

My First Medical Writing

SECTION EDITOR



Evguenia Alechine
ealechine@gmail.com

Editorial

In this release of My First Medical Writing, I have the pleasure to share great articles written by two aspiring medical writers. Nesrine Benhizia-Benaouicha, MD, is a clinical trial manager and academic medical writer at the emergency department in Nantes University

Hospital, France, with extensive experience in clinical trial management and recruitment in the ER. Sofia Polcownuk has a PhD in biology from the University of Buenos Aires, Argentina, and is currently a research associate at the University of Glasgow, UK, focused on understanding the gut-brain axis. It has been a pleasure working

with both Nesrine and Sofia in publishing their first articles in *Medical Writing*. If you're an aspiring medical writer eager to gain experience in this field, this space offers you an opportunity to publish your work and start creating your portfolio.

Evguenia

Clinical trial management and patient recruitment in the emergency department

Everyone is probably familiar with *ER*, an American television series created by Michael Crichton that aired on NBC for 15 years. In that fictional emergency room, many popular topics were discussed between patients and physicians, for example, HIV status, the catastrophic situation in Congo-Kinshasa and Darfour, deafness and sign language, euthanasia, and Social Security problems.¹ However, did you know that in a real ER, or emergency department (ED) as it is more formally known, the physicians are also conducting and discussing clinical research projects?

Emergency medicine is a universal and transversal discipline at the junction of several disciplines. It is a science of acute pathologies and the overall management of the patient. The major asset of emergency medicine lies in the diversity of its practices, which includes triage, pre-hospital emergency care, emergency response for disaster management, etc. Otherwise, within the ED, physicians don't just manage critical situations, they also conduct research, as in any other other speciality. This is made possible due to the recognition of emergency medicine as a stand-alone speciality, which is the case in the US and in 17 countries in the European Union with national and international scientific conferences.²

The strength of a discipline's research is also measured by its organisation and the dissemination of knowledge. In a recent Canadian survey assessing the level of development of the emergency medicine system in 36 countries, 70% of the nations had national emergency medicine

research.³ Emergency medicine is widely represented in the international scientific literature. There are six international Anglo-Saxon and two European indexed journals dedicated to emergency medicine, including the *American Journal of Emergency Medicine* and the *European Journal of Emergency Medicine*. The major generalist scientific journals (e.g., the *New England Journal of Medicine*, the *Lancet*, and the *British Medical Journal*) also devote considerable space to clinical research in emergency medicine. Clearly, research is a priority for emergency medicine as it is for non-



Nesrine Benhizia-Benaouicha, MD
Nantes, France
nesrine.benhizia@gmail.com

emergency medicine.

Research provides the foundation for everything we do in medicine. In particular, bedside clinical research, in which patients are prospectively enrolled in clinical trials, including those that compare therapeutic strategies, is important to efficient and cost-effective patient care.⁴ However, bedside research in the emergency



Photo: Alamy

context presents a number of challenges. Indeed, the emergency and pre-hospital environments are unlike any other clinical environment and require special consideration to allow the successful implementation of clinical trials.⁵ In addition, research projects in emergency medicine are not limited to this speciality but often involve the collaboration of multiple specialities such as cardiology, neurology, infectious disease, etc., due to its transversal nature and that the ED is the gateway for the patient who enters the hospital. Rightly so, emergency departments across the world are becoming increasingly crowded. The numbers and the complexity of patients arriving in the ED are increasing.⁶ The caregivers have neither the time nor the resources to help with research, making it a challenging environment to incorporate clinical research in addition to providing effective and timely care.

