced environmental change, such as climate change, is one of the biggest threats to global health. Annual reviews by the Lancet Countdown Commission on health and climate change clearly summarise the consequences of the increased frequency of heatwaves, increased likelihood of extreme weather events, increased spread of infectious disease, and corresponding economic losses.[2] These pressing findings are consistently paired with an overview of the potential health benefits of coordinated climate action and climate justice. Especially the vulnerabilities of minorities and populations in the Global South need to be considered. According to the authors of many published comments and editorials, the gravity of the health effects, and the opportunity to still improve health outcomes, serve as an urgent call to action for healthcare professionals to raise their voice.

Meanwhile, the healthcare sector itself contributes to environmental change by constituting around 4% to 5% of the global carbon footprint and frequently larger shares in high-income countries.[3] Research in the Netherlands, for example, indicates that the Dutch healthcare sector accounts for 7% of the annual carbon footprint and 13% of raw material extraction[4] – a stark contradiction when considering healthcare's all-time mission to heal and prevent harm. Not surprisingly, many countries have a growing movement of bottom-up healthcare initiatives that strive to make healthcare delivery more sustainable. In addition, multiple European governments have made an explicit pledge since the 2021 UN Climate Change Conference in Glasgow to ambitiously reduce healthcare's negative impact on the environment, in line with the European Green Deal.

Reducing carbon footprint

A quickly expanding body of literature focuses on more detailed examinations of the carbon

footprint of healthcare and ways to reduce its impact. Especially in the acute care sector, evidence is starting to accumulate of the environmental impacts of single-use medical items, medication such as anaesthetic gasses, and energy usage of highly demanding heating, ventilation, and air conditioning systems.[5] Where possible, recommendations to reduce the carbon footprint are made based on life cycle assessments of products or care pathways – an extensive methodology for environmental impact quantification. Generally, one can rank the expected environmental benefit of choices using the "R-levels" of circularity: to Refuse or Reduce usage of a product or service (largest benefit) or to Recycle or Recover once disposing (smallest benefit).[6] The higher the level, the more environmentally friendly the choice is (see Figure 1). Much work remains to be done, however, to make underlying research data findable, accessible, interoperable, and reusable.

Carbon footprint thinking, however, might be limited in its reductionist perspective on the impact of healthcare. Essentially, the focus of carbon footprint research is to quantify and minimise the negative effects of regular care delivery – a type of environmental efficiency, in a way. The healthcare sector is therein framed as an isolated service, which needs to transition to a more environmentally sustainable way of operating. In order to do so, suggestions have been made previously to make environmental sustainability an integrated characteristic of healthcare quality assessment.[7] Yet in daily practice, this frequently raises discussions regarding compatibility with patient safety, maintenance of high-quality care, and sectoral challenges such as financial and staffing issues. Moreover, focusing on the carbon footprint of healthcare might downplay concern for other environmental impacts such as water usage and ecotoxicity.

A positive alternative

Handprint-thinking can be a positive and activating addition to further develop our engagement with environmental sustainability. Unlike footprint-thinking, it requires us to think about ways to consciously *increase* our impact in contributing to a healthy life on this

