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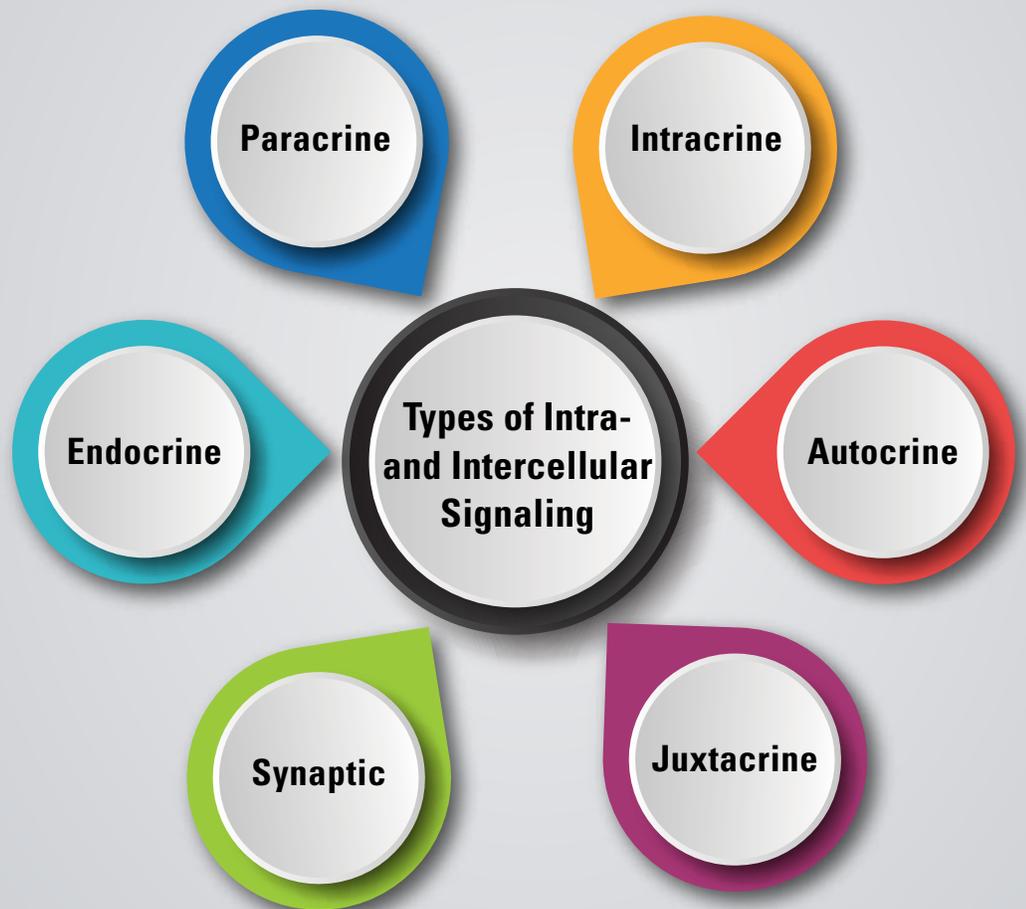
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Melissa L. Bogen, ELS

Sherry Bowen, MA, ELS

Lori De Milto, MJ

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CONTACT: American Medical Writers Association, 30 West Gude Drive, #525, Rockville, MD 20850-4347. Phone: (240) 238-0940; Fax: (301) 294-9006; Email: amwa@amwa.org.

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How Cells Communicate, Part 2: Sending and Receiving Signals

By Laurie Endicott Thomas, MA, ELS / Author and freelance medical writer; Madison, NJ

The human body is a macro-organism that is made up of trillions of micro-organisms: cells. The human body can function as a single, integrated organism because of the ways in which its cells communicate with each other, as tissues, as organs, and via the pathways that connect them. Part 1 of this series introduced the endocrine system and the concept of feedback loops. This article, which is part 2 of a 3-part presentation, will describe the kinds of chemicals that carry messages between cells and the receptors that receive those messages.

MESSAGING AND MESSENGERS

The messages that are passed from one cell to another can be categorized according to the distance that the message travels (Table 1).

Many different kinds of chemicals can serve as messengers that can carry a signal from one cell to another. These chemicals can be sorted into 4 broad categories:

- **Hormones** are the signaling chemicals used by the endocrine system (distant effects).
- **Neurotransmitters** are the signaling chemicals used by the nervous system. They usually work within the synapse between 2 nerve cells or between a nerve ending and some other cell (eg, a muscle or gland).
- **Cytokines** are signaling proteins of the immune system. Normally, they have paracrine effects (local effects).
- **Eicosanoids** are produced by the oxidation of polyunsaturated fatty acids, such as arachidonic acid. They can have autocrine, paracrine, or endocrine effects.

Even though these categories are handy for initially differentiating the body's chemical messengers, the boundaries between these categories are sometimes unclear. Hormones can also have local (paracrine) effects on the tissue that produced them; some neurotransmitters can enter the bloodstream and have endocrine-like effects on distant tissues; and

Table 1. Types of Intra- and Intercellular Signaling

Type of signaling	Description
Intracrine	Messenger is produced within a cell and has an effect within the cell.
Autocrine	Messenger is released by the cell and produces effects by interacting with receptors on the outer surface of the cell that released it.
Juxtacrine	A signal transmitted along a cell membrane can affect the emitting cell or the cells that it is touching.
Synaptic	Messenger (neurotransmitter) is released into a narrow gap between cells and interacts with the cell on the opposite side of the gap.
Paracrine	Messenger is released by the cell and diffuses over relatively short distances, to have effects on nearby cells. The diffusion may produce a concentration gradient. Cells exposed to a high concentration of signal may respond differently than the cells that receive a weaker signal.
Endocrine	Messenger is released into the bloodstream and has effects on target cells in distant tissue. A single hormone can have different effects on different kinds of tissue.

if cytokines enter the bloodstream in large enough amounts, they can produce a systemic effect, such as a fever.

The signaling molecules belong to several different chemical classes: lipids, phospholipids, amino acids, monoamines,

proteins, glycoproteins, and even some gases. Note that some hormones are proteins, some are lipids, and some are glycoproteins. In contrast, all cytokines are small proteins.

Some signaling molecules, such as the neurotransmitters, cannot easily pass through cell membranes. These molecules are often made ahead of time and stored in membrane-bound vesicles within the cell.¹ They are released when the vesicle is brought to the surface of the cell, so that the vesicle's membrane fuses with the cell membrane, releasing the vesicle's content. This process is known as exocytosis. Other signaling compounds, such as eicosanoids, can easily pass through cell membranes. For this reason, they cannot be stored inside a cell. Instead, their production is tightly regulated.²

Because the fat-soluble signaling molecules (including the steroid hormones) can easily pass through cell membranes, they can reach receptors that are inside a target cell. However, the fat-soluble molecules must generally be bound to a transport protein to be carried in the bloodstream. For example, most of the testosterone in the bloodstream is bound to albumin or sex-hormone-binding globulin. Yet as long as these fat-soluble compounds are bound to their transport protein, they cannot pass into the cell to reach a receptor that is inside the cell. Only a tiny proportion of the testosterone in the bloodstream is "free" (ie, not bound to a protein). Only the free testosterone molecules can enter the cell to exert their effect. Thus, conditions that alter the amount of sex-hormone-binding globulin in the bloodstream can alter the amount of free testosterone in the bloodstream and, therefore, the effect of testosterone in the body.³

In contrast, the water-soluble signaling molecules are easily transported in the bloodstream. However, they typically cannot pass through the cell membrane. Instead, they exert their effects by binding to the extracellular portion of a receptor protein that passes through the cell membrane of the target cell.

LIGANDS AND RECEPTORS

Signaling chemicals exert their effects by interacting with a protein that serves as a receptor. A chemical that binds to a receptor is called a ligand.

Protein Structure

To better understand how receptors work, you need to understand how the chemical messengers (ligands) can have such a precise fit with their receptors, and how a ligand's binding with a receptor can trigger effects. To understand that, you need to know something about the structure of proteins.

Proteins are made up of chains of amino acids. Up to 20 different amino acids can be used in making proteins, and a protein molecule can be thousands of amino acids long. All of the amino acids used in making proteins have the same basic

structure. They consist of a central carbon atom with an amine group (-NH₂) and a carboxyl group (-COOH) and a side chain (R). The amino acids within the protein are held together by peptide bonds, which are formed by the reaction between the carboxyl group of one amino acid and the amine group of the next one. As a result, the peptide chain will have an amine group (the N-terminal) on one end and a carboxyl group (C-terminal) on the other (Figure 1).

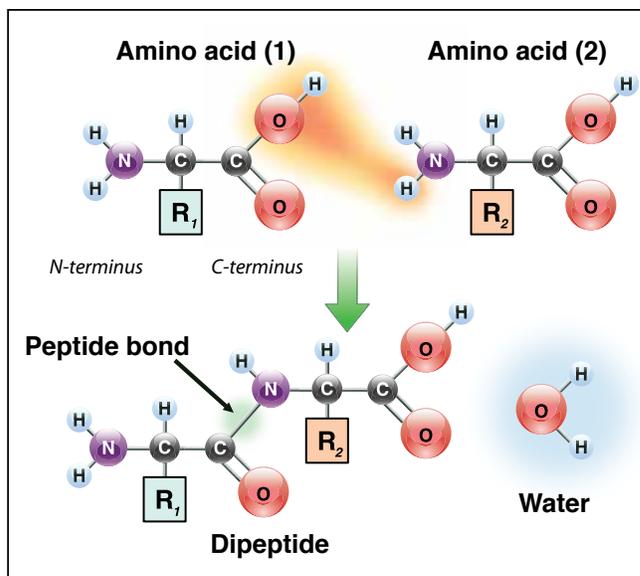


Figure 1. Protein molecules are made up of chains of amino acid residues, held together by peptide bonds. Reprinted from https://en.wikipedia.org/wiki/Peptide_bond#/media/File:Peptidformationball.svg.

A protein is merely a peptide chain that is at least 50 amino acids long. Each gene tells the cell which amino acids to use, and in what order, when building a peptide chain. This ordering of the amino acids is called the primary structure of the protein (Table 2 and Figure 2).

As the primary structure of the protein chain is being made, portions of it tend to take on a particular shape (secondary structure), which is determined by hydrogen bonding. Because of the way that electrical charge is distributed over the surface of the amino acid residues in the peptide chain, the amine group from one amino acid residue within the chain will be attracted to the carboxyl group of another amino acid residue a few units away, to form a weak hydrogen bond. Because of these hydrogen bonds, some portions of the peptide chain will twist into a spiral called an alpha helix. Other portions will form a flat zigzag (beta sheet).

Each of the 20 amino acids that are used in making proteins has its own unique side chain, which gives it unique chemical properties. Some of these side chains are either polar or electrically charged. As a result, they are attracted to water.

Table 2. Protein Structure

Primary	The exact sequence of amino acids, which are held together by peptide bonds.
Secondary	The pattern of hydrogen bonds between the amine hydrogen and the carboxyl oxygen atoms in the peptide backbone. It determines the 3-dimensional shape of local segments of the protein (eg, alpha helix or beta sheet).
Tertiary	The overall 3-dimensional shape of the protein, as a result of the interactions and bonds of the side chains of the amino acids.
Quaternary	The number and arrangement of multiple protein molecules in a multisubunit structure.

Others are neutral and nonpolar. As a result, they are hydrophobic (ie, they repel water but are attracted to oily materials [lipids]). Because of these interactions between the side chains, the protein will take on a fairly predictable 3 dimensional shape called the tertiary structure.

Many proteins are made up of more than one peptide chain. The number and arrangement of the protein subunits in a multisubunit complex is called the quaternary structure of the protein.

The precise, predictable shape of a receptor allows it to bind specifically to some ligands but not others. However, the action of binding to the ligand can produce a change in the shape of the receptor protein. It is this conformational change that then triggers the receptor's physiological effect.

Types of Receptors

The signaling chemicals (ligands) bind specifically with a particular receptor, just as a key fits a particular lock. The receptors are named after their ligand. Receptors are divided into families (indicated by a subscript number), and the families into subtypes (as indicated by a subscript letter). For example, 14 different receptors for serotonin (5-HT) have been discovered. They are divided into 7 families: 5-HT₁ through 5-HT₇. The 5-HT₁ family includes 5-HT_{1A}, 5-HT_{1B}, 5-HT_{1D}, 5-HT_{1E}, and 5-HT_{1F}.⁴

These various subtypes of receptor are expressed by different kinds of cells. For this reason, a single ligand can have different effects on different kinds of tissues. In the upper respiratory tract, histamine binds to H₁ receptors, which trigger allergy symptoms. But in the lining of the stomach,

histamine binds with H₂ receptors, which trigger the release of stomach acid.⁵

Receptor expression is typically dynamic. Chronic stimulation of receptors often results in a decreased receptor response, either through a decrease in the number of receptors or through homologous desensitization, which refers to an uncoupling of some receptors from their intracellular signaling cascade.⁶ Repeated stimulation of a receptor can also result in heterologous desensitization, which refers to desensitization of not only the stimulated receptor but also other receptors that work through a similar mechanism.⁷

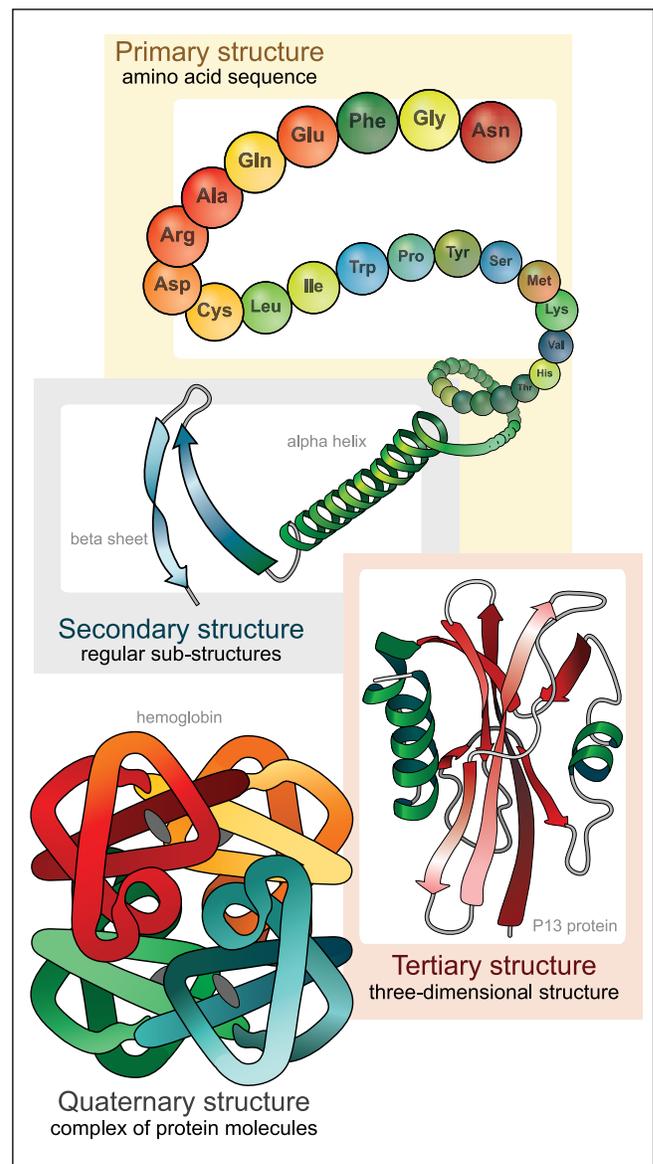


Figure 2. The primary, secondary, tertiary, and quaternary structure of proteins. Reprinted from http://www.clerk.com/cliparts/o/a/b/d/12641392801203977540Main_protein_structure_levels_en.svg.hi.png.

There are 4 main types of receptor proteins. Types 1 through 3 are transmembrane receptors, which means that they pass through the cell membrane. They remain anchored in the cell membrane by one or more transmembrane domains, which are hydrophobic alpha helices. A transmembrane receptor must have one or more domains that are outside the cell, where they can interact with the ligand. They must also have one or more domains that are inside the cell, so that they can interact with molecules that are inside the cell.

Type 1 receptors are also called **ionotropic receptors** or **ligand-gated transmembrane ion channels**.⁸ When the proper ligand binds to a type 1 receptor, the change in the receptor's shape allows small, electrically charged particles (ions such as K^+ , Na^+ , Ca^{++} , and Cl^-) to pass through the membrane.

Type 2 receptors are also called **metabotropic receptors** or **G-protein-coupled receptors**. Sometimes, they are called 7-transmembrane domain receptors because they cross the cell membrane 7 times.⁹ Type 2 receptors do not directly open a channel. Instead, they are linked to another small protein (a G protein) that is found inside the cell. When the ligand activates the receptor, the receptor then causes a conformational change in the G protein. The G protein then activates another molecule within the cell, which is called the secondary messenger. In some cases, the secondary messenger can bind to and open ion channels somewhere else on the cell membrane. In other cases, the secondary messenger will activate other intermediate molecules inside the cell. The regulation of the secondary messenger allows the signal to be amplified or suppressed within the cell. Hundreds of G-protein-coupled receptors have been discovered. Examples include the adrenergic receptors, which are the targets of the catecholamines, especially norepinephrine and epinephrine.