With this in mind and considering the complexities of implementing a protocol in an emergency context, when designing project research, investigators need to make sure the intervention and flowchart of the trial are not overly complex and should demonstrate that participants are available for recruitment into their studies. Hence, emergency medicine researchers should optimise the design and implementation of trials to accommodate the ED setting that must include only key intervention and data points while adhering to the regulatory framework of clinical research. In order to do that, they should work with clinical research staff early in the protocol development. That staff can include clinical project managers, study coordinators, biostatisticians, pharmacists, and medical writers. They would help to guide investigators during the trial design in an effort to maximise study efficiency in the ED environment. Therefore, involving clinical research staff is an important way to improve successful implementation, in order to take advantage of the millions of ED patients who could be eligible to participate in clinical trials. It is also essential to provide evidence that a sufficient number of eligible subjects can be enrolled in the protocol in a timely manner, which is crucial to receiving funding.

When implementing trials in the ED, one must focus on identifying participants who meet eligibility criteria to enter prospective studies. In each trial, inclusion and exclusion criteria must

be defined, for example, you must be female (inclusion criteria) and not be pregnant (exclusion criteria). The screening and identification of participants are other significant challenges in the ED, where timing from arrival to the need for treatment is tight (e.g., a research project about acute pain management, acute health failure, etc.). Physicians identify potential obstacles to

recruitment, such as real-time identification of eligible participants and consent issues. That said, there are specific strategies to enhance recruitment into trials.

For example, when using Electronic Medical Records (EMR), software can provide a timely and efficient method of identifying participants. This software connects to EMR for screening of existing medical data and when a study matches

the patient's medical record, an alert is sent in real-time through central paging to the physician and study coordinator. For example, we want to select patients who have a prescription for a particular antibiotic. When the physician prescribes this antibiotic in the EMR, an alert is sent with this message: "This patient is potentially eligible for project X, please contact research member staff". Such software has been used successfully to recruit participants into prospective studies. There has been an increase in the number of enrolments in a study using clinical trial alerts within an EMR.⁷

But this software is not the only tool used to alert research staff of potential participants. Other alerts include study documentation sheets included in kits (e.g., in lumbar puncture kits for meningitis studies), advertising posters, and leaflets with concise information about ongoing recruitment for studies.

Another way to further research is when research staff, physically present in the ED, work closely with clinical teams and can be involved from identification and recruitment of the patient to the final follow-up visit in the trial. They can manually review electronic medical records of admitted patients to screen potential participants. A study coordinator or a specific research staff member (e.g., a study nurse), who is either dedicated to reviewing current patients in the ED or the alert in central paging, is essential to capture all eligible participants.⁸ Many academic EDs have invested in research personnel. The skills and experience of these individuals to enrol patients into interventional clinical trials are proven. The funding is often being shared across

multiple projects. Therefore, there needs to be enough volume of patients and studies to justify the effort and cost of their full-time presence.⁹

Moreover, research staff support physicians to obtain informed consent from the patient to take part in a clinical trial, which must be written, dated, and signed. According to Good Clinical Practices, a clinical trial may be undertaken only if the trial subject had the opportunity, in a prior interview with the investigator, to understand the objectives, risks, and inconveniences of the trial and they are able to give informed consent, or a legal representative may do so when the patient is not able to give informed consent. But, obtaining consent in the ED is nearly always problematic. The time frame available to recruit participants in emergency medical clinical trials is often far tighter than for standard trials.¹⁰ Patients are frequently sedated, unconscious (e.g., cardiac arrest), or, when conscious, are stressed and highly dependent on the medical team. Likewise, the legal representative is rarely on the spot.¹¹

Exception From Informed Consent (EFIC) has been used successfully to enrol participants into research in the pre-hospital and ED setting when a patient or their legal representative are not available. EFIC allows the enrolment of participants into studies without prior consent when the following criteria are met:

- it must be a life-threatening situation,
- available treatments are unproven or unsatisfactory,
- participation in the research holds out the prospect of direct benefit to the participants,
- and the clinical investigation could not practicably be carried out without the exception and the Office of Human Research Protections, which must allow using this EFIC.¹²

However, even if consent is waived before enrolment, the notification must be done and consent obtained from the patient or legally authorised representative as soon as possible.