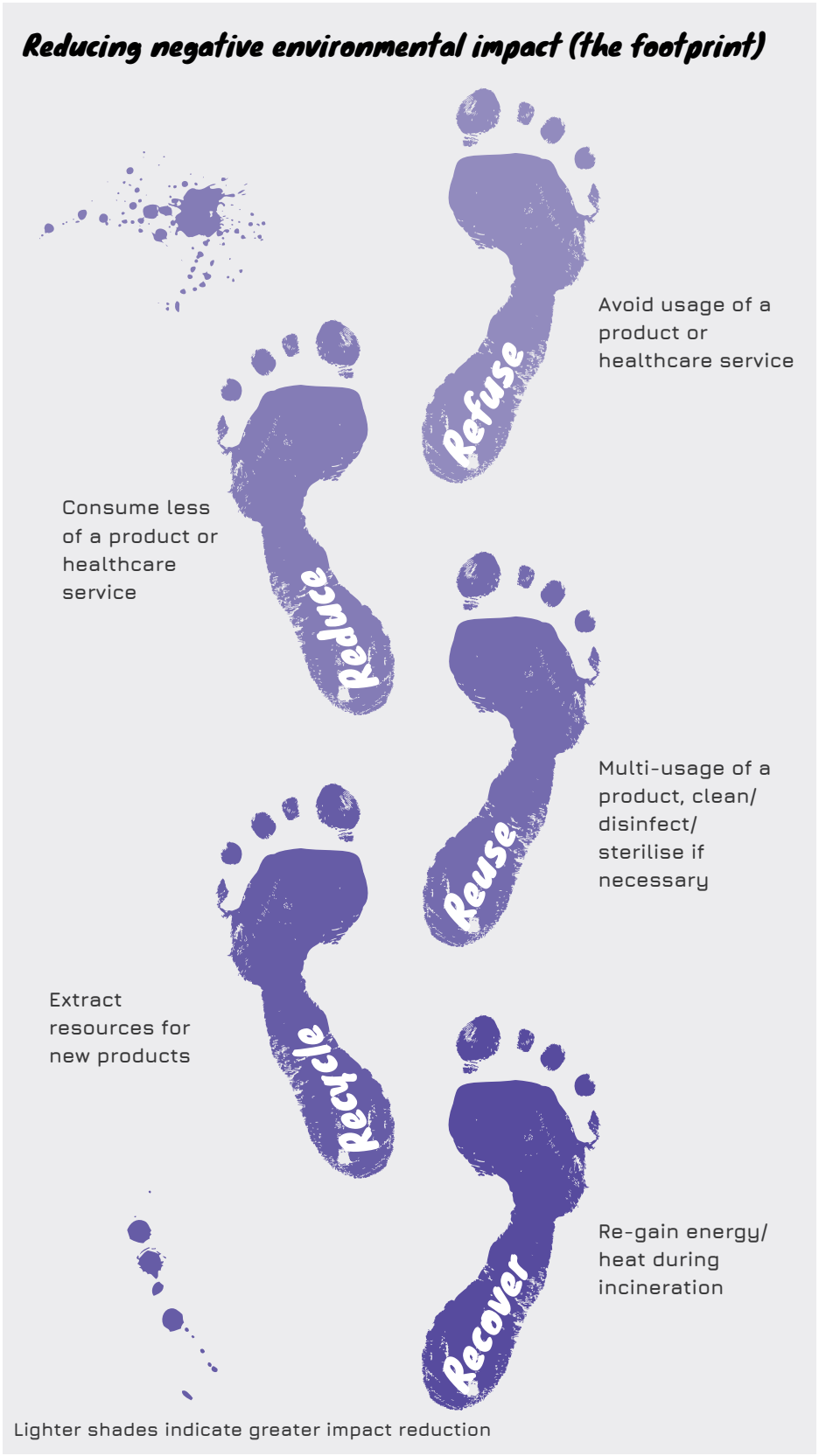

Figure 1. The R levels of circularity

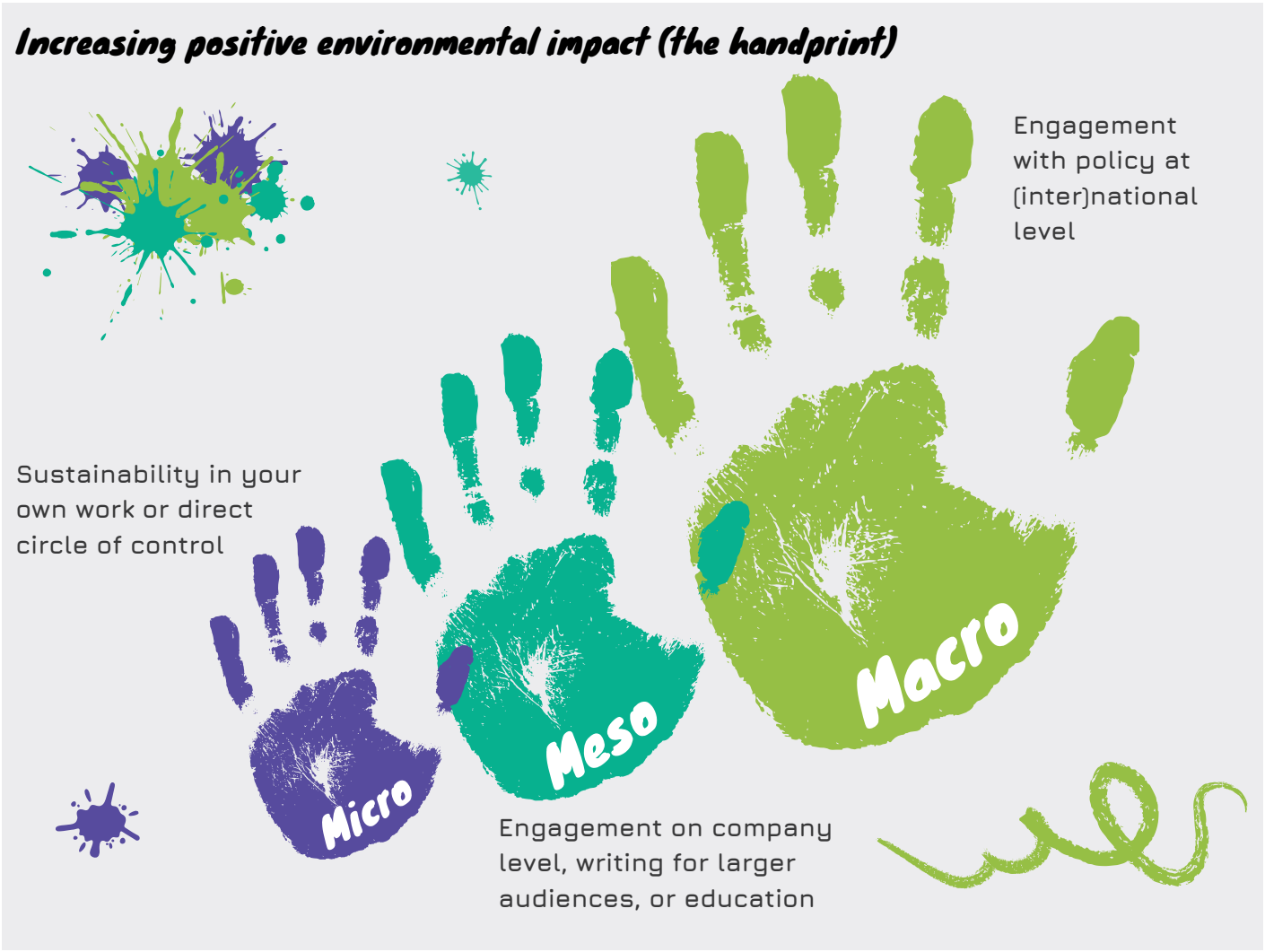

Figure 2. The handprint levels of positive environmental impact

planet.[8] We can have an impact on a micro, meso, or macro level (Figure 2). For example, by making food choices that benefit both our health and the environment (micro), by partaking in local initiatives for more vegetation in the places we live (meso), and by advocating for policies that address health inequities which would be enlarged due to climate change (macro). In medicine, this coincides with a transition to prevention of disease through healthy behaviour and healing environments, which frequently overlaps with climate-friendly measures.[9] In literature, these environmentally friendly and health promoting options are frequently referred to using the term "co-benefits".

The healthcare sector could be one of the leading voices in a regenerative movement that strives to safeguard planetary health. On an individual level, healthcare professionals are regarded as a trusted source for personal advice and healthy behaviours. On a societal level, they have the authority – and quite possibly the responsibility – to represent public interests in health and wellbeing. This also became apparent during the last coronavirus pandemic, as health professionals took a leading role in vaccination campaigns and media debates regarding preventive measures. A recent review of physicians' perspectives to prescribe interventions or behaviours which benefit both the patient's and the planet's health, however, pointed out that understanding and guiding policy statements to be able to do so are frequently missing.[10]

> Especially in the acute care sector, evidence is starting to accumulate of the environmental impacts of single-use medical items

Picking up the pen

Medical writers and communicators are naturally in a strategic position to pick up the pen to lead and inspire action for planetary health. As previously written in this journal: "Sustainability is not just a lifestyle choice – it is a professional responsibility."[11] Communication regarding the co-benefits for planetary and human health is crucial to drive conversation and knowledge attainment regarding the benefits of handprint-thinking. Education of healthcare professionals, and related industries, should be one of the key focus areas to get the message of planetary health across.[12] In addition, medical writers can engage their readers to consider implications of research and healthcare policies for both the planet and the individual, and aid in valorisation of findings in environmentally inclusive policies. The audience of these writings can vary: a small group

in one's network (micro), a larger company or organisation (meso), or an institute for policymaking on a national and international (macro) level.