Type 3 receptors are also called **kinase-linked and related receptors** and have a single extracellular domain containing the ligand binding site, a single transmembrane alpha helix, and an intracellular domain, which often has an enzymatic function. The receptor tyrosine kinases are part of a larger family of protein tyrosine kinases, many of which do not have transmembrane domains. The insulin receptor is a type 3 receptor.¹⁰

Type 4 receptors are also called **nuclear receptors**. However, they are generally found in the cytoplasm. They migrate to the nucleus after they bind to their ligand. They can bind directly to DNA and regulate the expression of adjacent genes. For this reason, they are classified as transcription factors. Nuclear receptors have a C-terminal ligand-binding region, a core that recognizes a particular DNA sequence, and an N-terminus that can interact with other factors that can alter the activity of the receptor. Examples include receptors for steroid hormones and thyroid hormones.¹¹

LIGAND-RECEPTOR BINDING

This ligand-receptor bond is usually a result of ionic bonds, hydrogen bonds, and Van der Waals forces, rather than resulting from covalent bonding.¹² For this reason, the bond between the ligand and its receptor is reversible. The reversal is called dissociation.

The strength of the intermolecular forces that hold the ligand and its receptor together is called the binding affinity.¹² If a ligand has high affinity for a receptor, there will generally be a high degree of occupancy (ie, more of the receptors will be bound with ligand). This relationship is important in radiology. By giving a patient a dose of a radiolabeled ligand with high affinity for a particular receptor, radiologists can get an image of the distribution of that receptor in tissue, such as in the heart or the brain.¹³ Note, however, that high affinity does not necessarily result in longer residence time (the duration of the ligand-receptor complex).

You might expect that high-affinity binding would be more likely to produce a physiological effect, as some of the binding energy could be used to create a conformational change. However, some ligands can bind tightly to a receptor without triggering the receptor's normal physiologic response. One example is naloxone (Narcan[®]). Naloxone is useful as an antidote to opioid overdose because it has extremely high affinity for μ -opioid receptors but does not produce the normal physiologic effects of an opioid drug.¹⁴

Ligands can be classified according to the effect that they exert on their receptor (Table 3). Many drugs work on receptors, often by mimicking or blocking the natural ligand. Drug designers often try to develop a compound that will selectively bind to only some subtypes of receptors. Typically, the goal is to develop a drug that would have the desired effects without producing undesired side effects.

Many drugs work by allowing the natural ligand to have more of an effect. For example, the selective serotonin reuptake inhibitors (SSRIs) and the serotonin and norepinephrine

Table 3. Types of Ligands

Agonist	Triggers a physiological effect by binding to a receptor
Full agonist	Maximally stimulates the receptor
Partial agonist	Only partially activates the physiological response
Antagonist	Binds to the receptor without triggering the physiological effect
Inverse agonist	Has the effect that is opposite to an agonist, but can be blocked by an antagonist

reuptake inhibitors (SNRIs) allow the respective neurotransmitters to remain for a longer period in the synapse, so that they have more time to interact with their receptors. As a result, these drugs increase serotonergic (and sometimes noradrenergic) signaling.¹⁵

Some other drugs work by mimicking a natural ligand. The dopamine agonists that are used for treatment of Parkinson's disease activate the dopamine receptors in the brain.¹⁶ Thus, these drugs have an effect similar to that of natural dopamine, which is in short supply in patients with Parkinson's disease.

A full agonist is a substance that maximally stimulates the receptor. In other words, it has high positive intrinsic activity. In contrast, a partial agonist is a ligand that produces less of an effect at the receptor. It has low positive intrinsic activity. In the absence of a full agonist, the partial agonist can provide some stimulation to the receptors. However, if the full agonist is present, a partial agonist acts as a competitive antagonist. By competing with the full agonist for receptor occupancy, it can produce a net decrease in receptor activation. Many phytoestrogens (plant-derived estrogens) are partial agonists of estrogen receptors and end up having a net antiestrogenic effect by competing with the full agonist for receptor occupancy.¹⁷ Some drugs, such as buspirone, have a mix of full agonist and partial agonist effects on different receptor subtypes.¹⁸

Antagonists occupy receptors but block the receptor's physiologic effect, which is why they are sometimes called blockers. Antagonists themselves have zero intrinsic activity (ie, they have no physiologic effect if the natural ligand is not present). Antihistamines are histamine receptor antagonists. There are 4 types of histamine receptors.⁵ Antagonists of each of those types have potential clinical uses. H₁ blockers are used for treating allergic reactions. H₂ receptors are used for suppressing the release of stomach acid. H₃ antagonists are being investigated for use in narcolepsy and Alzheimer's disease. An H₄ antagonist is being investigated for the treatment of atopic dermatitis.¹⁹

Inverse agonists have an effect that is opposite to that of an agonist. To have this effect, the ligand's receptor must have some basal level of activity, even if the ligand is absent. By blocking these receptors, the inverse agonist can produce a lower level of activity than is seen even in the absence of the ligand. Thus, an inverse agonist has negative intrinsic activity. Many antipsychotic, antidepressant, and other psychiatric medications have been shown to have inverse activity at various types of receptors.²⁰

SIGNAL TRANSDUCTION PATHWAYS

Many receptors can be viewed as an intermediate point in a signaling pathway. When activated, these receptors pass along some sort of signal that is eventually carried to some other

target in the cell, where the physiologic effect is produced. These pathways and what happens inside cells when those messages are received will be discussed in more detail in part 3.

Laurie Endicott Thomas is the author of Thin Diabetes, Fat Diabetes: Prevent Type 1, Cure Type 2 (www.thindiabetes.com).

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Understanding Rigor and Reproducibility for Grant Applications: A Survey of Faculty at an Academic Health Center

By **Kerry L. Evans, PhD** / Editor, Science Communication Group, University of Arkansas for Medical Sciences, Little Rock, AR

ABSTRACT

Objective: The objective of this survey was to evaluate the perception and implementation of the NIH Initiative to Enhance Rigor and Reproducibility (NIH RR Initiative) at the University of Arkansas for Medical Sciences (UAMS). This survey focused on 2 aspects of this initiative—the scientific premise and robust and unbiased results—and how editors in the university’s Science Communication Group can help faculty address this requirement in their grant applications.

Methods and Materials: A 13-question survey was administered via SurveyMonkey to 160 investigators at UAMS. The survey distinguished between respondents who receive NIH funding and those who had served on an NIH study section (reviewed grants) since the NIH RR Initiative was implemented (on January 25, 2016).

Results: The response rate was 30%; 68.75% of respondents said that they currently receive (or will be receiving) NIH funding, and 38% said that they had attended an NIH study section since the NIH RR Initiative was implemented. Overall, 38.5% of respondents were “very familiar” with the initiative, 56.4% were “somewhat familiar,” and only 5.1% were “not familiar.” Of those respondents who had attended a study section (served as a grant reviewer), 38.9% said that only 25% of applications addressed rigor and reproducibility in a distinct section of the grant proposal, but 27.8% said that 75% of applications addressed it in a distinct section. Sixty-one percent of study-section members agreed with survey definitions of “significance” and “scientific premise,” and 28% strongly agreed.

Conclusions: While the sample size was small, the survey results suggest that most study-section members at UAMS understand the NIH RR Initiative, but that other faculty are less well-informed. Current strategies taken by the Science Communication Group to implement the NIH RR Initiative, such as addressing the scientific premise and robust and unbiased results in distinct sections of the proposal, appear to align with grant reviewers’ expectations.

INTRODUCTION

Rigor and reproducibility are hallmarks of quality research, but there is growing concern about the fact that some biomedical research is not reproducible.^{1,2} Because of this, the National Institutes of Health (NIH) announced in October of 2013 the Initiative to Enhance Research Rigor and Reproducibility, an initiative that includes all NIH Institutes and Centers.³

Under this initiative (NIH RR Initiative), applications must address 4 key topics^{4,5}:

- 1. Scientific premise of the proposed project.** “The scientific premise for an application is the research that is used to form the basis for the proposed research question.”⁵ This requirement is factored into the reviewers’ score for the significance of each application.
- 2. Rigorous experimental design.** “Scientific rigor is the strict application of the scientific method to ensure robust and unbiased experimental design, methodology, analysis, interpretation, and reporting of results.”⁵ This requirement is factored into the reviewers’ score for the approach.
- 3. Considerations of sex and other relevant biological variables.** “NIH expects that sex as a biological variable will be factored into research designs, analyses, and reporting in vertebrate animal and human studies. Strong justification from the scientific literature, preliminary data, or other relevant considerations must be provided for applications proposing to study only one sex.”⁵
- 4. Authentication of key biological and/or chemical resources.** Cell lines, specialty chemicals, antibodies, and other biologics whose quality could influence the research data should be authenticated.^{4,5}

The Science Communication Group (SciCom) at the University of Arkansas for Medical Sciences (UAMS) is an editing resource for faculty who are applying for extramural research funding; UAMS is Arkansas's only academic health center and receives nearly \$39 million in NIH funding.⁶ SciCom serves investigators in all UAMS colleges and from organizations that partner with UAMS for research. The group's main goal is to help applicants produce competitive grant proposals, but they also edit manuscripts for submission to peer-reviewed journals. SciCom services range from simple grammatical assistance to more substantive editing. They also mentor UAMS investigators by providing grant-writing workshops throughout the year.

Because the NIH RR Initiative is still relatively new, SciCom has accrued very few data on how investigators should effectively address rigor and reproducibility in their applications. However, once the NIH RR Initiative was announced, SciCom devised a plan for addressing the RR topics discussed above. First, SciCom suggests that investigators address the scientific premise under the heading "Scientific Premise for the Proposed Project" within the Significance section, and the following comment is attached:

"In the Significance section, applicants are asked to 'Describe the scientific premise for the proposed project, including consideration of the strengths and weaknesses of published research or preliminary data crucial to the support of your application.'⁷ On a website created by NIH to provide guidance on rigor and reproducibility, NIH advises the following: 'It is expected that this consideration of general strengths and weaknesses could include attention to the rigor of the previous experimental designs, as well as the incorporation of relevant biological variables and authentication of key resources.'^{8,9}

Second, SciCom suggests that investigators address rigorous experimental design under the heading "Robust and Unbiased Results" in the Approach section, and the following comment is attached:

"Describe the experimental design and methods proposed and how they will achieve robust and unbiased results. Explain how relevant biological variables, such as sex, are factored into research designs and analyses for studies in vertebrate animals and humans. For example, strong justification from the scientific literature, preliminary data, or other relevant considerations, must be provided for applications proposing to study only one sex. See NOT-OD-15-102 for further consideration of NIH expectations about sex as a biological variable."¹⁰

If applicable, more detail about biological variables can be provided within the descriptions of experimental design and methodology.

Since the NIH RR Initiative was implemented, it has become evident that many investigators at UAMS either are unaware of this new initiative or do not fully understand how to implement it in their applications. To better understand how they can help UAMS investigators navigate the NIH RR Initiative, SciCom surveyed faculty at UAMS to determine how they perceive and understand this initiative.

METHODS

SciCom designed a web-based survey to understand how faculty at UAMS perceive and understand the NIH RR Initiative (IRB #206490). The survey consisted of 13 questions, 3 of which were open-ended, and it identified respondents who currently receive NIH funding and/or who had served on an NIH study section since the NIH RR Initiative was implemented.¹¹

SciCom generated and distributed the survey via SurveyMonkey, and the responses were anonymous. The survey was sent by email to 160 individuals; 39 completed the survey, and 9 partially completed it. The survey remained open for 7 days, and a reminder email was sent after 5 days to recipients who had not opened the survey. The first question—"Do you currently receive NIH funding?"—appeared in the body of the email message. Upon answering the question, the survey opened in a new window and was accompanied by a message that described the survey goal and format.

The survey recipients were identified in 3 ways. First, because most investigators in the UAMS basic science division receive NIH funding, the survey was sent to all of the basic sciences faculty. Second, an email was sent to the deans of the UAMS College of Public Health, the College of Pharmacy, and the College of Nursing in which we asked for a list of faculty members who had served on a study section since January 25, 2016 (the date on which the NIH RR Initiative was implemented). Third, we queried NIH RePORTER for a list of currently funded research grants at UAMS. The email addresses for all recipients were available on the UAMS website.

RESULTS

Forty-eight people responded to the survey, giving a response rate of 30%; 68.75% of respondents said that they currently receive (or will be receiving) NIH funding, and 38% said that they had attended an NIH study section since the NIH RR Initiative was implemented on January 25, 2016 (data not shown).

A major goal of this survey was to understand how familiar UAMS faculty are with the NIH RR Initiative. We asked, "How familiar are you with the NIH Initiative to Enhance Rigor

and Reproducibility?” Out of all of the respondents, the majority (56.4%) were “somewhat familiar” (Figure 1, all). To determine which respondents had attended a study section since the NIH RR Initiative was implemented, the survey asked, “Have you attended an NIH study section since January 25, 2016?” Of those respondents who answered “yes,” 61.1% were very familiar with RR, and the rest (38.9%) said that they were somewhat familiar (Figure 1, SS). Considering these data, it is not too surprising that 55.6% of respondents who had attended a study section said that they disagree/strongly disagree that “the majority of investigators submitting grant applications fully understand the concept of rigor and reproducibility” (Figure 2).

It was possible that faculty from certain research disciplines were more or less familiar with the NIH RR Initiative, so the survey asked the respondents to identify their primary research disciplines. The majority of respondents (32.6%) identified “other,” while 19.8% of respondents identified “cell biology” as their discipline (Figure 3). Based on the pool of survey recipients, SciCom concluded that most of the “other” investigators belong to the nursing discipline. Interestingly, all of the respondents who listed their research discipline as neuroscience (10.9%) reported being very familiar with the NIH RR Initiative, whereas a large majority of respondents from the cell biology and “other” disciplines reported being somewhat familiar with the Initiative, and only respondents from the “other” category reported being unfamiliar with the Initiative (data not shown).

Because their primary goal is to help investigators prepare competitive grant applications, SciCom wanted to know what steps they could take to effectively address the NIH RR Initiative in grant proposals. To that end, the survey asked, “In your experience as a reviewer, what percentage of applications address rigor and reproducibility in a distinct section?” Of those respondents who had attended a study section, the majority (38.9%) said that only 25% of applications address RR in a distinct section (Figure 4). The survey also asked, “In the Research Strategy, is it helpful for rigor and reproducibility to be addressed under a distinct section heading(s)?” The majority of respondents (59%) indicated that it was helpful for RR to be addressed under a distinct heading; surprisingly, 41% indicated that it was not helpful (data not shown).

As editors, we find that the terms “premise” and “significance” are often misunderstood by grant writers. To understand how study-section members understand

Q: How familiar are you with the NIH Initiative to Enhance Rigor and Reproducibility?

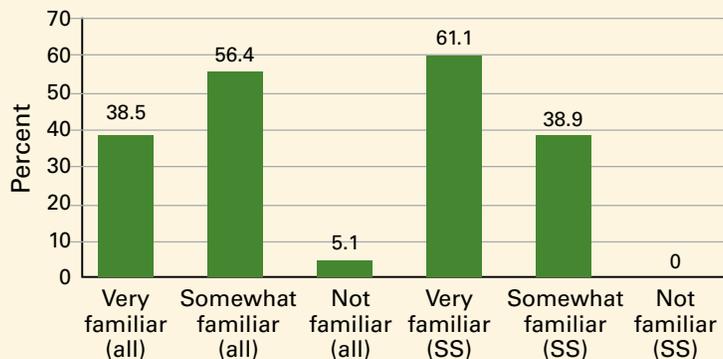


Figure 1. Most respondents are familiar with the NIH RR Initiative. *n*=39 total responses (all); *n*=18 respondents who had attended a study section (SS).

Q: To what extent do you agree or disagree that the majority of investigators submitting grant applications fully understand the concept of rigor and reproducibility?

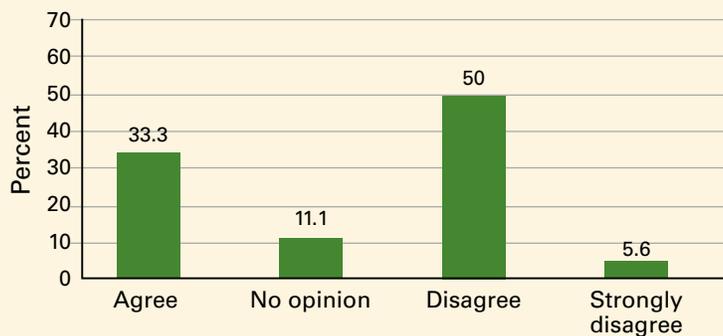


Figure 2. Most study-section members disagree that the majority of investigators submitting grant applications understand the concept of rigor and reproducibility. *n*=18 responses.