Finally, research staff members are also involved in the follow-up of the patients. Indeed, a key for a successful study is time to follow-up with participants. The follow-up in emergency medicine clinical trials must be short (e.g., hospital discharge or on day 28) and by phone. Clearly, the longer the follow-up, the greater the risk of losing patients. There is also the risk of protocol violations and refusing patient refusal to schedule a follow-up visit. These risks can be minimised with strict oversight by research staff members. Indeed, they should be in close contact with participants and record telephone follow-

ups in a log, keeping track of the best times to contact the patient. While it is generally ideal to have a phone follow-up, this can also be done through research units with their research staff (e.g., study nurses) scheduling follow-up visits according to the availability of physicians. Furthermore, if participants should be given study-specific visits, consider who have physical and logistical difficulties returning for follow-up.

Otherwise, if participants are compensated for transport costs to themselves and their visits are at no cost, they are more likely to remain in the study.

Clinical research in emergency medicine is an evolving field. Currently, new projects are being developed in the field of big data, artificial intelligence, and machine learning. Artificial intelligence can improve emergency care, help with diagnosis and manage patient flows. Research in emergency medicine has a bright future ahead.

References

1. The Emergency Room series. Available from: [https://en.wikipedia.org/wiki/ER_\(TV_series\)](https://en.wikipedia.org/wiki/ER_(TV_series))
2. Adnet F. La recherche en médecine d'urgence : vers la création d'une discipline scientifique majeure. *Réanimation*. 2004;13: 463–4.
3. Arnold JL, Dickinson G, Tsai MC, Han D. A survey of emergency medicine in 36 countries. *Can J Emerg Med*. 2001;3:1–3.
4. Brown SGA, Isbister GK. Clinical research is a priority for emergency medicine but how do we make it happen, and do it well? *Emerg Med Australas*. 2014;26(1):14–8.
5. Cofield S, Conwit R, Barsan W, Quinn J. Recruitment and retention of patients into emergency medicine clinical trials. *Acad Emerg Med*. 2010;17(10):1104–12.
6. Fisher J, Sokolove PE, Kelly SP. Overcrowding: harming the patients of tomorrow? *Acad Emerg Med*. 2009;16(1):56–60.
7. Embi PJ, Jain A, Clark J, Harris CM. Development of an electronic health record-based Clinical Trial Alert system to enhance recruitment at the point of care. *AMIA Annu Symp Proc*. 2005:231–35.
8. Isaacman DJ, Reynolds EA. Effect of a research nurse on patient enrollment in a clinical study. *Pediatr Emerg Care*. 1996;12(5):340–2.
9. Hollander JE, Sparano DM, Karounos M, Sites FD, Shofer FS. Studies in emergency department data collection: shared versus split responsibility for patient enrolment. *Acad Emerg Med*. 2004;11(2):200–3.
10. Herlitz J. Consent for research in emergency situations. *Resuscitation*. 2002;53(3):239.
11. Lemaire F. European Society of Intensive Care Medicine statement: clinical research in the intensive care unit. *Intensive Care Med*. 2002;28:1218–9.
12. Ernst AA, Fish S. Exception from informed consent: viewpoint of institutional review boards – balancing risks to subjects, community consultation, and future directions. *Acad Emerg Med*. 2005;12(11):1050–55.

A gut-feeling: How intestinal diseases can affect our sleep

Do you lie awake at night feeling that something bad may happen? You might think that you are crazy, but don't worry, you are not alone. Almost every animal carries in their gut microorganisms such as bacteria, forming the microbiota, a complex community of different species living in their intestines. These microorganisms influence our health and fitness. There is a deep connection between what is happening with the microbiota in our gut and changes in our sleep patterns. The bacteria in our intestines can influence sleep by communicating with the brain through the gut-brain axis.

Gut-brain axis

The gut and the brain have a close relationship and communicate with each other in two different ways:

- The nerves around the intestine, the enteric system, receive and send signals to and from the brain.
- The microbiota themselves send messages to the brain.