The urgency of the global climate and environmental crises requires each of us to act on a level that suits our (professional) interests and capabilities. Possibilities to make a positive contribution to planetary health are plenty, including the way medical writing is practiced and the content of the writing itself. The choice really lies with each and every individual to make. Kindly do ask yourself: "How am I part of the solution today?"

Disclaimers

The opinions expressed in this article are the author's own and not necessarily shared by the Leiden University Medical Centre (LUMC) or EMWA.

Disclosures and conflicts of interest

The author declares no conflicts of interest.

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Author information

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Sustainability spotlight: Egid van Bree, MD

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Medical Writing (MEW): Hi Egid, thank you for taking the time to speak with us to tell us about how to integrate sustainability in your work as a medical doctor and researcher. To start, can you tell us how your involvement with sustainability began and how you came to be involved with the Dutch Green Health Alliance (Groene Zorg Alliantie)?

EvB: When I was a medical student, I was a member of Dutch Medical Student Union and there was a specific working group looking at sustainability issues in healthcare. I served in this working group and through this, I met other like-minded healthcare professionals and groups that aimed to make healthcare more sustainable; some were also focussed on international/global health and planetary health. Around two years ago (during the peak of the COVID pandemic), our working group and these other groups (about 11 or so) organised an online meeting to see how we could support each other by collaborating and sharing knowledge. This online meeting was the start of the Green Health Alliance.

Our association is now a thriving network of 40+ so-called "national commissions" and 100+ "green teams". National commissions are groups organised at the level of national healthcare professional associations (e.g., gastroenterologists, general practitioners, nurses). Green teams are local groups, for example, a given department in a hospital, that try to do things on a daily basis. Our two key pillars are 1. to help connect people and groups so they can collaborate and share knowledge; and 2. to act as a voice for change through advocacy and involvement in the political discussion and debate in the Netherlands.

"Planting seeds" and grassroots action are ways to overcome resistance and facilitate change.

MEW: In speaking with others involved in sustainability endeavours, it seems that a common challenge that they encounter is overcoming the resistance in others. Have you encountered "resistance"? If so, in what form and can you share how you overcame this resistance? Can you share a "success story" with us?

EvB: This past May, I was involved as a reporter during the Green Week of the Royal Dutch Medical Association (Koninklijke Nederlandsche Maatschappij tot bevordering der Geneeskunst, [KNMG]). I think this is a nice example of how "planting seeds" and grassroots

Szechuan Egglant with Tofu

Makes 4 servings

Adapted from the Vancouver Sun Six O'Clock Solutions
Pacific Press Books, 1995 (my go-to for workday dinners)

Ingredients

- 350 g aubergines or Japanese eggplants, trimmed and cut into 5 x 1 cm pieces
- 90 ml vegetable oil
- 15 ml chopped garlic
- 15 ml chopped fresh ginger
- 20 ml hot bean sauce
- 125 ml vegetable stock
- 25 ml dark soy sauce
- 5 ml sugar
- 170 g packaged fried tofu, diced
- 7 ml sesame oil
- 7 ml Chinese brown vinegar or rice vinegar
- 45 ml chopped green onions, divided

Directions

- In a wok or large heavy frying pan, heat vegetable oil over high heat. Add aubergine/egglant, reduce heat to medium-low; stir-fry until soft and golden (about 5 min). Remove and set aside.
- Add garlic, ginger, and bean sauce to the wok/frypan. Stir-fry for 10 seconds. Add stock, soy sauce, sugar; bring to boil over medium-heat. Add tofu; cook for 1 minute.
- Then return eggplant to the frypan and cook for 2 minutes or until the sauce has been absorbed. Add sesame oil, vinegar, and 30 ml green onions. Stir until heated through.

- Place in a serving dish and sprinkle with remaining 15 ml green onions.
- Serve with rice.