Research Disciplines of Respondents

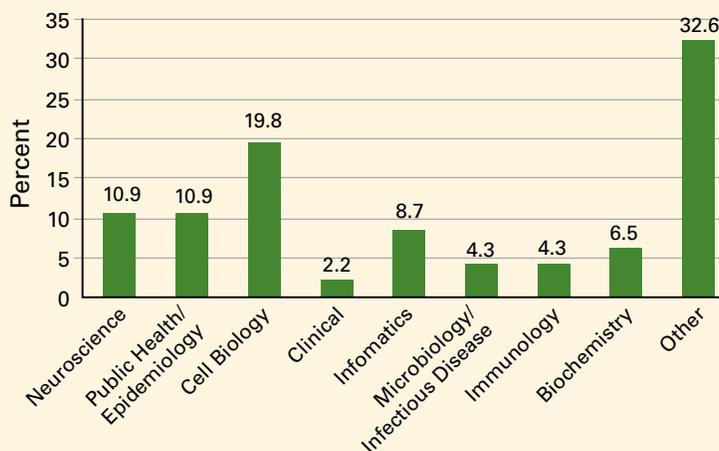


Figure 3. Respondents were asked to mark their specific research discipline(s); some respondents marked multiple categories. *n*=39 responses.

these terms, the respondents were asked to what extent they agree or disagree that:

“Discussion of the scientific premise is a retrospective on the strengths and weaknesses of prior research and how these strengths and weaknesses inform the proposed study. Significance is a prospective discussion of how the proposed research will impact the field and human health.”

Sixty-one percent of study-section members responded that they agree with these definitions, and 28% strongly agreed (Figure 5).

Finally, the study included 3 open-ended questions at the end of the survey. One of these questions was “What is the most important topic to address related to scientific premise?” One study-section member noted that

“Multiple items must be covered, but most important to me, which is sometimes not covered, are appropriately identified strengths and weaknesses of prior work in the field.”

A second study-section member responded that

“Ensuring everyone is on the same page that this is about PRIOR work, how balanced it is and whether it justifies and informs the current study and design.”

The last question of the survey produced the most passionate responses. It asked the respondents to “please provide any specific comments on rigor and reproducibility.”

One respondent who receives NIH funding but is not a study-section member said that

“Admittedly, completely addressing this in an application is very difficult. Many applicants will likely struggle with this section until a culture of ‘rigor and reproducibility’ has developed. Reviewers need to take this into account in their evaluation process. And reviewers would do well to write reviews that help the investigators (regardless of funding status) improve these sections.”

DISCUSSION AND CONCLUSIONS

The UAMS SciCom group offers editorial assistance to faculty investigators seeking extramural research funding. SciCom conducted this survey to determine how faculty at UAMS perceive and understand the NIH RR Initiative, which was implemented in early 2016. The results of this survey will help SciCom to guide investigators more effectively through the grant-writing process.

Q: What percentage of applications address rigor and reproducibility in a distinct section?

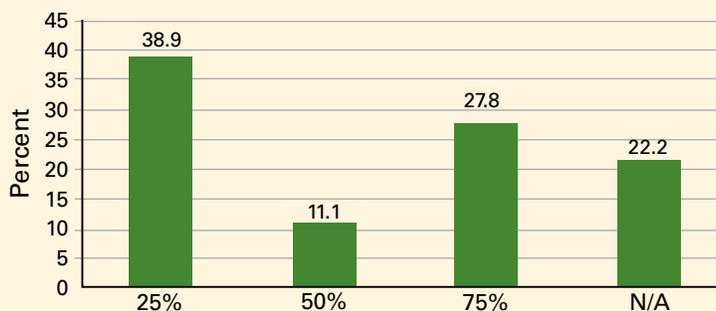


Figure 4. Relatively few applications address the rigor and reproducibility requirements within distinct sections of the application. $n=18$ responses.

Scientific Premise vs Significance

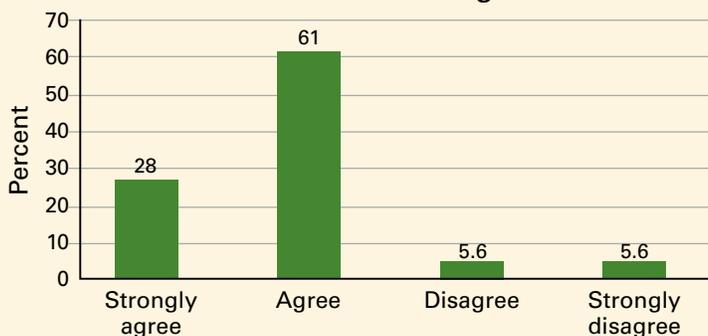


Figure 5. Most study-section members agree with SciCom definitions of “premise” and “significance.” Respondents were asked to what extent they agree or disagree that: “Discussion of the *scientific premise* is a retrospective on the strengths and weaknesses of prior research and how these strengths and weaknesses inform the proposed study. *Significance* is a prospective discussion of how the proposed research will impact the field and human health.” $n=18$ responses.

While the survey respondents reported being at least somewhat familiar with the NIH RR Initiative, it is clear that faculty at UAMS would benefit from a better understanding of this NIH requirement. Although SciCom educates all of the investigators who work with them about the NIH RR Initiative, they do not edit all of the grant proposals submitted from the UAMS campus. Therefore, SciCom should consider additional strategies for educating UAMS faculty about this NIH requirement.

SciCom recently held a “Fund My Grant” panel discussion between investigators and study-section members. Although the discussion was aimed at early-stage investigators and focused on all aspects of funding, panelists were encouraged to discuss the NIH RR Initiative. In addition, SciCom typically holds at least one annual grant-writing workshop. All of these activities are opportunities for SciCom to discuss not only the NIH RR Initiative, but any new

requirements set forth by key funding agencies. Although the survey sample size is small, it appears that respondents from cell biology and “other” disciplines may need more education about RR, and future outreach strategies could target these disciplines more specifically. In fact, one strategy could simply be making educational materials available online (eg, slides from the SciCom grant-writing workshop).

One topic that was discussed at the “Fund My Grant” panel was the issue of sex as a biological variable. Because the main focus of the survey was the distinction between scientific premise and significance (and because SciCom wanted to keep the survey brief), sex as a biological variable was not specifically addressed. Nevertheless, it is an important topic. The NIH strongly recommends that animal studies use both male and female animals. However, investigators insist that this is often not financially feasible. Thus, SciCom suggests that applicants propose to validate their key experimental findings in both sexes but conduct the majority of their work with one sex, an approach that was also affirmed by the “Fund My Grant” panelists. Alternatively, researchers might present preliminary data for both sexes to show that a specific phenotype is not sex-dependent.

SciCom’s current approach for incorporating RR into applications appears to be effective; they will continue to include distinct subsections titled “Scientific Premise for the Proposed Project” and “Robust and Unbiased Results” within the Significance and Approach sections, respectively. Accordingly, SciCom needs to specifically educate investigators about the nature of the scientific premise—something that was echoed by a number of survey respondents. In SciCom’s experience, most applicants confuse premise for significance or preliminary data. The scientific premise should be a retrospective discussion of prior work in the field. The applicant should address how past approaches to research in a specific discipline have hindered or advanced the field. Then, they should describe how the approach taken in the current proposal reflects this prior work.

Although the survey sample size was very small and some responses were likely affected by recall bias, these data provide a snapshot of the status of the NIH RR Initiative on the UAMS campus; a more rigorous survey with more respondents is required to draw definitive conclusions. The SciCom group encourages other institutions to submit similar surveys to their faculty—the process is simple and cost-effective, and the results could be quite informative.

Acknowledgments

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Author contact: klevans@uams.edu

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Results From the 2016 Freelance Medical Communicator Tools of the Trade Survey

Monica Nicosia, PhD / Freelance Medical Writer, Nicosia Medical Writer LLC, Bryn Mawr, PA

ABSTRACT

Objective: To collect and analyze data about the software, apps, and other tech tools that freelance medical communicators use in their daily work.

Methods: I administered a 34-question survey via SurveyGizmo and recruited participants primarily via fliers handed out at the 2016 Medical Writing & Communication Conference, announcements posted on the AMWA Engage forum, and various LinkedIn venues.

Results: Of 381 people who started the survey, 79% completed it. Participants were primarily from the United States (70%); 85% were women; 61% were 40 to 59 years old; 52% were full-time freelancers; and 67% were writers as their primary function. Most participants worked on laptops (63%) powered by Microsoft Windows (70%) and backed up with an external hard-drive (66%) and/or an online/cloud service (52%). The most commonly used online/cloud-based backup services were Dropbox (29%), Carbonite (19%), and Google Drive (15%). Among the survey responders who had a business website (52%), 54% had designed it themselves. For accounting/bookkeeping, 42% used spreadsheets and 20% did not use any software/app. For time tracking, 32% used spreadsheets and 35% did not use any software or app. Also, 42% did not use any citation/reference management software. When asked about the one essential tool they would recommend to colleagues, the most popular responses were Microsoft Word, Adobe Acrobat, and PerfectIt for the software app category, and multiple and/or large monitors, a laptop, and an external back-up hard drive for the device category.

Conclusions: While this survey study is not intended to be a purchasing guide, the information it provides could help new and current freelance communicators identify new options and narrow down choices.

INTRODUCTION

In addition to producing quality deliverables that satisfy their clients' needs, freelance medical communicators (freelancers) have to juggle multiple business management-related tasks such as time tracking, bookkeeping, and invoicing. Old-fashioned approaches to handling some of these tasks involve the use of cumbersome spreadsheets and piles of receipts stuffed in boxes or drawers. Technological solutions include software, apps, and online services. In setting up their business, freelancers also have to decide which services to use for their business website and email.

Given the large number of available options, freelancers can spend countless unbillable hours researching and assessing the tools that they might want to demo or buy. To narrow down choices, it might be helpful to know which tools colleagues use in their work. This information has not been included in past medical communicator surveys conducted by the American Medical Writers Association (AMWA)^{1,2} or the European Medical Writers Association (EMWA),³ which instead have focused on analyses of types and hours of work, billing methods, and income. Further, while providing very useful guidance, current published literature⁴⁻⁸ on the practice of running a freelance business does not include updated and systematically gathered data on the specific tools used by these professional medical communicators. One source that does have some pertinent information is a self-published 2016 survey of software and equipment recommended by medical writers.⁹ However, this informal survey relied primarily on 4 open-ended questions that, while informative, are difficult to analyze.

To address this gap, this article describes the design, implementation, and analysis of an online survey that collected data about the software, apps, and other tools used by freelancers in their daily work.

METHODS

Survey Design

I used an online survey platform (standard license, SurveyGizmo; Widgiz, LLC dba SurveyGizmo, Boulder, Colorado) to design, administer, and analyze a 34-question survey (online supplemental material). The survey had 3 parts (or pages) and required participants to answer all the questions in each part before they could proceed to the next part. Selected responses to a few questions generated conditionally displayed questions that were not mandatory. The survey platform allowed backward navigation to completed parts of the survey. To initiate the survey, participants had to scroll down to the bottom of the introductory explanatory page and click on a button marked NEXT. The introductory information stated that the survey was open to currently working freelance (ie, self-employed) medical communications professionals (eg, writers, editors). The first part of the survey asked 9 work-history related questions; all but 1 of these questions permitted selection of a single answer (Figure 1). The second part of the survey asked 19 questions on tools of the trade. The third part of the survey asked 6 demographic questions and allowed participants to provide their email address if they wanted to receive an Adobe portable document format (.pdf) copy of the survey summary findings (the only incentive offered for participation). Email addresses were stripped from responses prior to data analysis.

Prior to launch, the author and a colleague tested the survey usability and technical functionality. SurveyGizmo (the

survey platform host) estimated that it would take participants approximately 6 minutes to complete the survey.

Participant Recruitment

The survey, which opened October 3, 2016, and closed December 15, 2016, could be accessed through a direct link hosted by SurveyGizmo and the author's business website. Methods used to elicit survey participation included fliers handed out at select freelance sessions held at the AMWA Medical Writing & Communication Conference (October 5-8, 2016, Denver, Colorado) and multiple announcements posted on the AMWA *Engage* forum, the author's LinkedIn profile, several LinkedIn professional groups (AMWA, Professional Medical/Scientific Writers, EMWA, AMWA-Delaware Valley Conference), and via Twitter. Several AMWA chapters encouraged survey participation by including an announcement regarding the survey in an email to their chapter membership. Two freelance medical writer colleagues promoted the survey by sharing the link in their monthly newsletter and business Facebook page.

Data Handling and Statistical Analysis

The day after the survey closed, I exported survey data from SurveyGizmo as raw data in Excel format and as SurveyGizmo-generated Excel, Adobe .pdf, and PowerPoint reports summarizing results of each question. To generate word cloud graphs, I copied the responses from the raw data Excel report into a Word document, then edited them to apply more uniform

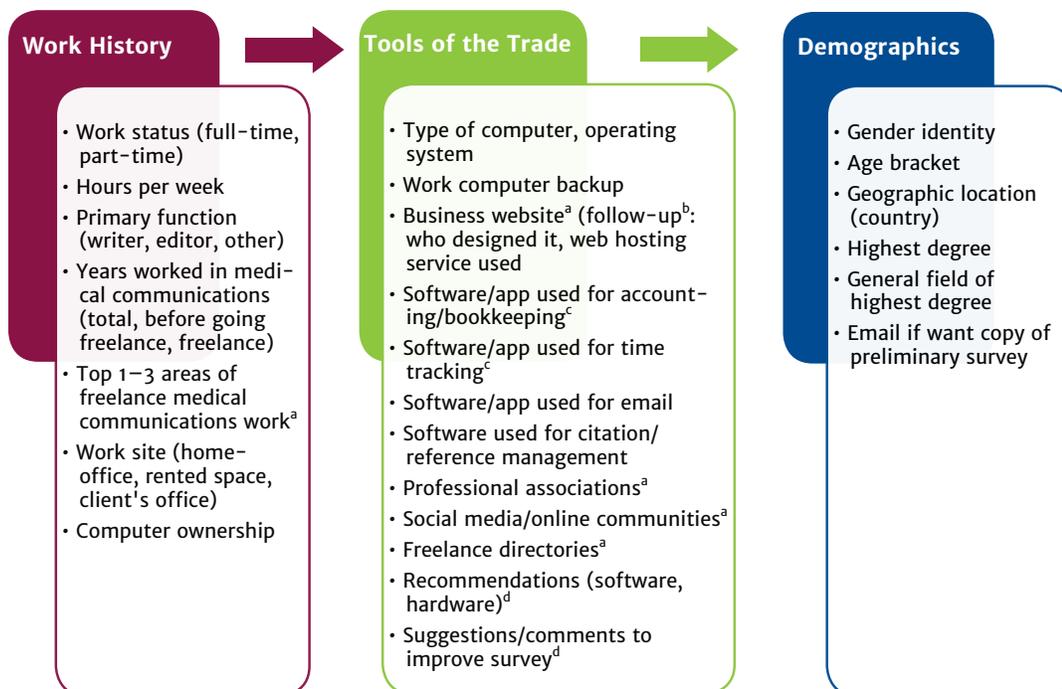


Figure 1. Survey structure. ^aMultiple answers allowed. ^bParticipants who answered that they did have a business website were asked 2 follow-up questions about it. ^cParticipants who said that they used a spreadsheet were asked 1 follow-up question about it. ^dOpen-ended questions.

terminology and to eliminate outlier responses (eg, “none,” “I don’t know”). Then, I copied and pasted the edited comments into an online word cloud-generator app (www.jasondavies.com/wordcloud) and produced the figures using the “Spiral Rectangular” and “One word per line” options.

Statistical analyses comprised descriptive statistics (ie, percentages) for each survey question. Some responses to open-ended (“Other”) questions were manually grouped and/or allocated into wider categories to simplify analysis.

RESULTS

Demographics Data and Work History

Of the 381 people who started the survey, 324 (85%) answered all 9 questions in the first part of the survey, 307 (81%) answered the last mandatory single-response question in the second part of the survey, and 300 (79%) completed all 34 questions. Review of IP addresses found no indication of potential duplicate entries by the same user.¹⁰

Table 1 summarizes the demographic characteristics of the 300 participants who completed the entire survey. Participants were primarily from the United States (70%). Most were women (85%) and most (61%) were 40 to 59 years old. Table 2 summarizes participants’ work history. A slim majority (52%) of participants were full-time freelancers, 62% worked an average of 21 or more hours per week, and 67% selected “writer” as their primary function. Most (54%) survey responders had worked ≥6 years as freelance medical communicators. The most commonly reported (≥20%) areas of freelance medical communication work were scientific publications (60%), continuing education for healthcare professionals (39%), regulatory documents (23%), patient education materials (22%), and promotional materials (21%) (Figure 2).

Office Characteristics

The vast majority of 324 survey responders reported that they owned their business computer (97%) and worked >50% of their billable time in a home office (95%). A few participants primarily worked in rented office space (2%), a client’s office (2%), or in other locations (0.9%) including owned office space ($n = 2$) and a coffee shop ($n = 1$).