The microbiota releases small molecules, called neuropeptides, and hormones. In the intestine, these molecules are absorbed and finally reach the blood. Through the circulatory system, these signals contact the brain where they bind to receptors, unleashing different physiological or behavioural changes.

Sleep problems and gut disease

Researchers have found a strong relationship between insomnia and gut disorders. Patients who suffer from intestinal problems often report more frequent night-time awakenings, while other patients who suffer from more aggressive gut diseases, like colorectal cancer, also report that the duration and quality of sleep are affected.¹ The bacterial composition of the gut in patients with cancer is different compared to healthy people and this difference in the microbiota is strongly associated with the quality of sleep.¹



Sofia Polcownuk, PhD
Glasgow, UK
sophiepol8@gmail.com

Red flag for colorectal cancer

Experiencing some discomfort in our intestine once in a while is normal, but when it occurs often, we need to be alert. Intestinal inflammation and changes in our bowel habits or sleep patterns have been researched as red flags for the beginning of colorectal cancer. These changes may potentially allow an earlier diagnosis, improving treatment and survival.²

Colorectal cancer and microbiota disruptions

Our gut bacteria help us maintain intestinal homeostasis by regulating biological functions (like immunity), protecting our intestine, and regulating our metabolism. Colorectal cancer is

Amongst the small molecules that the bacteria produce, short-chain fatty acids are very important.

These molecules are produced when the bacteria ferment the fibre we eat and have a positive effect on the gut, in particular on the intestinal mucosa. In the gut of patients with intestinal problems, like inflammation, there is a reduction of these molecules compared with healthy individuals.



one of the most common cancers worldwide and one of the most aggressive gut diseases. Nowadays, there is evidence about how gut bacteria can make us more susceptible to this pathology and affect its progression. These bacteria can produce small molecules involved in tumour growth or suppression.³ Amongst the small molecules that the bacteria produce, short-chain fatty acids are very important. These molecules are produced when the bacteria ferment the fibre we eat and have a positive effect on the gut, in particular on the intestinal mucosa. In the gut of patients with intestinal problems,

like inflammation, there is a reduction of these molecules compared with healthy individuals. Abnormal levels of these fatty acids can indicate gut microbiota dysregulation and a loss of bacterial diversity, which can trigger intestinal diseases like colorectal cancer.^{4,5}

Patients with colorectal cancer have less specific types of so-called “good bacteria”, like *Lactobacillus* and *Bifidobacterium* spp., and more that can cause inflammation, like *Escherichia* and *Klebsiella* spp. Studies analysing faeces from patients with colorectal cancer with poor sleep quality revealed an increasing amount of “bad

bacteria” while healthy individuals who reported good sleep had more “good bacteria”.⁶

We dreamed even before we had a brain

Sleep has been conserved throughout evolution. Even the most primitive animals that have a less complex brain than humans need sleep. Interestingly, since during sleep we are in our most vulnerable state, there must be something behind this behaviour that pushes all animals to risk their lives every day to sleep.⁷ Indeed, while we are sleeping, we think that everything is on pause but