Tips

- If you don't have fried tofu on hand, you can use pressed firm tofu instead.
- Press tofu by wrapping the tofu between a cheese cloth or tea towel, placing it on a plate, and putting cutting board on top. Let sit for about 30 minutes to get the moisture out.
- Hot bean sauce is also known as "chilli bean paste", "spicy broad bean paste", "broadbean, chilli sauce" or "tobanjan" to name a few.

action is a way to overcome resistance and facilitate change.

Going back to the Dutch Medical Student Union, this union is a branch of the KNMG, and our working group pushed to get sustainability onto the KNMG's agenda. However, at the time, there was little recognition from the top to make this a priority. But now, 2 to 3 years later, the KNMG started hearing how local groups of their membership wanted to organise local activities simultaneously to raise awareness and promote sustainability. Thus, they realised that their members are interested in sustainability and got involved as the coordinating entity, and the Green Week event was born. Parallel to this, draft policies on healthcare and sustainability from the EU were being created and the KNMG needed support from someone with this expertise during the review process. The board members, who knew me from the time I was a part of the student working group, consulted me as an expert to advise on these policies. This eventually led them to hire me as a reporter during the Green Week to report on the different activities. In one district, they showed films on sustainability, another held activities in an edible forest, and others held lectures and discussions. During the week, I also worked together with a colleague who acted as a cameraman, and at the end of each day, we created short videos to summarise the highlights to upload onto the KNMG website.

MEW: It sounds like it was a fun, intense week as a reporter. And this is indeed interesting and encouraging to hear how your earlier work and efforts and grassroot activity led the KNMG to embrace sustainability. Do you have any other last tips to share, especially to get governing bodies to act?

EvB: Yes, when dealing with entities that are slower to change, be patient and persistent while pushing as many buttons as possible. Repeat arguments. And when you invite them to participate, make it easy for them to participate. Do you know that train analogy? It's like you do the work to get the train moving and then invite the others to jump on. And plant as many seeds as possible.

CONTACT US

If you have ideas for themes or would like to discuss any other issues, please write to mew@emwa.org.

Upcoming issues of **Medical Writing**

December 2023: **Biotechnology**

Biotechnology uses biological systems and living organisms in R&D and production processes. Biotechnologies include biologic and biosimilar pharmaceuticals like monoclonal antibodies, vaccines, and advanced therapy medicinal products, for example, gene and cell therapies and tissue engineered products. In addition, biotechnologies support the product lifecycle, for instance, in non-clinical work using in silico, in vitro, and animal testing methods. Also, support services personnel like those in biobanks and supply chains require an understanding of biotechnology. This issue focuses on the crucial role of writing and communications in biotechnology and product development.

Guest Editors: Jennifer Bell
The deadline for feature articles has now passed.

March 2024: **Translation**

Medical translation is a complex and demanding field requiring specialised knowledge, skills, and expertise. In this issue, we explore a range of topics, including the role of medical translation in clinical trials and regulatory affairs, the importance of terminology management, the use of technology and machine translation, ethical and legal considerations, the impact of cultural differences, quality assurance and risk management, and the emerging trends and challenges in the field.

Guest Editors: Ana Sofia Correia and Claire Harmer
The deadline for feature articles is December 1, 2023.

June 2024: **Soft Skills for Medical Writers**

Medical writing is a highly specialised field that requires a unique combination of technical knowledge, writing skills, and soft skills to produce high-quality work. While technical knowledge and writing skills are undoubtedly important, it is how one interacts with people that can truly set medical writers apart and enable them to succeed in their careers. This issue will focus on how soft skills are used within the different areas of the medical writing industry, and we hope it will provide valuable insights and inspiration for medical writers at all stages of their careers.

Guest Editors: Clare Chang and Nicole Bezuidenhout
The deadline for feature articles is March 1, 2024.

September 2024: **Clinical Trial Transparency and Disclosure**

The clinical trial transparency and disclosure space continues to grow at pace. With the EU Clinical Trial Regulation being applicable since the 2022 launch of the Clinical Trials Information System comes increased requirements for public-facing documents. Provision of a summary of clinical trial results in lay language is also now mandatory in the EU. Challenges continue in balancing protection of personal data of trial participants with transparency, especially in the wake of the COVID-19 pandemic. All of these bring opportunities for medical writers to drive best practice in authoring clinical trial documents with disclosure in mind.

Guest Editors: Holly Hanson and Alison McIntosh
The deadline for feature articles is June 1, 2024.

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