Table 3 summarizes data regarding survey participants’ office practices. Most reported using a laptop (63%) to perform >50% of their freelance medical communications work; 70% identified Microsoft Windows and 30% Apple OS as the operating system of their business computer. The majority of survey participants used an external hard drive (65%) and/or an online/cloud-based service (52%) to back up their work computer. The other systems mentioned by participants who selected “Other” as their response (7%) included flash drives, USB keys/sticks, and multiple computers. A small propor-

Table 1. Participant Demographics

Characteristic	N (%)
Responders (n = 381)	
Complete	300 (79)
Partial	81 (21)
Gender identity (n = 300)	
Woman	254 (85)
Man	46 (15)
Age, years (n = 300)	
20–29	7 (2)
30–39	45 (15)
40–49	90 (30)
50–59	92 (31)
≥60	66 (22)
Geographic location (n = 294)	
United States	207 (70)
United Kingdom	34 (12)
Canada	22 (7)
Germany	5 (2)
India	5 (2)
Other ^a	26 (9)
Highest degree (n = 300)	
Associate	1 (0.3)
Bachelor	79 (26)
Master	73 (24)
Advanced	139 (46)
Other	16 (5)
Professional associations (multiple responses allowed)	
American Medical Writers Association	217 (72)
European Medical Writers Association	33 (11)
International Society for Medical Publication Professionals	18 (6)
Drug Information Association	20 (7)
National Association of Science Writers	17 (6)
Regulatory Affairs Professionals Society	8 (3)
Other	88 (29)
None	50 (17)

^aOther countries include: 2 participants each from Australia, France, Iran, Japan, Mexico, New Zealand; 1 participant each from Brazil, Greece, Israel, Italy, Malaysia, Netherland, Portugal, Taiwan, Trinidad and Tobago.

Table 2. Participant Work History

Characteristic	N (%)
Work status as a freelancer (n = 324)	
Full time	170 (52)
Part time	154 (48)
Average hours per week worked as a freelance medical communicator (n = 324)	
<15	74 (23)
16-20	48 (15)
21-30	85 (26)
31-40	77 (24)
>41	40 (12)
Primary function (>50% billable hours per week) (n = 323)	
Writer	216 (67)
Editor	85 (26)
Other	22 (7)
Total years worked in medical communications, as an employee and as a freelance (n = 323)	
<1	16 (5)
1-2	26 (8)
3-5	35 (11)
6-10	53 (16)
11-15	51 (16)
16+	142 (44)
Total years employed as a medical communicator before going freelance (n = 322)	
None	105 (33)
<1	7 (2)
1-2	31 (10)
3-5	53 (16)
6-10	60 (19)
11-15	36 (11)
16+	30 (9)
Total years worked as a freelance medical communicator (n = 323)	
<1	37 (11)
1-2	48 (15)
3-5	64 (20)
6-10	71 (22)
11-15	37 (11)
16+	66 (20)

Table 3. Participant Business Practices

Characteristic	N (%)
Type of computer used for most (>50%) freelance medical communication work (n = 307)	
Laptop	193 (63)
Desktop	111 (36)
Tablet	3 (1)
Backup for work computer (multiple answers allowed)	
External hard-drive	201 (65)
Online/cloud-based service	161 (52)
Other	21 (7)
No back-up	19 (6)
Having a business website (n = 307)	
Yes	161 (52)
No	146 (48)
Who designed the business website (n = 160)	
I designed it myself	87 (54)
I paid someone to design it	57 (36)
A relative/friend designed it at no charge	16 (10)
Online freelance directories used to promote business (multiple answers allowed)	
AMWA Freelance Directory	116 (38)
EMWA Freelancer Directory	16 (5)
None	143 (47)
Other ^a (fill in the blank)	61 (20)
Social media and online communities used for freelance medical communication business (multiple answers allowed)	
LinkedIn	252 (82)
AMWA Engage	150 (49)
Twitter	80 (26)
Facebook	40 (13)
None	29 (9)
Other (fill in the blank)	8 (3)

^aAnswers written in by ≥5 participants included Editorial Freelancers Association (n = 12), Medcomms Workbook and/or Networking (n = 11), Board of Editors in the Life Sciences (n = 8), and Copyediting-L (n = 5). AMWA, American Medical Writers Association; EMWA, European Medical Writers Association.

tion of participants (6%) reported no backup. Among the 161 responders who used an online/cloud-based service to back-up their work computer, the top 3 options were Dropbox (29%), Carbonite (19%), and Google Drive (15%) (Figure 3).

Communications and Marketing

Of the 52% of participants who had a business website, 54% reported having designed it themselves, and 36% had paid someone to design it for them (Table 3). Among respond-

ers with business websites, the most commonly used website hosting services were GoDaddy (15%), Bluehost (10%), Wix (8%), and SquareSpace (6%) (Figure 4). Many responders (35%) used other services.

The most commonly reported software/apps used for business email were Gmail (53%), Outlook (50%), and Apple Mail (12%) (Figure 5). The top 3 social media and online communities used by participants for their freelance medical communication business were LinkedIn (82%), AMWA *Engage* (49%),

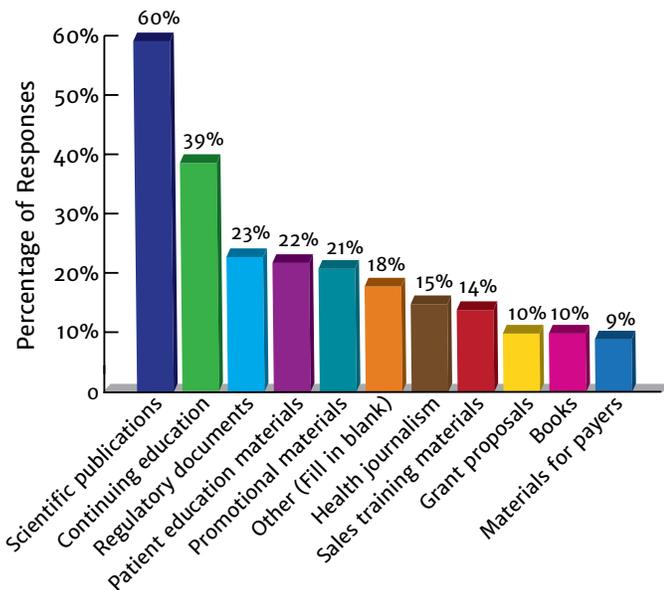


Figure 2. Participants' top 1 to 3 areas of freelance medical communications work (maximum 3 answers allowed).

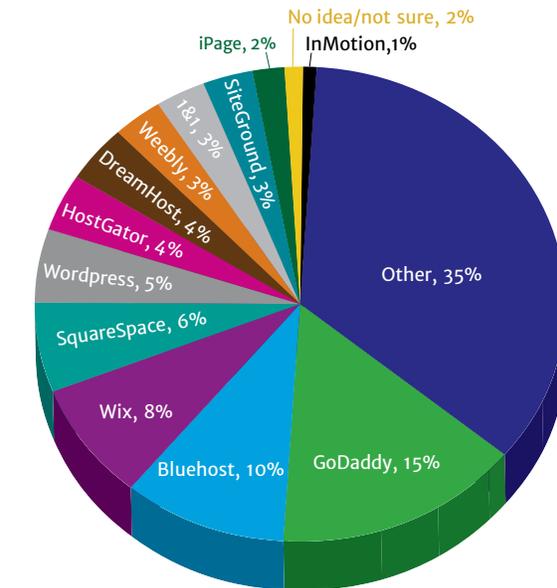


Figure 4. Web hosting service used for business site (1 answer allowed).

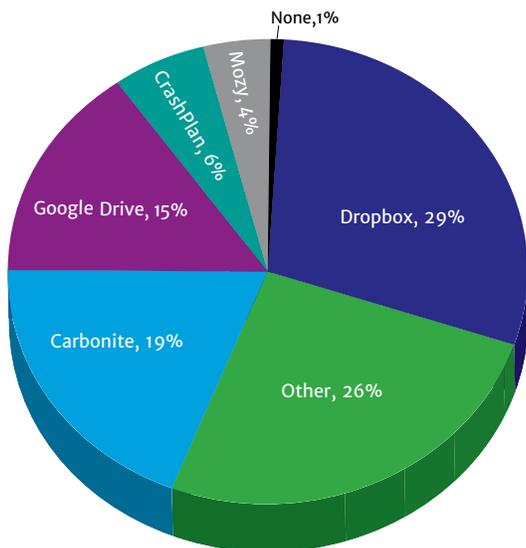


Figure 3. Online/cloud-based service used to back up work computer (1 answer allowed).

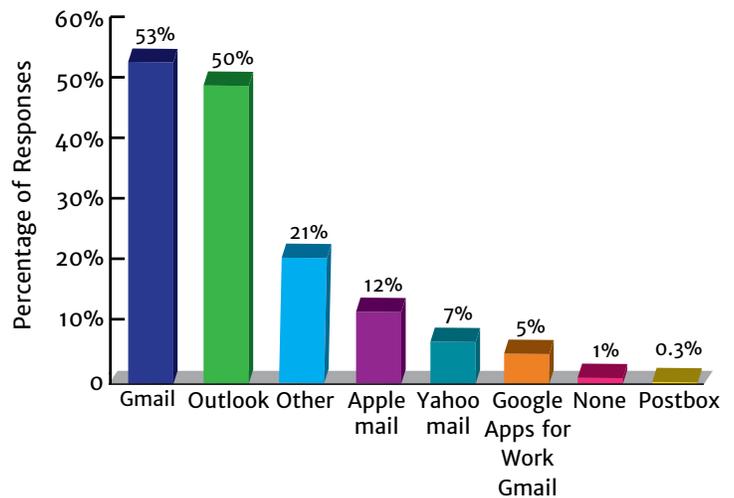


Figure 5. Software/apps used for email (multiple answers allowed).

and Twitter (26%); 9% of responders did not use social media or online communities for their business (Table 3).

Accounting/Bookkeeping and Time Tracking

Of 307 responders to the question about which software or apps they used for accounting/bookkeeping, most used spreadsheets (42%) or nothing (20%) (Figure 6). The accounting/bookkeeping software or apps identified by ≥ 5 participants were QuickBooks Online (12%), Quicken Home & Business (8%), QuickBooks software (5%), FreshBooks (2%), and Wave (2%). Of 129 responders who identified spreadsheets as their accounting/software system, 96% used Microsoft Excel, 3% Google Sheets, and 1% Apple Numbers.

Of 307 responders, 40% did not use any software or app for time tracking and 32% used a spreadsheet (Figure 7). The time tracking software or apps identified by ≥ 5 participants were Toggl (6%), Trax-Time (4%), FreshBooks (2%), and Harvest (2%).

Other Tools

Of 307 responders, 42% did not use any citation/reference management software (Figure 8). Endnote (47%), Reference Manager (8%), Mendeley (6%), and Zotero (5%) were the most commonly identified citation/reference management software programs.

Word cloud graphs in Figure 9 show responses to 2 open-ended questions that asked participants which single essential software/app (panel A) and hardware/specialized device (panel B) they would recommend to their fellow freelance medical communicators. In these graphs, the size and weight of the font reflects its frequency; thus, more frequently used words are displayed in a larger and bolder font than less frequently used words. Among 225 answers, the most commonly suggested software/app were Microsoft Office/Word ($n = 58$), Adobe Acrobat ($n = 20$), the Microsoft Word proofreading software add-in PerfectIt ($n = 18$), and EndNote ($n = 17$). Among 203 answers, the most commonly suggested hardware or specialized device were a large screen and/or multiple monitors ($n = 53$), a laptop ($n = 28$), an external hard drive for backup ($n = 26$), and a digital recorder or other audio recorder ($n = 13$).

DISCUSSION

As previously mentioned, the information gathered by this survey has not been included in past medical communicator surveys conducted by AMWA^{1,2} and EMWA.³ Neither does the current published literature⁴⁻⁸ on the practice of running a freelance medical communicator business include updated and systematically gathered data on the specific tools used by these professionals. Thus, the 2016 Freelance Medical Communicators Tools of the Trade Survey pro-

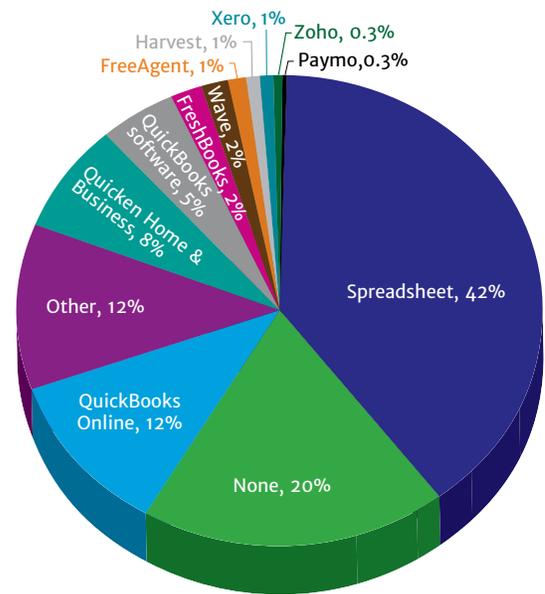


Figure 6. Software/app used for accounting/bookkeeping (1 answer allowed).

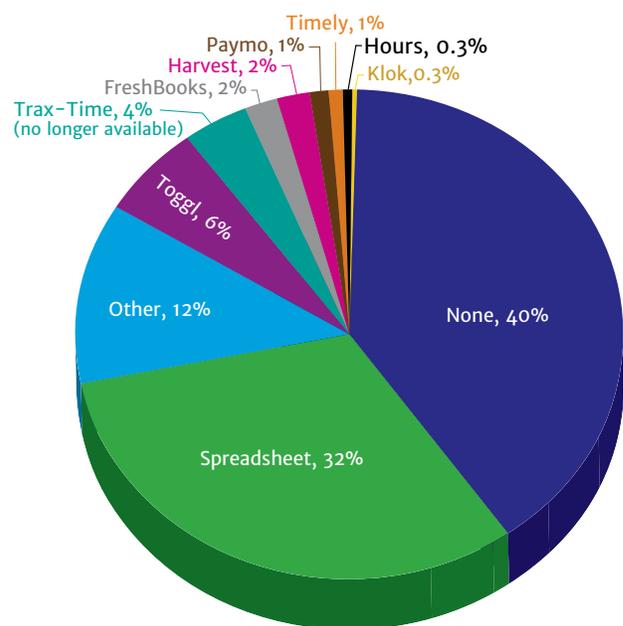


Figure 7. Software/app used for time tracking (1 answer allowed).

vides the first systematically acquired snapshot of freelance medical communicator business-related practices.

The Tools of the Trade survey completers ($N = 300$) included 217 AMWA members (72% of the participant pool) and 33 EMWA members (11%). The 2015 AMWA salary survey reported that 451 freelancers participated in that survey.¹ AMWA had publicized the 2015 salary survey by direct email and postcards to their membership list, which are methods not

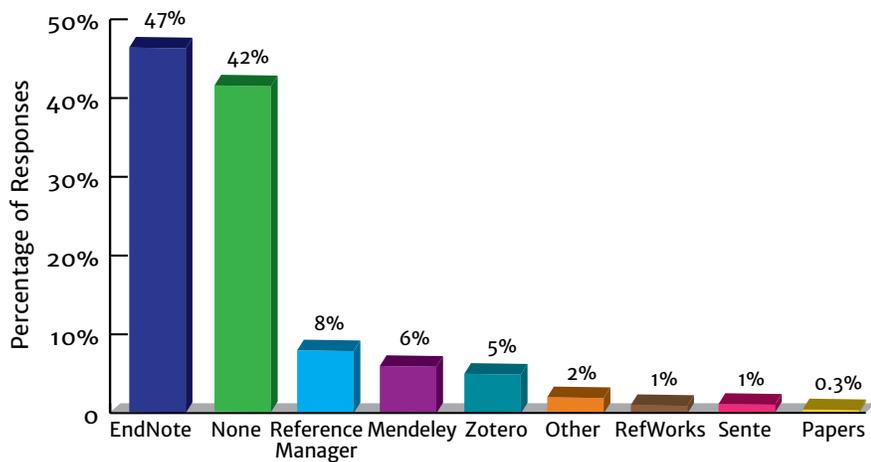


Figure 8. Citation/reference management software (multiple answers allowed).

accessible to non-AMWA-sponsored research projects such as the current survey. As AMWA does not have firm data on how many of its members are freelancers, I used the published literature to derive data to generate an estimate. A report on the 2016 AMWA membership survey¹¹ noted that of 1074 responders, 42% reported being freelance/self-employed. This report also said that the AMWA membership comprises approximately 4100 members. With the assumption that the response rate of freelancers to the salary survey was in proportion to their membership, an estimated 1722 AMWA members are freelancers. Thus, the 217 AMWA members who participated in the present survey might represent 13% of the estimated total AMWA freelance population. A report on the 2016 EMWA member survey¹² stated that membership comprises approximately 1000 people and found that of 286 responders, 37% were freelance. Again, with the assumption that the freelance response rate was in proportion to their membership, approximately 370 EMWA members are freelance. Thus, the 33 EMWA members who participated in the present survey might represent 9% of the estimated total EMWA freelance population.

Because these are estimates only, it is not possible to ascertain whether the Tools of the Trade survey participants were representative of the overall AMWA and EMWA freelance populations.

The current survey findings indicate that the participating freelancers tend to work on laptops (63%) powered by Microsoft Windows (70%) and backed up with an external hard-drive (65%) and/or an online/cloud service (52%). The most commonly used online/cloud-based backup services were Dropbox (29%), Carbonite (19%), and Google Drive (15%). The 6% of participants who reported not using a backup for their work computer risk losing their work on a daily basis to cyber-attacks and computer malfunctions. Among the slight majority of survey responders (52%) who had a business website, 54% had designed it themselves. GoDaddy (15%) and Bluehost (10%) were the most commonly used website hosting services. Gmail (53%) and Outlook (50%) were the most popular software/apps used for business email.