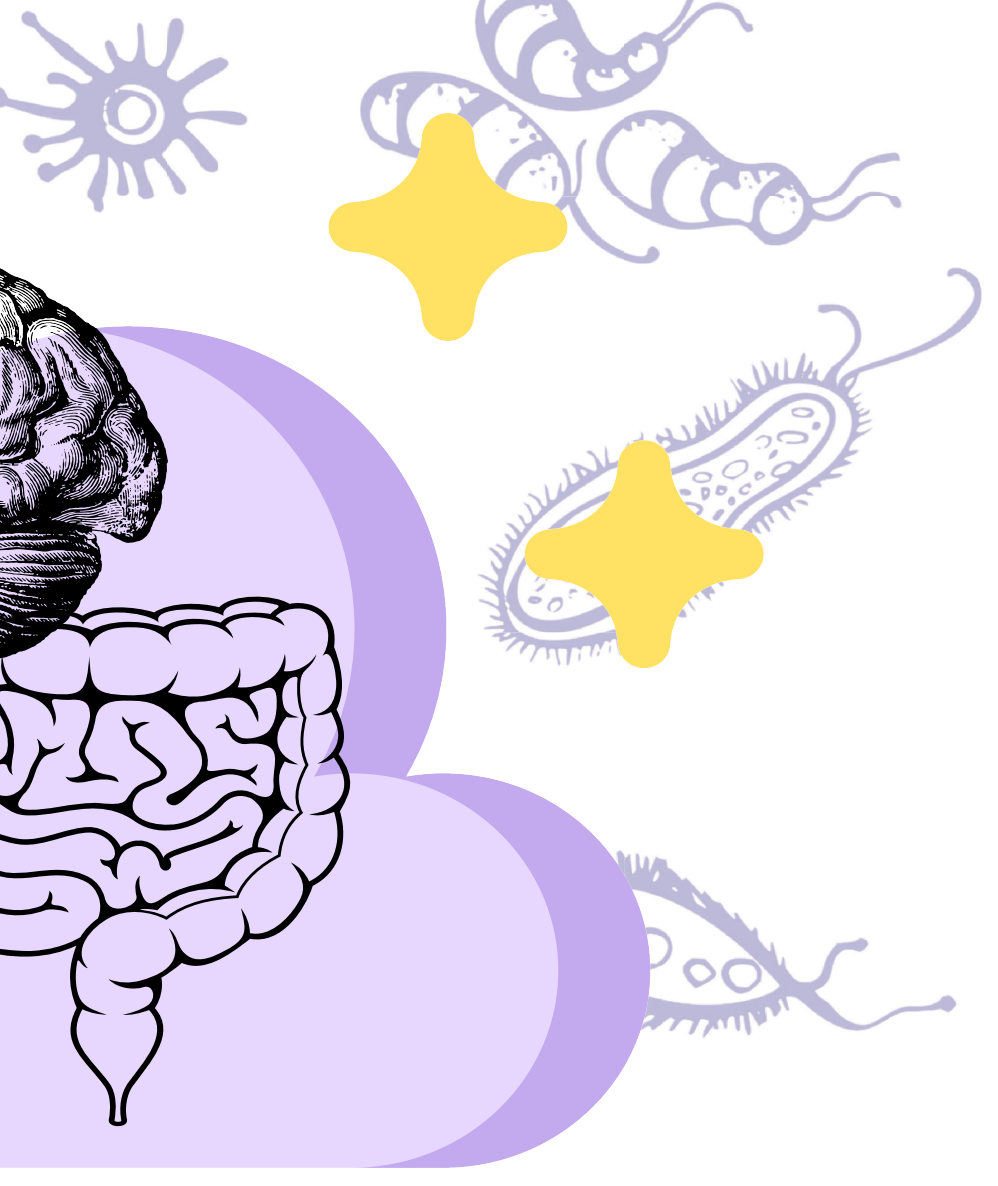
This is called the hash, pound, or number character. A hashtag is a keyword or set of keywords that is preceded by the # character. It is used in social media to create a thread of conversations around a specific theme or topic conveyed in short texts or microblogs. It is commonly used in Twitter, Instagram, YouTube, Pinterest, etc.

A dictionary of most common hashtags can be found at <https://www.hashtags.org/definition/~h/>. For your info, EMWA is compiling a list of standardised hashtags for our social media use.