LinkedIn (82%) and AMWA *Engage* (49%) were the 2 most popular social media/online communities used by participants for their freelance businesses. Because I used both of these platforms to advertise the survey, the survey recruitment methods might have artificially enriched the participant pool with LinkedIn and/or AMWA *Engage* users. However, evidence from another survey corroborates LinkedIn's popularity with freelancers: a 2017 survey of freelance marketing practices found that 95% of 239 participants selected LinkedIn as 1 of the top 3 social networks they used for business.⁶ Unfortunately, the self-published report of this survey did not describe how participants were recruited to complete the survey, so it is not possible to evaluate its potential bias.



Figure 9. Word clouds of edited responses to questions asking for (A) 1 essential software app and (B) 1 essential hardware or specialized device to recommend to fellow freelance medical communicators.

Many participants had low-tech approaches to some business-related tasks. For accounting/bookkeeping, 42% percent used spreadsheets and 20% did not use any software/app. For time tracking, 32% used spreadsheets and 40% did not use any software or app. Also, 42% did not use any citation/reference management software. When asked about the one essential tool they would recommend to colleagues, the most popular responses were Microsoft Word, Adobe Acrobat, and PerfectIt for the software app category, and multiple and/or large monitors, a laptop, and an external backup hard drive for the device category.

This survey had a solid completion rate: of 381 people who started the survey, 79% completed all the questions. The main survey limitations are reliance on self-reporting and selection bias. In using the information from this survey, one should keep in mind that the survey asked participants to report what technology they used for various business-related activities, without asking them to rate whether they liked the technology they were using. Only the 2 open-ended questions asked participants to make recommendations. This survey report is not intended to be a purchasing guide, and people should do independent research, consult with colleagues, and use their own judgment when deciding how to set up their office and which tools to buy.

The survey results suggest that many freelancers do not use much technology to help them run their business. The survey did not investigate personal motivations behind these business practices. Through informal communications, it seems that some people prefer paper-based systems or simple electronic spreadsheets; some are not comfortable using new software or apps; some don't trust cloud-based applications; and some are not aware of the availability of time-saving, often low-cost tools. As freelancers, we have to be computer-savvy enough to efficiently write and edit our projects, communicate with our clients, and market ourselves. While we don't have to be on the cutting edge of technology to do our job well, we also should not lag too far behind. My approach is to strive for the middle and, when affordable and convenient, take advantage of well-tested technology to help me work more efficiently. Factors to consider in deciding whether to incorporate new tools into one's business practice include desired features, cost, potential for time saving, ease of use, ease of integration into work routines, and system requirements.

Hopefully, the information provided in this report will help both new and established freelancers identify new options and narrow down choices.

In conclusion, The Tools of the Trade survey provides valuable data on the kinds of software, apps, and other devices freelance medical communicators use to handle routine business tasks. Anecdotal evidence indicates that participation in the survey might have prompted some participants to explore incorporating some new tech tools into their business practice. A few participants commented that they found the survey edu-

cational because they had not been familiar with some of the included software or apps. Repeated surveys (perhaps every 2 to 3 years) would provide updated data and allow an assessment of trends. It will be interesting to see if and how the patterns of technology use change over time.

Acknowledgments

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Author contact: Monica@NicosiaMedicalWriter.com

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Avoiding Predatory Publishers in the Post-Beall World: Tips for Writers and Editors

By **Ray Hunziker** / Senior Editor, ProEd Communications, Inc., Beachwood, OH

In January 2017, the medical publishing world was rocked by the news that the *Scholarly Open Access* blog that included “Potential, Possible, or Probable Predatory Scholarly Open-Access Publishers” was now offline. More commonly known as *Beall’s List*, the blog was created in 2012 by Jeffrey Beall, a librarian at the University of Colorado Denver. It included lists of publishers, standalone journals, and meetings for medical professionals that Beall deemed “predatory,” and which were designed to bilk unwary authors and meeting attendees out of financial resources. The removal of the content could have been a result of professional and/or legal threats. At the time, this could not be confirmed; however, this did appear in a recent article in *Biochemica Medica* titled “What I Learned From Predatory Publishers.”¹

Although the open access (OA) movement is a laudable effort to make the results of medical, scientific, and technical research freely available to researchers and the public around the world, it unwittingly has become host to predatory publishers and standalone journals. The predators’ “business model” is almost elegantly simple. In the most common form of OA publishing, the Gold OA or “author pays” model, publishing costs are borne by the authors through article processing costs (APCs). This is in sharp contrast to the traditional model in which publishing costs are largely defrayed through journal subscriptions. The predatory publishers/journals collect lucrative OA APCs through fraud and misrepresentation.

Using free services such as Hotmail, predators massively spammed scientists with flattering emails soliciting submissions, often failing to mention APCs, which were sometimes much higher or much lower than legitimate OA journals (eg, *PLoS* and *BMC* journals). Faux journal websites created with free design software to accept submissions were amateurish but effective. Authors who submitted a manuscript would initially be thrilled that the manuscript had been accepted,

often with few to no peer review comments. However, the excitement would soon be tempered by receipt of an invoice in order to publish the manuscript. Authors who refused to pay the invoice could find their submission effectively held hostage, with the journal unresponsive to requests to withdraw the submission. In addition, ethical prohibition against duplicate submission meant that the unpublished work could not be submitted elsewhere. If authors paid the invoice, they would usually find that the online published article appeared exactly as submitted, with no evidence of peer review, editing, or graphic design. With little overhead other than cheap hosting services to house PDFs of the original submissions, a stable of “journals” could be created quickly, even by “publishers” consisting of one person.

Once these publishers had a taste of the potential profits, it was perhaps inevitable that they would branch out into other areas. Predatory publishers large enough to become profitable used their war chests to establish new divisions devoted to organizing meetings, congresses, and symposia. Like their journals, these meetings were of low quality. A common trick was to book large ballrooms at a hotel located in a popular tourist city. By subdividing the larger rooms, small presentation rooms were created so that multiple meetings could be held at the same hotel on the same weekend, all run by a shoestring staff from the predatory organizer. The sources of profit were registration fees (significantly higher than meetings by legitimate societies) and abstract submissions (recruited by spamming in the same manner as for journal manuscripts). Additionally, the meeting organizer would require speakers and regular attendees to use the organizer’s preferred travel vendor, which was—surprise—another division of the predatory parent company.

Other clever predators have metastasized into ancillary services associated with scholarly publishing, such as providing metrics. Unlike those of the established metrics pro-

viders (eg, Thomson Reuters Impact Factor®, Scopus), these metrics are either totally fictitious or, if actually calculated, are essentially worthless because they are not accepted by most institutions as valid measures of journal impact and performance. It remains to be seen what will evolve next, as the predators have created a bona fide ecosystem of low-quality, low-impact, low-value products and services.

Sadly, the victims were often researchers in developing nations, hungry to publish for career advancement and eager to network with peers from developed nations, and willing to pay OA APCs or meeting registration fees out of their own pockets.

Beall's List was initially one of the few, and certainly the most famous, of the online resources designed to help researchers identify predatory publishers and meeting organizers (and, more recently, bogus metrics providers). It was essentially an assortment of blacklists—those that Beall considered “potential, possible, or probable predatory” vendors. Many considered it a valuable resource, but it was not without numerous critics.^{2,3} Some pointed out that, as the work of one person, the evaluations were subjective and Beall’s criteria were insufficiently transparent. As an outspoken critic of OA, Beall was sometimes accused of having an agenda to discredit the OA movement. (Indeed, the publishers and journals listed were only OA; subscription-based publishers and publications

were not evaluated.) Still others felt that the blacklist approach was less desirable than a whitelist approach listing publishers/journals that had been thoroughly vetted and approved as legitimate and ethical. Regardless of opinion, there is no denying that *Beall's List* was a popular place to verify whether a prospective journal or meeting was likely a predator.

Evaluating a journal before submitting material is a core responsibility of the authors. For example, the International Committee of Medical Journal Editors states that “authors have a responsibility to evaluate the integrity, history, practices and reputation of the journals to which they submit manuscripts.”⁴ But how? Or, if you plan to attend a meeting, how can you be sure it is legitimate?

While this article is not definitive nor a systematic review of all resources available, it comprises my own musings from more than 20 years as a medical editor. As do others, I still struggle with the question, “Is this journal/meeting legitimate, or a predator?” The question often comes from colleagues, seeking to guide clients and external medical experts in selecting a journal that may accept their manuscript submission, or a meeting to which to submit an abstract. It is surprising how often my answer is not 100% certain. There are startup journals that continuously surface; some are legitimate, while others are predatory. I have developed a list of criteria that is frequently updated (Figure 1). This list includes tips and is by

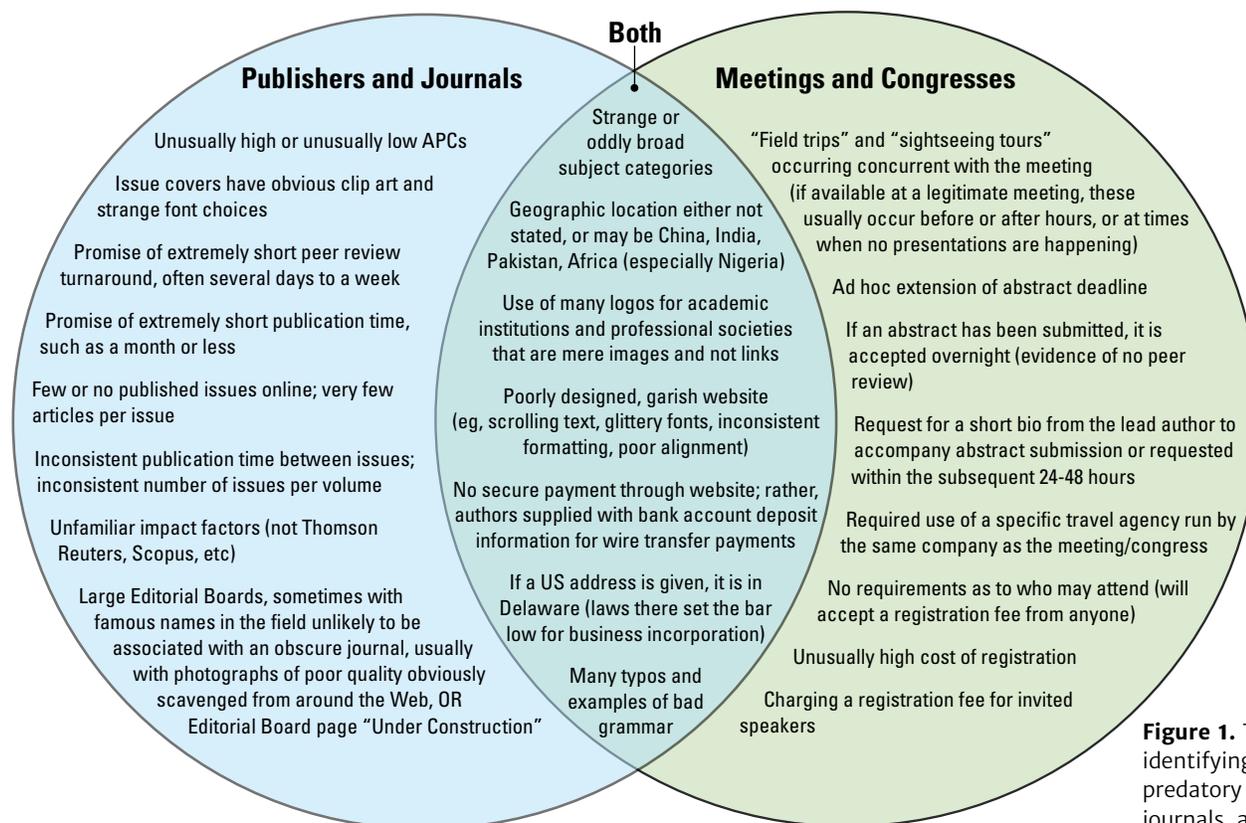


Figure 1. Tips for identifying potential predatory publishers, journals, and meetings.

no means exhaustive, in no particular order, and drawn from my experience and study of websites and communications from known predators. I would also caution against putting too much weight on any single criterion. But if you answer “yes” to the majority of the characteristics in Figure 1, there is an excellent chance that you’ve identified a true predator, one that should be avoided at all costs.

The best defense against the predators is common sense, tempered with a healthy dose of caution. Awareness of this enemy is the first step to avoiding it.

In addition to these tips, there are online resources to consult. Although not up to date, a number of sites have archived versions of the *Beall's List(s)*. A quick Google search will identify the available copies of the list. This is still a good place to start, but it should not be the only resource. Rather, I would recommend a combination of resources, possibly including new whitelists and blacklists that are now available (eg, from Cabells International, <https://www.cabells.com/>), although these are pay-to-play services. The *Think. Check. Submit.* initiative (<http://thinkchecksubmit.org/>) is a collaboration of industry and professional societies, and its 3-step system is easy to use and available in many languages. Laine and Winkler produced a valuable resource for the World Association of Medical Editors website.⁵ For meetings, an excellent example by Cobey et al recently appeared in the *Journal of Oncology Practice*.⁶

The best defense against the predators is common sense, tempered with a healthy dose of caution. Awareness of this enemy is the first step to avoiding it. Although Figure 1 lists other criteria, what are considered the most useful for identifying a predatory publisher/journal are bad grammar (numerous typos, sentence fragments, inconsistent capitalization, hor-

rible punctuation) and poor website design (think Web design circa 1995). For meetings, be suspicious of a company running multiple meetings at the same venue on the same dates, and those that force you to use only their own preferred travel vendor. Often this is a first, obvious way to identify a predator! Also, be alert for lists of Editorial Boards or Congress Faculty that (a) contain a larger-than-expected number of members, (b) are more geographically diverse or from widely divergent fields, and (c) contain headshots/photos that appear to have been pirated from other sources (eg, unclear/fuzzy, pixelated, or with wide variation in background colors/scenery). Often, these experts are unaware that they have been virtually abducted to serve on these fictitious boards/faculty.

Predatory publishers, journals, and meeting organizers pose a serious threat to the integrity of science. Therefore, it is necessary to be vigilant and to carefully evaluate if a publisher/provider is reputable before submitting an article or abstract; it is also a professional and ethical responsibility. Although *Beall's List* is no longer available, there are numerous online resources to help authors, medical writers, and editors. Remember—if it feels wrong, it probably is. Simple common sense is the best guide!

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Missing Data in Clinical Studies

Helen Bridge, DPhil / Clinipace Worldwide, Glasgow, UK

Thomas M Schindler, PhD / Boehringer Ingelheim Pharma, Biberach, Germany

You may think that this topic does not concern medical writers. You may think this is something for data managers or statisticians. Well, you may need to think again. Each and every study you write about in a publication or a study report will have dealt with the problem of missing data. Moreover, the way this problem was handled by those conducting the study can have far-reaching consequences for the validity of the conclusions. The complexity of clinical studies means that everything is related to everything else, so the issue of missing data is linked to many other aspects, from study design to patient retention, data analysis, and the conclusions that can be drawn. Because of this, every scientific report about a clinical study must take note of the extent to which data are missing and how this unfortunate but inevitable fact has been handled.

Why Are Data Missing in Clinical Studies?

In an ideal world and an ideal clinical trial, all patients would come to all visits, all patients would take their medication each day at the right time, and all patients would undergo all procedures as planned. No pieces of equipment would fail, all shipments would occur as they should, all laboratory analyses would be done under the conditions specified, and no samples would be lost. No study investigators or patients would move or decide to leave the study and nobody would have an accident, fall ill, or die during the study. Only in such a scenario could the medical writer be absolved of having to talk about missing data. But as seen from this non-exhaustive list, in the real world things are never perfect and the issue of missing data will invariably arise.

What Are the Issues?

We cannot assume that we will obtain all the data for all the patients in a clinical study. This may or may not be a problem, depending on the quantity and nature of the missing data.

There can be no doubt about it: the more data are missing, the shakier the results and conclusions become. It is very difficult to say when a critical limit of missing data has been reached because the size of the study, the indication being studied, the magnitude of difference between treatments, and the frequency and nature of the assessments must all be considered. However, if the trial is testing for a difference in outcome events (these are any medically important events [eg, heart attacks in patients at high cardiovascular risk]), then even a small number of missing data may be important. If outcome data are missing for a sizable proportion of the patients, the whole trial may become invalidated.

A second issue with missing data arises when the pattern of missing data differs between the treatment groups. This is likely to introduce bias in the interpretation of results. Data can be missing for various reasons. On the one hand, it could be pure chance that values are missing. For example, a patient misses a study visit because her car broke down and she could not get to the study site. Or a patient decides to leave the study because he needs to move for his wife to take up a new job in a different region. On the other hand, the fact that data are missing could be related to the outcome that is being measured and/or the study treatment. For example, we might have a much higher dropout rate in one treatment group than in the other. This may happen for many reasons (eg, because one of the treatments is causing adverse events that lead to discontinuation or because a treatment shows no efficacy and therefore patients stop participating). Then there are cases in which it is difficult to know whether data are missing by chance or because of the treatment. Consider a drug that may cause dizziness and a patient who has a traffic accident on her way to the study clinic and ends up in hospital. Is this a chance event or related to the treatment?

Statisticians have developed a theoretical framework to categorize the reasons for missing data. In brief, they distin-

guish data that are “missing completely at random (MCAR)” from data that are “missing at random (MAR)” and data that are “missing not at random (MNAR).” As the elaboration of these concepts is beyond the scope of this paper, please consult the reading list.

In a randomized trial comparing 2 treatments, missing data because of chance events should not be much of a problem provided they are rare. We would expect chance events to occur with similar frequency in both treatment groups, and therefore no bias is being introduced. However, “missingness” related to the treatment or outcome variable leaves us on very difficult ground.

Suppose we have a study comparing 2 treatments, the new wonderdrug (WD) and placebo. If WD were to cause adverse events that lead to dropout of patients while patients in the placebo group carry on, we risk underestimating the size of the treatment effect. Conversely, if WD has good efficacy and no tolerability issues and the patients taking it remain in the study while patients in the placebo group drop out because they see no improvement, we risk overestimating the size of the treatment effect.

The goal of randomization is that the 2 treatment groups will have similar characteristics at the start of the study. If many patients in one group but not in the other withdraw from the study, the 2 groups may no longer be comparable at the end. This is a serious conceptual problem. For example, if a sizable proportion of patients in the WD group drops out because of tolerability issues, we will not only have more missing data in this group, we will also have a different group of people at study end. By exposing patients to WD, we unintentionally “select” those patients who are able to tolerate the treatment. Hence, at study end we arrive at a comparison of the placebo group with all its initial demographic and disease characteristics and a modified WD group that consists only of those patients who have tolerated the treatment. Their demographic and baseline disease characteristics may be quite unrepresentative of the initial population. This will make it very difficult to draw any conclusions about the efficacy or safety of the 2

treatments because the statistical techniques commonly used to analyze clinical trial data require us to compare randomized treatment groups.

When reporting clinical studies, medical writers need to be alert to signs that missing data are not due to chance and therefore have the potential to cause bias. Signs to watch out for include differences between treatment groups in the proportions of patients with missing values or the reasons for withdrawals. Clusterings of withdrawals or missed visits around certain points in time should also raise suspicion. A starting point could be the tables detailing the disposition of patients. If you detect any issues, it is advisable to ask the statistician to provide further information on the missing data.

Now let’s look at an example of what missing data can look like for individual patients. Let’s assume that we are looking at a trial in patients with type 2 diabetes. We want to find out what effect our new drug has on the long-term marker for blood sugar levels (hemoglobin A1c [HbA1c]). We are looking at the change from baseline to study end as our primary endpoint for efficacy. Table 1 depicts the data of 5 patients during the course of the study.

In this example, we have all values only for patient 1, who has completed all visits. Thus, only for her can we easily calculate the change from baseline. Data analysis will be more complicated for the other 4 patients because they have data missing for some visits. Would it therefore be a good idea to ignore the data from patients 2 through 5 (ie, concentrate the analysis only on “completers”)? No, it would not. Looking at the table does not tell us the reasons why the data are missing, and this is a common situation in real clinical trials. We may know the broad reasons why some patients withdrew (eg, “adverse event” or “lack of efficacy”) and the reason why a patient died, but patients who are lost to follow-up or who missed some visits may not have detailed reasons recorded. The patients who missed visits in our example may have done so because of the severity of their disease, or because they had adverse events, or because of chance events having nothing to do with their health. The patients who attended all visits could be the

Table 1. Data from 5 Patients in a Study with the Primary Endpoint of Change from Baseline in HbA1c

	Study start/ Baseline	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5/ Study end	Comment
Patient 1	X_0	X_1	X_2	X_3	X_4	X_5	Completer
Patient 2	X_0	X_1	X_2	-	-	-	Withdrew at Visit 2
Patient 3	-	X_1	X_2	X_3	X_4	X_5	No baseline value
Patient 4	X_0	X_1	X_2	X_3	-	-	Died after Visit 3
Patient 5	X_0	-	-	-	X_4	-	Did not attend all visits

younger patients with fewer comorbidities who are fit and mobile enough to make it to every planned visit. We cannot know whether, in focusing on only the “completers” (or “observed cases”), we would be selecting patients who share certain characteristics that are not typical of the population as a whole. If we were to disregard all the patients with incomplete data, we would not only risk bias, but would also lose a lot of valuable information. Whatever the reasons for the missing data, these patients may be representative of actual clinical practice.

What Can We Do About Missing Data?

A number of different statistical methods exist for handling missing data, and the risk of bias in a particular situation will vary, depending on the method chosen.

Imputation Methods

For both ethical and economic reasons, it would be wise to use all the data that we have gathered during a clinical study. Thus, we need to find ways to use the data we have in the best and most appropriate way. One method that has been used for many years is the so-called “last-observation-carried-forward” approach, or LOCF. The LOCF method is very simple, as it fills in (or “imputes”) the missing data items with the last observation that was obtained at a previous time point (Table 2).

After having performed LOCF, we can now easily calculate the change from baseline to study end (for patient 3, we use the data from Visit 1 as a starting point). This method looks convenient as it fulfills our aim to use all the data we have gathered and provides a mechanism for filling in the missing values. (A similar imputation method is BOCF, ie, “baseline observation carried forward,” wherein a patient’s baseline value is carried over.)

Although appealing in its simplicity, the LOCF method is likely to introduce bias and may even lead to wrong conclusions. Suppose, for example, we perform a study in a population of patients with depression. In such a group of patients, some will improve spontaneously in their condition. If many

patients in the active treatment group in the study drop out because of adverse events and the LOCF method were applied, this would likely result in underestimation of the treatment effect of the drug. The reason for this is that not all the spontaneous improvements in the active treatment arm would have had a chance to surface and be recorded. Conversely, suppose we perform a study in a population of patients who have a condition that worsens over time. The condition in the group of patients that received placebo would continue to worsen, resulting in a worse score at study end. Further, some patients in the active treatment group might leave the study prematurely due to adverse events. The LOCF method would mean using an earlier, better score for these patients than the scores they would have had at study end had they stayed in the study as their condition continued to worsen over time. This would likely favor the active treatment and result in overestimation of the treatment effect. Because of the potential for introducing bias and incorrect conclusions, regulators and leading statisticians urge clinical researchers to stop using the LOCF method.

Not all methods for imputing missing values carry as great a risk of bias as LOCF. Instead of filling in each missing value with a single “replacement” value (as with LOCF and BOCF), a more sophisticated form of imputation, which minimizes bias, is so-called multiple imputation (MI). The MI method involves using the data collected in all patients, whether they have complete data or some missing values, to model the distribution of the missing data. This model is then used to generate a series of values (this is the “multiple”) to fill in each missing observation. This produces a series of different data sets, each consisting of all the observed values and imputed values for the missing data. The prespecified analysis methods can then be used on each of the generated data sets, and an overall estimate of treatment effect is derived by combining all the results.

Methods Involving Statistical Modeling

A very different approach to handling missing data is to use a model that can take account of all the available information

Table 2. Data from 5 Patients in a Study with the Primary Endpoint of Change from Baseline in HbA1c with Missing Data Being Filled in by LOCF

	Study start/ Baseline	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5/ Study end	Comment
Patient 1	X_0	X_1	X_2	X_3	X_4	X_5	Completer
Patient 2	X_0	X_1	X_2			X_2	Withdrew at Visit 2
Patient 3	-	X_1	X_2	X_3	X_4	X_5	No baseline value
Patient 4	X_0	X_1	X_2	X_3		X_3	Died after Visit 3
Patient 5	X_0	-	-	-	X_4	X_4	Did not attend all visits

from patients with complete data as well as those with some missing values. This makes it unnecessary to fill in the missing values with substitute values. An approach of this kind frequently used in clinical trials in which the same continuous outcome variable is measured repeatedly at different time points is a family of analyses called mixed-effects models for repeated measures (MMRM). In effect, these analyses combine the information available for individual patients who have missing data with information from the patients who have complete data to predict what the responses of the patients with missing data would have been.

Suppose a patient showed a small improvement from baseline early in the trial, then withdrew after 3 weeks, while most other patients in the same treatment group tended to show larger improvements in the first 3 weeks and then continued to improve until the end of the study. In an MMRM analysis, the pattern seen in the data collected from the patient before withdrawal will feed into the overall estimate of treatment effect, as will all of the data collected from the other patients. So, in this example, the model will assume that the withdrawn patient, like the other patients, would have continued to improve after week 3, but—based on the data from the first 3 weeks—that this patient's improvement would have been smaller than average.

By comparison with single imputation methods like LOCF and BOCF, MMRM has the clear advantage of using all the available information for each patient (instead of just 1 value) to arrive at an estimate of treatment effect. It has also been shown to produce much less biased estimates than LOCF.

Sensitivity Analyses

There is no single best solution to the missing data problem that will produce unbiased results in all circumstances. As well as choosing a method that is appropriate to the particular situation, it is important to demonstrate the robustness of the results by carrying out sensitivity analyses. These should include analyses using different missing data handling methods from the one that was used in the primary analysis. For example, if MMRM is used for the primary analysis, the sensitivity analysis might include LOCF, BOCF, and MI. Or if LOCF were used for the primary analysis in a long-term trial with many patient withdrawals, it would be helpful to include a sensitivity analysis based on the completers only. If the results from the primary analysis and the various sensitivity analyses are similar, then we can be confident that the results are not being unduly influenced by the method used for handling missing data. If, on the other hand, the results differ substantially, then the issue of missing data needs further investigation and discussion.

What Can Be Done to Avoid Missing Data?

“No amount of statistical expertise can make up for the absence of real data” (MG Kenward, 2013). Preventing missing data in the first place, therefore, needs to be a top priority. A number of measures can be taken at the trial protocol stage to help limit the quantity of missing data. Most importantly, trials need to be designed so that they interfere only minimally with the “normal life” of the study participants. That means study visits should be scheduled at convenient times and should not take too long. If it is possible to design the trial so as to minimize the number of visits and assessments, this is likely to help retain patients in the study. Likewise, generous visit windows make it easier for patients to fit study visits around other commitments. The longer the follow-up period, the more patients are likely to withdraw, so using a short follow-up period at least for the primary endpoint can help minimize the impact of missing data. Endpoints that are difficult or time-consuming to measure, or that require invasive procedures, tend to result in a high quantity of missing data. If endpoints can be chosen that are easy to measure, this is likely to reduce the amount of missing data.

As we have seen, missing data that arise due to adverse events or lack of efficacy are especially problematic because they tend to be associated with a particular treatment and therefore risk biasing the results of a study. Withdrawals due to tolerability issues can be minimized by allowing flexible dosing. Withdrawals due to lack of efficacy are a common problem when patients receive placebo, so using an add-on design, in which patients receive active treatment or placebo in addition to standard treatments, can help to avoid withdrawals for this reason. Should a patient nevertheless need to discontinue study treatment, the sponsors should ask for permission to continue to collect data from them and plan the study so that discontinuation of treatment does not necessarily mean the patient has to withdraw from the study.

Precautions can also be taken to limit missing data during trial conduct. Engaging the participants by giving clear explanations of the study purpose and the procedures will most likely reduce the number of patients who withdraw from the study. The choice of investigators and trial sites can take into consideration their track record at following up patients and collecting complete data. Sites can be chosen that are conveniently located and easily accessible, with facilities that make it easier for patients to attend visits (such as plentiful parking and on-site child care). Investigator training and communication with patients can emphasize the importance of patients remaining in the trial until the end.

Realistically, it will never be possible to prevent missing data altogether. In order to ensure that data are collected from enough patients to enable valid conclusions to be drawn,

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ANOTHER Ethics Column??

By **Tamara Ball, MD** / Principal Medical Writer, INC Research/inVentiv Health Clinical, Raleigh, NC; Everyday Ethics Editor, *AMWA Journal*

If you've been an AMWA member for any period of time, you may have noticed that professional ethics pervades our organizational culture. Nowhere is this more evident than on the AMWA website (Table 1), where a foundational document—the “AMWA-EMWA-ISMP Joint Position Statement on the Role of Professional Medical Writers”—can be found. The Statement begins,

“Professional medical writing support helps authors and sponsors to disclose their research in peer-reviewed journals and scientific congresses in an ethical, accurate, and timely manner, with the ultimate aim of advancing patient care.”¹

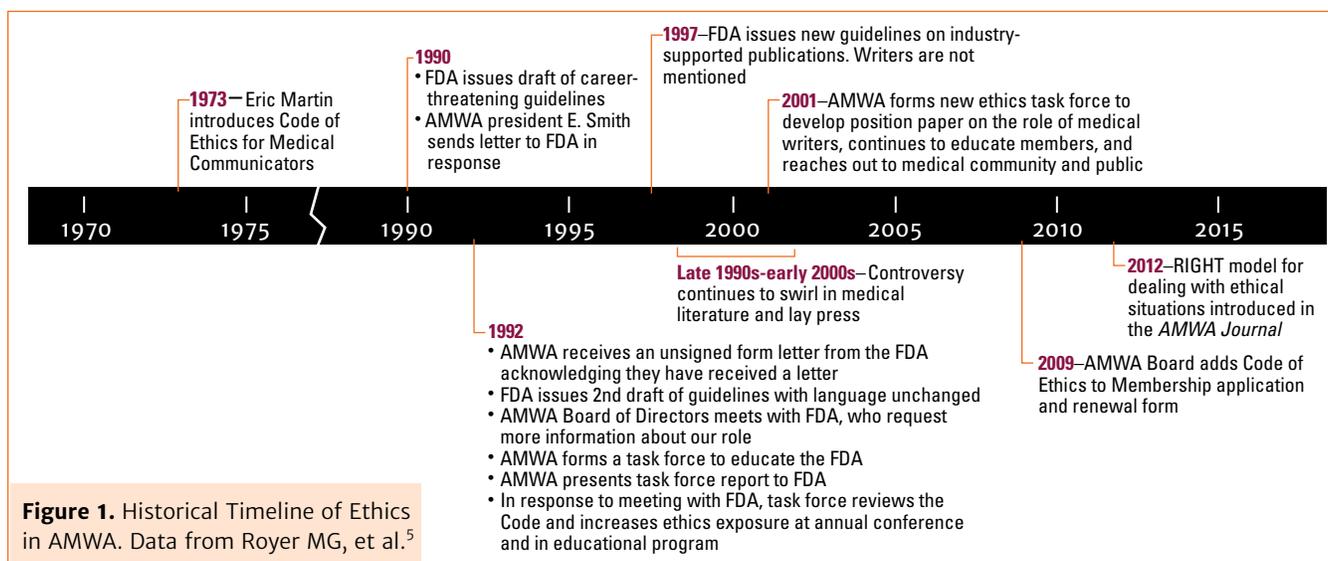
AMWA's ethical backbone, the Code of Ethics, sits beneath the Joint Statement. Nearly every component of AMWA's extensive education program incorporates ethics in some fashion, including Workshops, Essential Skills, Online Learning, and Self-Study Workbooks. Members can draw attention to their own ethical savvy in their Personal Profile or Freelance Directory listing. In addition, the Medical Writing Certified[®] credentialing examination includes ethics in the outline used to prepare potential test takers, and ethics is frequently a topic of conversation on *Engage*, AMWA's online community. A search of AMWA's website using “ethic” as the search term delivered 166 hits, 81 of which were *Journal* entries. With all of these resources, you may be wondering, “Why on earth do we need an Ethics Column? What more could possibly be said?” I believe that ethics is not simply a list of facts or guidelines to be memorized; rather, ethics is the embodiment of core values that manifest our beliefs and guide our actions. As such, ethics is a living, evolving part of who we are as individuals, professionals, and members of the larger community. Thus, it warrants our continued attention and ongoing exploration.

AMWA has a long history of commitment to professional ethics (Figure 1). It began in 1973 when—after being urged for a decade to do so—the AMWA Board of Directors approved

Table 1. Ethics-Related Resources from the AMWA website

AMWA-EMWA-ISMP Joint Position Statement on the Role of Professional Medical Writers
Education Program Workshops Essential Skills Online Learning Self-Study Workbooks Medical Writing Certificate Outline
Opportunities to Highlight Ethics Knowledge Personal Profile Freelance Directory
<i>AMWA Journal</i>
<i>Engage</i>

the Code for Medical Communicators proposed by Eric Martin, PhD.² Throughout the 1980s, the use of medical communicators was a subject of considerable debate. Advocates felt that communicators improved the quality of documents and the efficiency with which they were produced, while opponents felt that their use encouraged bias, especially when a communicator's contribution went unacknowledged or their financial relationship to industry was not disclosed³—practices that were unfortunately common at that time. In 1991, the US Food and Drug Administration (FDA) drafted career-threatening guidelines that imposed severe limitations on the use of industry-sponsored communicators⁴; AMWA responded vigorously. For AMWA, the conflict ultimately resulted in a review of what has now become the AMWA Code of Ethics and an energetic expansion of the topic that informs the details of its practice in the educational program.⁵ Workshops on ethics proliferated, presentations on ethics were included in the Annual Conference,⁵ and Workshop leaders were encouraged to include consideration of professional ethics in all of their presentations. The Code was added to the AMWA membership and renewal form in 2009.⁶ Although



membership awareness has improved, there remains much to be done.⁷ This column aspires to be a continuation of AMWA's focus on professional ethics.