This is called the “at” sign or symbol. The @ sign is part of email addresses and social media user names (“handles”). Our EMWA handles are as follows: @Official_EMWA (Twitter), @EMWA (LinkedIn), and @europeanmedicalwritersassociation (Facebook)

The two most important keys on your keyboard



a lot of things are taking place. When we are sleeping the pituitary gland in the brain releases growth hormone which helps our bodies to grow and repair. During sleep, we also consolidate what we have learned and memorised the day before.^{8,9}

How bacteria affect our sleep

Researchers in the last decade have shown that sleep is affected by external and internal cues, like circadian rhythms and feeding. Our eating habits can affect our microbiota composition and therefore the amount and type of metabolites they release. Studies in mice depleted of microbiota showed impairment of sleep associated with a drastic reduction in serotonin levels, an important regulator of sleep. Thus, microbiota imbalance can affect our sleep by altering the intestinal balance of neurotransmitters.¹⁰

Changes in the diversity of our gut bacteria can affect our intestinal function and make us more vulnerable to intestinal diseases. How can we know if something is going wrong in our gut microbiota? Because the gut communicates with the brain through the gut-brain axis – signals

coming from the microbiota can affect our behaviour. Nowadays, more studies show that by tracking our changes in mood, sleep, or eating habits, we can modify our lifestyle to improve our gut and overall health.¹¹

How can we help our bacterial community and improve our sleep?

Diet and lifestyle are important factors to achieve overall health, prevent gut disorders, and reduce the predisposition to developing more serious diseases. Eating more fibre-rich foods, vegetables, and fruits, and avoiding antibiotics when they are not needed, can help you to keep a healthy gut.¹²

Despite all the information available nowadays, further research is needed to understand the link between gut disease, microbiota, and sleep. Studies with animal models like mice and fruit flies can help researchers understand behavioural changes in the early stages of the disease. In the future, we could use sleep tracking as a diagnostic tool to detect gut dysfunction at its onset and help prevent the development of more aggressive pathologies like colorectal cancer.

References

1. Chen W, Liu F, Ling Z, Tong X, Xiang C. Human intestinal lumen and mucosa-associated microbiota in patients with colorectal cancer. *PLoS One*. 2012;7(6):e39743.
2. Hippisley-Cox J, Coupland C. Identifying patients with suspected colorectal cancer in primary care: derivation and validation of an algorithm. *Br J Gen Pract*. 2012;62(594):e29–37.
3. Belkaid Y, Hand TW. Role of the microbiota in immunity and inflammation. *Cell*. 2014;157(1):121–41.
4. Zackular JP, Baxter NT, Iverson KD, Sadler WD, Petrosino JF, Chen GY, Schloss PD. The gut microbiome modulates colon tumorigenesis. *mBio*. 2013;4(6):e00692–13.
5. Parada Venegas D, De la Fuente MK, Landskron G, et al. Short chain fatty acids (SCFAs)-mediated gut epithelial and immune regulation and its relevance for inflammatory bowel diseases. *Front Immunol*. 2019;10:277.
6. Smith RP, Easson C, Lyle SM, et al. Gut microbiome diversity is associated with sleep physiology in humans. *PLoS One*. 2019;14(10):e0222394.
7. Keene AC, Duboue ER. The origins and evolution of sleep. *J Exp Biol*. 2018;221(Pt 11):jeb159533.
8. Tarasiuk A, Berdugo-Boura N, Troib A, Segev Y. Role of growth hormone-releasing hormone in sleep and growth impairments induced by upper airway obstruction in rats. *Eur Respir J*. 2011 O;38(4):870–7.
9. Rasch B, Born J. About sleep's role in memory. *Physiol Rev*. 2013;93(2):681–766.
10. Ogawa Y, Miyoshi C, Obana N, et al. Gut microbiota depletion by chronic antibiotic treatment alters the sleep/wake architecture and sleep EEG power spectra in mice. *Sci Rep*. 2020;10(1):19554.
11. Smith RP, Easson C, Lyle SM, et al. Gut microbiome diversity is associated with sleep physiology in humans. *PLoS One*. 2019;14(10):e0222394.
12. Liu X, Cao S, Zhang X. Modulation of gut microbiota-brain axis by probiotics, prebiotics, and diet. *J Agric Food Chem*. 2015;63(36):7885–95.