"A profession is a disciplined group of individuals who adhere to ethical standards. This group positions itself as possessing special knowledge and skills in a widely recognised body of learning derived from research, education and training at a high level, and is recognised by the public as such."⁸

People with extensive training often wish to be recognized as professionals engaging in a profession rather than as technicians providing a service or workers doing a job. The crucial element that transforms an occupation into a profession is a shared ethic. Thus, medical communicators need a solid understanding of basic ethics and a maturing awareness of its nuances, not in the least due to the strong link between ethics and professionalism.

This ethic is often expressed as a Code of Ethics (Code) that sets the minimal acceptable moral behavior for that profession. Codes can be used to teach or remind members of their professional obligations and, when shared with employers and consumers, can enhance trust in and respect for the profession. Most commonly, the Code is self-defined, collectively accepted, and regulated by a professional organization through a licensing process.⁹ Of note, AMWA's focus has always been on professional education; the organization has never issued a license to "practice medical communication." Medical communicators who initiate or renew an AMWA membership are asked to agree to the Code because "membership in AMWA is an honor and a trust"⁶; thus, adherence is entirely self-regulated.

AMWA's Code consists of a preamble and 8 principles that guide ethical conduct in medical communications (Figure 2).¹⁰

Though it reflects essential truths of our profession, AMWA's Code is not a static collection of statements. It is subject to review and modification and can be revised in response to a change in industry standards, innovation in science and technology, evolution of the media used to communicate the message, and shifts in societal norms or the political atmosphere. Since its introduction in 1976, the AMWA Code has been reviewed and modified 3 times (1989, 1994, 2008), with the greatest change occurring in 1994 when "scientific rigor" and "fair balance" were added to Principle 2 in response to changes in emphasis at the FDA. Other changes were editorial in nature.⁵

When communicators execute their duties with ethics in mind, there are advantages for everyone. First, there is an increased trust when an employer knows that through an organization like AMWA, the potential employee has had exposure to professional ethics. This is especially important at this time, when employers can be overwhelmed by the endless parade of service providers on the internet.¹¹ Employers need a filter to distinguish between those who may or may not violate professional ethical norms and become a liability for the company. Today's economy is increasingly driven by the transfer of specialized knowledge, and this is accomplished most efficiently when governed by a code of ethics. Further, advocating for our professionalism may enhance our employability and increase our job longevity.¹²

As part of agreeing to the Code, AMWA members pledge to "expand and perfect their professional knowledge and communications skills" (see Principle #5; Figure 2).¹⁰ AMWA membership makes it more likely that we meet our continued education goals. When members gather at an annual conference or chapter event, it affords them the opportunity to connect with like-minded individuals who share their work and a place to turn for professional advice. And when we behave

AMWA CODE OF ETHICS

Preamble

The American Medical Writers Association (AMWA) is an educational organization that promotes excellence in medical communication and recommends principles of conduct for its members. These principles take into account the important role of medical communicators in writing, editing, and developing materials in various media and the potential of the products of their efforts to inform, educate, and influence audiences. To uphold the dignity and honor of their profession and of AMWA, medical communicators should accept these ethical principles and engage only in activities that bring credit to their profession, to AMWA, and to themselves.

Principle 1. Medical communicators should recognize and observe statutes and regulations pertaining to the materials they write, edit, or otherwise develop.

Principle 2. Medical communicators should apply objectivity, scientific accuracy and rigor, and fair balance while conveying pertinent information in all media.

Principle 3. Medical communicators should write, edit, or participate in the development of information that meets the highest professional standards, whether or not such materials come under the purview of any regulatory agency. They should attempt to prevent the perpetuation of incorrect information. Medical communicators should accept assignments only when working in collaboration with a qualified specialist in the area, or when they are adequately prepared to undertake the assignments by training, experience, or ongoing study.

Principle 4. Medical communicators should work only under conditions or terms that allow proper application of their judgment and skills. They should refuse to participate in assignments that require unethical or questionable practices.

Principle 5. Medical communicators should expand and perfect their professional knowledge and communications skills.

Principle 6. Medical communicators should respect the confidential nature of materials provided to them. They should not divulge, without permission, any patent, proprietary, patient, or otherwise confidential information.

Principle 7. Medical communicators should expect and accept fair and reasonable remuneration and acknowledgment for their services. They should honor the terms of any contract or agreements into which they enter.

Principle 8. Medical communicators should consider their membership in AMWA an honor and a trust. They should conduct themselves accordingly in their professional interactions.

Original: Eric W. Martin, PhD, 1973

First revision: June 1989

Second revision: April 1994

Third revision: June 2008

ethically, we are more likely to obtain the recognition, respect, and reward a professional traditionally merits.¹³

As we have transformed medical communications into a true profession, talented people have been attracted to it as a viable career option, which has resulted in an influx of new members over the years 2014-2016 (written communication, Sharon L. Ruckdeschel, AMWA Director of Membership & Systems). It is especially important, and some would contend that it is our collective responsibility, to introduce the Code to new members early in their careers. How are they to know what professional behaviors are expected of them if they are not provided a guide? Unsurprisingly, a 2005 AMWA survey revealed that member familiarity with guidelines was associated with compliance with those guidelines.⁷ Therefore, members exposed to the Code may take action consistent with the Code, perhaps resulting in increased respect for our profession. Through this column, I seek, in part, to expose newcomers to ethics-related concepts and remind established members that the principles stand, ready to serve as their professional moral compass when needed.

Ethical conundrums occur with disquieting frequency, many would say every day. Some situations are big, some not so big. We can *hope* to take appropriate ethical action based on instinct and experience, or we can prepare ourselves to meet these challenges by using a more systematic approach. I propose that we explore the experience of our colleagues through the lens of the RIGHT model. This model for dealing with ethical situations was developed by AMWA workshop leaders who taught ethics, has been experienced by many AMWA members, and was presented in an excellent article published in a 2012 issue of the *AMWA Journal*¹⁴ (http://cymcdn.com/sites/www.amwa.org/resource/resmgr/journal/Issues/2012/2012v27n1_online.pdf).

The 5-step RIGHT model was designed to be simple and, thus, memorable, and to be applicable to most, if not all, possible ethical situations our diverse membership might encounter (Figure 3).¹⁴ **R** is *recognizing* the ethical situation, which includes naming the issue, identifying who is directly involved, and listing all stakeholders (those who could possibly be affected by the final decision). **I** is *investigating* the facts and assumptions, which includes identifying relevant ethical codes, statutes, regulations, and laws that may apply and taking stock of your own competencies and biases, and considering potential conflicts of interest. **G** is *gauging* the situation, which is the step in which decisions are made. Communicators list every potential action and the likely effect on each stakeholder. The best decisions maximize benefit and minimize cost and risk. **H** is *handling* the situation. Now that the What and Why have been determined, communicators need to consider Who, When, Where, and How the decision will be implemented. **T** is *tailoring* the decision, which involves a backward look at the RIGHT model experience to determine whether there are lessons to be learned moving forward.

Ethical thinking compels us to be guided by, but not shackled by, the Code. Proper use of the Code involves careful consideration of the unique situation in question.¹⁵ A benefit of AMWA membership is being an active participant in a community of peers who are

Figure 2. AMWA Code of Ethics.¹⁰

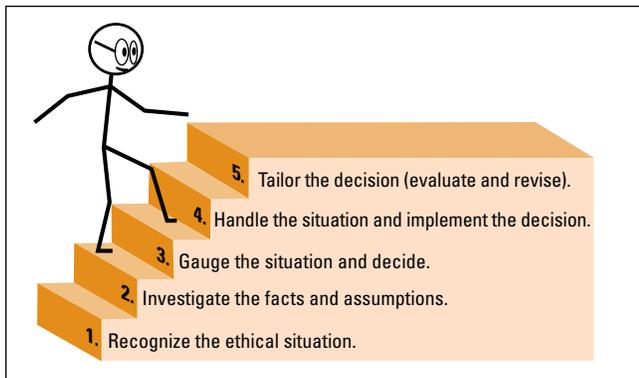


Figure 3. The RIGHT model for making ethical decisions. Reprinted from Hamilton CW, et al.¹⁴

uniquely willing to share their knowledge and experience for the betterment of each other, the association, and the profession. With that in mind, I encourage members to share with each other ethical situations they have experienced. Please send essential details of the situation, a list of stakeholders, proposed solutions, and, if the situation has been handled, how it was handled and the follow-up results. Please consider following the RIGHT model. Both newcomers and seasoned AMWA members are encouraged to submit thoroughly anonymized “cases” that may serve as a springboard for discussion in this column. An interactive ethics column is a new way of exercising our ethical muscle at AMWA, and the discussion may generate a renewed awareness of the ethical principles that govern our profession. Please send cases to tballmd@gmail.com. I may not be able to publish all cases, but I will eventually return your message.

Cheers!

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it is important to consider the likely number of missing values when planning the trial and to allow for them when calculating how many patients to recruit.

Summary and Conclusion

The phenomenon of missing data is ubiquitous in clinical studies. Both the extent of missing data and the structure of missing data can introduce bias into study results and lead to wrong conclusions. The traditionally used LOCF method to fill data gaps is problematic in many ways. It is better to employ a method that reduces bias, such as MI or MMRM, to account for missing data. Medical writers should be aware of the extent of missing data and should describe the methods that have been used to deal with this issue.

Additional Reading

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Social Media and Health Literacy

By **Helen Osborne, MEd, OTR/L** / President of Health Literacy Consulting, Natick, Massachusetts, and founder of Health Literacy Month

What exactly are social media? I wonder about that sometimes. If social media are limited to Facebook, Twitter, LinkedIn, and the like, then I'm not a big fan or frequent user.

But if social media are defined more broadly, count me in! In my way of viewing it, social media include all sorts of electronic communications that are interactive, immediate, and often inclusive of more formats than just the written (ahem, typed) word.

Social media can be a powerful tool for health literacy—helping medical writers, clinicians, and other professionals communicate health information in ways that patients and the public can understand. Social media also can be a wonderful way for professionals or patients to directly communicate with one another.

Here are examples of ways that social media can enhance the work of health literacy. As you can see, there are abundant opportunities for medical writers to get involved.

Social media to help professionals learn from each other:

- **Health Literacy Discussion List.** This list is hosted by the Institute for Healthcare Advancement (IHA). Honestly, I don't think I'd be nearly as savvy about health literacy if it wasn't for this online discussion group. It's been a constant presence in my business life for many years. (I once co-moderated this list. Now Julie McKinney does a stellar job.) Participants include health literacy researchers, practitioners, teachers, and advocates worldwide. Topics range from plain language basics to good sources for health images to higher-level concepts such as links between health literacy and social justice. How does this fit into my definition of social media? Discussion can be immediate, with many postings a day, though sometimes a week goes by without any. While not exactly multimedia, postings often include links to articles and videos. What

Helen Osborne, the 2017 Alvarez Award Winner, helps professionals communicate health information in ways that patients and the public can understand.

Helen is president of Health Literacy Consulting, founder of Health Literacy Month, and producer/host of the podcast series Health Literacy Out Loud. Helen also is a member of the national Patient Centered Outcomes Research Initiative (PCORI) Advisory Panel on Communication & Dissemination Research.

Helen brings clinical experience, educational training, and the patient perspective to all her work. She speaks about health literacy at conferences worldwide. She also serves as a plain language writer/editor on a wide range of health-related materials. Helen is the author of several books, including the AMWA award-winning *Health Literacy from A to Z: Practical Ways to Communicate Your Health Message, Second Edition*, which is considered by many as the most important health literacy text today.

To learn more about Helen's work, please visit the Health Literacy Consulting website at www.healthliteracy.com. You can also listen to her Health Literacy Out Loud podcast interviews at www.healthliteracyoutloud.org.



does this mean for medical writers? Those who write consumer-facing medical materials no doubt are expected to be savvy about health literacy and plain language. This free online discussion group is a great forum to post questions, search the archives, and learn about best practices. Here's the link: <https://www.iha4health.org/our-services/health-literacy-discussion-list>.

- **Health Literacy Out Loud (HLOL) podcasts.** At the risk of being self-serving, I want to mention this no-cost way for medical writers to stay up to date about issues related to health literacy, patient education, and health communication. I started this series in 2008 and have since posted more than 165 audio interviews with those “in the know” about health literacy. In about 20 minutes, you get to hear my conversations with experts about what to do, why to do it, and how to learn more about many aspects of health communication. Many listeners tell me that these podcasts help them stay current with research and practice. You can access all HLOL podcasts and many of the transcripts at www.healthliteracyoutloud.org.

Social media to help health professionals share information with patients:

- **Texting.** Today, patients (perhaps with caregivers) are responsible for the majority of day-to-day health care. This includes making decisions about what to eat, taking medications as directed, and keeping up with all needed appointments. Texting is now being used as a way to help. One example is Text4Baby, a free service that sends to-be and new moms timely messages about prenatal care and a baby’s development in the first year. This service was created by several reputable agencies, including the Centers for Disease Control and Prevention. Its use and effectiveness have been well researched. Why does this form of social media matter to medical writers? While projects like these can outwardly seem simple, there are many aspects that could benefit from skilled and savvy medical writers. Perhaps there are opportunities to help with programs like these. Here is the link to Text4baby: <https://text4baby.org>.
- **OpenNotes.** As described on its website, “OpenNotes is the international movement dedicated to making health care more open and transparent by urging doctors, nurses, therapists, and others to share their visit notes with patients.” This system of sharing a patient’s medical information is used in the Veteran’s Health Administration and is being adopted in hospitals and health centers across the United States. What role is there for medical writers? To make sense of their doctor’s notes, patients need to understand medical terms and concepts. When writing patient education materials, you can help by clearly defining key terms and then consistently using the same terms throughout. It’s not always clear which

to use. For instance, after explaining that “hypertension” and “high blood pressure” mean nearly the same thing, you and others on the writing team need to weigh which term would be more helpful to readers. Learn more about Open Notes at <https://www.opennotes.org>.

Social media for patients and caregivers to communicate with each other:

- **Twitter, Facebook, etc.** It’s almost inevitable that each of us will someday have a serious illness or find ourselves caring for someone who is sick. This experience can be scary and overwhelming. We may feel alone. Twitter, Facebook, and other social media offer ways for patients and caregivers to connect with, and support, each other. For example, Twitter has a growing number of tweet chat exchanges that use the same hashtag (#) to focus on a specific topic. A good place to find lists of hashtags, tweet chats, and more is the Healthcare Hashtag Project, <https://www.symplur.com/healthcare-hashtags>. Facebook, too, is a way for individuals to post updates and allow others to express support by commenting, liking, and sharing. What’s the relevance of these to medical communicators? Well, there’s the personal part of course. There’s also value for us as professionals. Regardless of our audience, it helps to frame medical information in the context of the patients’ experience of illness. My guru on using social media this way is Pamela Katz Ressler, MS, RN, HNB-BC. I encourage you to watch this video of Pam leading a panel discussion at Stanford Medicine X, “Communicating the Experience of Chronic Illness in the Digital Age”: <https://www.youtube.com/watch?v=rBdYLhiucnE&feature=youtu.be>.
- **CaringBridge.** This website offers a way for seriously ill patients and their friends, family, and caregivers to connect about issues they are going through now. This free service is not only convenient but also informative and interactive. Why is it of value to medical writers? None of us are exempt from illness, whether we are the ones who are sick or the ones caring for others. Medical writers can help by sharing news about useful, reputable social media sources like this. Here’s the link: <https://www.caringbridge.org>

Health literacy is about communicating health information in ways that people can understand. Today, that includes using social media for learning and sharing. It’s a powerful way we all can take health literacy action.

Have You Made Your Plans for the AMWA Conference in Orlando? It's 6 Weeks Away!

By Kelly Schrank, MA, ELS / 2016–2017 Annual Conference Administrator

There is still time to register for this year's conference and enjoy all of its social and educational opportunities! Whether you registered as a SuperSaver in the Spring or only plan to register before the regular pricing ends on September 30, you'll need a plan for what you want to learn and accomplish at the conference to make the most of your time and money.

Is this the year you... Transition from the bench to medical writing? Move to a new industry? Advance at your current employer? Master a new skill? Switch from writing to editing or from contributor to manager? Go freelance? There are sessions, workshops, and roundtables to help you with all of these goals.

Do you want to meet... People in certain industries, such as medical devices or academia? Those working in different areas, such as grant writing, health economics and outcomes research (HEOR), or continuing medical education (CME)? Folks who write in plain language or patient-centered publications? During the roundtables lunch on Friday (free with your registration), there will be tables for open discussions on topics such as these, as well as tables with facilitators to guide discussions on more specific topics.

Is your goal to... Get up to date with the industry by exploring some of the latest trends? There are sessions on technology—such as video, podcasting, and content management systems—to get you started. Do you need help incorporating storytelling or PR into your work? How



about medical devices or biologics or biosimilars? They are all covered in sessions at the conference.

Do you just want to... Strengthen your core skills? Delve more deeply into how to be an effective communicator? Dive

into a particular science topic? Learn how to better present data? These are all covered in workshops, sessions, and roundtables at various times throughout the conference.

Or are you looking for opportunities to... Develop your brand? Expand your network? Build your freelance business?

- You can attend the Intensive Session: Success Strategies for Showcasing Your Personal Brand (<http://engage.amwa.org/blogs/larry-lynam/2017/06/27/creating-our-brand>) for an in-depth workshop.
- You can network in so many ways! Watch AMWA Engage for blog posts on networking and other topics in the coming weeks. Until then, if you don't have business cards or a LinkedIn profile, work on that now!
- You can learn strategies to build your freelance business, no matter your level of experience or number of years in business, with sessions and roundtables that cover nuts and bolts, tech tools, social media, and business plans. And for the advanced freelancers, we are pleased to repeat our popular Freelance Jam Session.

There are so many options for learning and networking, so many people to meet, and so many new experiences to be had if you are willing to be open to what the conference has in store for you! But time is running out . . . this is your last chance to get your plans together. We look forward to seeing everyone in Orlando on November 1-4, having fun, learning new things, and growing as medical communicators!

Be Happy. Be Here.

By Rachel Spassiani, MA

Manager of Communications & Resources, AMWA



We know that our attendees love networking and value learning, but there is so much more to do and see at our conference this year! If you've made the decision to attend AMWA's Medical Writing & Communication Conference at the **Walt Disney World®** Resort, Florida, we want to share some fun facts with you about Orlando and **Walt Disney World®** Resort to ensure you make the most of your conference experience.

Getting to Orlando

The Orlando International Airport offers more flights to more places than any other airport in Florida. In fact, Orlando International Airport provides nonstop service to more major US destinations than most other cities in the United States.

The Orlando International Airport is about a 30-minute ride from the *Walt Disney World Swan and Dolphin*, and cabs can be expensive. Mears is the preferred service provider for transportation for the *Walt Disney World Swan and Dolphin* in Lake Buena Vista. A ride on the Mears Shuttle will cost about \$37.00* roundtrip for an adult. We recommend that you make your transportation reservations online prior to your arrival via our website, or use the code WEB10 when contacting Mears by phone. The concierge at the hotel can assist you with reservations for departure.

If you are planning to drive, there is plenty of parking available at the resort. Self-parking is \$20/day. Valet parking is \$28/day.*

Getting Around the Property

The 2017 AMWA Medical Writing & Communication Conference will take place at the *Walt Disney World Swan and Dolphin*. This hotel is situated in the heart of the **Walt Disney World®** Resort campus and offers easy access to all the amenities available on the Disney property. Guests enjoy complimentary and regularly timed transportation throughout the entire resort, so that you may come and go at your convenience. You may take the Friendship Boat from the hotel directly to the International Gateway's World Showcase entrance to **EPCOT®**. Or you may take a bus from the hotel to any of the theme parks or to the Transportation and Ticketing Center—which serves as the hub for all modes of transportation throughout the property (buses, boats, and the ever-popular monorail!). AMWA has secured specially priced Disney Meeting & Convention Tickets, including their Twilight Ticket, so you can spend your evenings in the theme parks at an affordable price. You may also pre-purchase Full-Multi-Day theme park tickets at a discounted rate (multi-day tickets include a complimentary +1Fun Bonus visit) online via our website.

2017 AMWA

Annual Conference Committee

Thank you, Annual Conference Committee members, for your hard work, thoughtful discussions, and industry insights in creating this year's conference program.

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Getting Something to Eat

There are many options for dining and entertainment in the area. If you would like to go somewhere specific or with a large group of people, we highly encourage you to plan ahead. **Walt Disney World®** allows visitors to make dining reservations in advance up to 180 days prior to their dining date. The easiest way to make your reservations is to use the Disney dining website: <https://disneyworld.disney.go.com/dining>. It is important to remember that if you want to eat at a restaurant in a theme park, you must have a valid admission ticket for that theme park.

There are plenty of dining options outside the theme parks, including 9 different restaurants within the conference hotel and dozens of restaurants at other hotels. *Walt Disney World Swan and Dolphin* is within walking distance of *Disney's Boardwalk Entertainment District* and a short bus ride away from *Disney Springs®*, a retail and dining paradise with more than 50 food options.

Getting Ready for #AMWA2017

Registrants should keep an eye out for AMWA's "Know Before You Go" message, which will be sent to all attendees just before the big event. This email will have important information, including schedule reminders, badge pickup times and location, and a preconference attendee list. In the meantime, get ready for an amazing AMWA experience. We can't wait to see you there!

More information is available at our website: http://www.amwa.org/Hotel_and_Travel.

** Please note that all prices are approximate and subject to change.*

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SHOWCASE PLAZA
IllumiNations: Reflections of Earth **FP+**
 Presented by Siemens
 Breathtaking fireworks, colors and lights set to a musical score. See Times Guide.

Boat & walkway to Epcot® Resorts & Disney's Hollywood Studios®

As to Disney properties/artwork: ©Disney



Brian Bass



Melissa L. Bogen



Lori De Milto



Cherie Dewar



Ruwaida Vakil

Q Have you ever had problems collecting payment from a client? How do you effectively handle this situation?

A I've only had a problem getting paid once in 20 years, but I've heard lots of horror stories about this from other freelancers. The first step is to find out whether (1) it is just a mistake, (2) the client has a long bill payment cycle, or (3) the client is deliberately trying to stall or avoid payment. If your client contact forgot to submit the invoice or accounts payable forgot to process it, then wait patiently for the payment. If the payment is large and you really need it, ask your contact to expedite it.

Some clients have a long bill payment cycle. Nearly all of my hospital clients, for example, pay at 60 days instead of 30. This is fine with me, and I don't consider this a problem getting paid.

But clients who are deliberately trying to stall payment or not pay freelancers are a real problem. The one time a client didn't want to pay me, I had a lawyer write a letter threatening legal action if the client didn't pay up. My check arrived a few days later.

If the threat of legal action doesn't work, actually hiring a lawyer to collect your payment may not be worth it. It could cost you more than you'll get from the client, and there's no guarantee that the client will pay you. Your best option may be to take the loss.

—Lori De Milto

Despite my 25+ years in the business, problems collecting have been extremely rare. Using two examples—the most innocuous and the most pernicious—I have described the situations below; how I was naive and/or made a mistake; how payment was resolved; and what I did differently after that to ensure to the best of my ability that the situations did not happen again.

Example #1: In my second year of business, an ad agency owed me \$750 for a small project. Payment was due upon

receipt of invoice or within 30 days. I had known the agency's president through my tenure as a full-time employee for pharma/biotech, so I trusted the client without a written contract. In fact, our prior relationship is why I was given the project in the first place. I let 30 days go by and then called the client to inquire about payment of my invoice; the accounting person said they had a glitch in their bookkeeping program and were late, but that I would receive the check very soon. I did not ask "how soon" but I did re-invoice to make sure no one could say they did not have the invoice. Another month went by without payment. I re-invoiced and called again; after that I called every week. Sometimes I faxed another copy of the invoice. Each time I was told "soon" and that they had a problem with bookkeeping. Finally, after 3.5 months, I received my check (no late fee was included).

My Error: I should or could have

- had a written contract (even though in this case it may not have helped).
- emphasized a 10% late fee in that contract (something that often "triggers" accounts payable).
- called the president the day after the invoice was overdue (in this case I believe I would have received payment promptly).
- requested an advance before starting.

Resolution: Payment was received after 3.5 months of persistent dunning by phone and fax.

Future Protection: Later I ran into the agency's president at an event and told him how sorry I was to know that his agency was doing so poorly that it could not pay its bills. He was shocked; when I told him my experience, he apologized and promised that it would never happen again and that, if it did, I should call him directly. I thanked him and said that I likely would request a 50% advance on future projects. The client called again, but I was quite busy with other paying clients, so I declined the offer.

Example #2: Approximately 15 years into my business, a pharma client owed me \$26,000.00 and refused to pay, first lying and later claiming lack of funds. Determined, I spent weeks and weeks of re-invoicing, emailing, faxing, telephoning, and paper mail. (Note that \$2,000.00 comprised a late fee, while \$12,000.00 was a kill fee I had written into the contract for early termination of the project.)

My Error: A physician colleague for whom I had worked quite a bit had referred me to this client. Even so, I should never have continued working after the first \$12,000.00 was unpaid. Moreover, I should not have continued working beyond \$5,000.00 (ie, I should have billed at \$5,000.00 and put in no more hours until that was paid).

Resolution: It took about 6 to 7 months of dogged follow-up, but I finally received a check for \$7,000.00. By then the company was in receivership with the surrogates trying to clear as much debt as possible, so they were happy to negotiate with me. (Note that early on, the client's CEO had cashed out several million dollars of stock and disappeared without shame. Several other vendors had tried desperately to collect; not one received payment of any kind. I was the only consultant to get paid anything. (One colleague took them to court for \$130,000.00 and got a *judgment* for that amount—but he never received a single dollar!) To what do I attribute my success? Even though I called constantly I was unfailingly polite and sympathetic, telling them how sorry I was that things had gone so badly, but that I was simply an individual freelance writer who had done this work in good faith. I was put off week after week but was nonetheless always courteous when I called/wrote/faxed/emailed. Finally, I was able to speak with a surrogate who was not only sympathetic but who also had authority; I told her that \$12,000.00 of the \$26,000.00 was a kill fee and that I would be willing to waive that debt and settle for 50% of the remaining \$14,000.00 owed *if they would pay me within 3 weeks*. Because they were trying to settle at least some debts, she agreed, sent me a waiver to sign, and I received the check as promised. The other vendors were amazed that I received anything at all. Persistence does pay, as does courtesy. I could afford to be doggedly tenacious because I had plenty of other work. Once I found out about the other consultants not being paid either, I became quite calm about it and, in fact, almost made a game out of it: every week I made a call, sent an email, fax or letter—and some weeks all of the above. It became a matter of principle: I was determined to keep trying as long as they were in receivership and there was even the slightest chance of getting paid. I consider myself lucky to have gotten \$7,000.00.

Future Prevention: Within a year the company was gone. I never looked back, obviously.

A few important lessons I learned from being burned:

- Always have a signed contract or agreement (even though that may not be sufficient, as you can see from Example #2 where I had an “ironclad contract”).
- Make sure you know the client is trustworthy before accepting the work, unless you have plenty of money to cover losses and are willing to take a risk for a fascinating project or potentially great client—or ask for an advance.
- Set a ceiling, ie, a maximum number of hours or dollars they can owe you before you cease working on the project until you are paid. I chose \$5,000.00, which seemed reasonable. Determine your own ceiling based on your needs.
- For foreign clients, where there is no possible legal recourse for collecting on unpaid invoices, request an advance for the amount of your ceiling.
- Do not bill once a month; rather, bill every 2 weeks or even every week if necessary.
- Insist on a 30-day turnaround for all invoices. (Credit cards today have to be paid in less than 30 days; leases and rents are paid once a month; certainly, medical writers should be paid within 30 days of invoice.) If the client's billing cycle is longer, then get the client to agree up front that you can bill before work is finished so that you still receive payment within your desired 30 days, and include a 10% late fee in your contract.
- *Never* agree to wait for payment by an agency or CRO “until their client pays them”—your contract is with the agency, not their client.

—Cathryn D. Evans

In 28 years, I am very fortunate to be able to count the number of collection problems I've had on 2 fingers. The best way to handle collection problems is to avoid them by working with good clients. But every good client is first a new client, and unless a new client comes to you pre-vetted, you're taking a bit of a risk until they prove themselves.

At the start of every new client relationship is a teleconference, when we talk about the client's needs and my capabilities. Whether the client brings it up or not, I also make a financial discussion part of the “getting to know you” call. In fact, I think they like it when I bring it up because most people don't like to bring up the topic of money. It also lets them know from the very start that I'm a business and that I mean business. I tell them about project estimating; invoicing, including progress billing on larger projects and projects with longer timelines; and that all invoices are due net in 30 days. Payment terms also appear on all of my invoices.

This conversation with new clients is excellent because it establishes a baseline of understanding for both of us. For example, if a client reliably pays on a 45-day cycle but I don't have that initial conversation with them, I wouldn't know it and might begin to think they're a problem client on Day 31. If I know in advance that a client's payment practices differ from my payment terms, I can choose whether or not to work with them. It puts the control for our financial relationship in my hands.

Even with the best controls in place, some new clients are collection problems. They chew up and spit out freelancers with every project because they have no intention of paying or no intention of paying on time, so no one in their right mind would ever work for them again.

I always follow up on projects after they've left my hands, which keeps the line of communication open even after invoicing. If there's a problem with the project that the client hasn't told me (whether or not it has to do with my work), this may enable me to find out so I can have an opportunity to address it or help the client address it. If there's going to be a problem with our business relationship, this open line of communication can serve as an early warning system. For example, if the client is uncommunicative or, worse, avoids me, I will be sure to send an email a few days before payment is due on my invoice to make sure the client knows I'm on top of it. Then if I don't receive payment on the day it's due I can place a phone call to my contact the very next day.

I would only be this quick and intense about following up if I had reason to suspect the client is going to become a collection problem. Otherwise, to do so would send a signal either that I don't trust the client or that I'm in dire financial straits, neither of which would be a good message to send to a new client.

Once I had a client who stopped responding to me after I sent my invoice for the first (and only) project. Shortly after delivery of the project my contact had informed me that he was pleased with my work and that I had delivered precisely and accurately on the assignment. But then he fell silent. About 1 week after payment was due I learned that my contact had left the company and that the person who took his place had decided to take the project in a different direction; a direction that included not paying me for my work, which he wasn't using. I sent a stern letter via certified mail, return receipt requested, explaining that the turn of events had nothing to do with the quality of my work, that I had an email detailing satisfaction with my work, and that if payment wasn't received by a specific date the next communication would come from my attorney. I copied my attorney on the email. I received a check on the date I had specified.

So, my recommendation for dealing with a collection problem is to do everything possible to avoid one. When a collec-

tion problem arises—which sooner or later it will—make sure you keep records of everything, especially client communications about your work, and take swift, stern action with specific consequences. Collection problems don't get better the longer you wait. The faster you take action, the more likely the client will realize you really do mean business and hopefully choose not to mess with you.

—Brian Bass

Q What is your advice to new writers just starting out? What are some things you wish you knew when you started out?

A Treat freelancing like the business that it is, because you can't succeed on talent alone. Be determined to succeed, and be prepared to work hard to build your business.

When I started out back in 1997, I wish I had known 2 key things: (1) more about medical writing, and (2) how to network strategically. If I had known more about medical writing, I wouldn't have wasted time and effort marketing to some people who would never hire me, because they only use scientific medical writers, and I do medical marketing communications. As I learned more about freelance opportunities in medical writing, mostly through AMWA, I adjusted my marketing. So, take the time to figure out where you fit within medical writing in terms of your experience, education, and capabilities, so you can position yourself to attract the right clients. Joining AMWA within a few months of launching my business and volunteering right away helped me build strong relationships with a lot of people. But I didn't network strategically. It took me years to realize that I needed to be more strategic about networking and to focus more of my time on people who could be the most helpful to me (and me to them). Now I spend most of my networking time and effort on my key contacts and on people who are most likely to become key contacts.

—Lori De Milto

Some things are absolutely necessary to a freelance business owner. Here are my suggestions:

- **An accountant.** Why attempt becoming an expert at accounting when my skills and interests are in editing and writing? I pay my accountant to keep up to date with the tax laws. I file quarterly taxes and prepare tax information for my accountant, who handles the paperwork.
- **A way to organize and total receipts for tax time.** I use <https://www.shoeboxed.com>. I send my receipts to them in an envelope; they scan and make the receipts available in various spreadsheets for easy integration with QuickBooks

or other accounting software. I print separate spreadsheets for each itemized category.

- **A DBA (“doing business as”).** Google “how to obtain a DBA in {insert your state}” for state-specific information. In New York at least, corporations, limited partnerships, and limited liability companies are required by statute to conduct activities under their true legal name. All other entities, such as sole proprietorships, file an assumed name certificate. This is the first step to creating a professional business profile.
- **A separate business checking account.** You need to be able to deposit checks made out to your personal name as well as to your business name.
- **IT support.** Either Geek Squad or a local computer person can help sort out any issues with software or combining hardware. Whenever I buy a new component such as a printer, new antivirus software, or a computer, I find it takes as long as 2 weeks before all the components are integrated seamlessly. I sometimes don’t find the issues until I use a component and some file or feature is not correctly linked with the other parts of my work station.

Things that are nice to have but I have managed without:

- An automated project timer
- An automated invoice system
- A website

I have used my own time sheets and a customization of Word’s invoice template since I went freelance in 1997. Faster, more streamlined methods of timekeeping and invoicing exist, but I am loathe to try something new because my existing methods work well.

Regarding a website: I know that a website provides a professional showcase and could be a way to increase my business, but I find LinkedIn allows me to post useful PDFs and detail my skills. I do not want to attract cold prospects and I have been happy with the growth of my business using just my natural networking techniques and LinkedIn.

—Melissa L. Bogen

Five years into my medical writing and editing career, I led a roundtable about my lessons learned. Looking back at those, here is my advice to writers beginning their careers:

1. Attend the AMWA classes on how to start a freelance career. The advice about setting up a business, contracts, and where to find clients is invaluable.
2. Network at as many AMWA events as you can attend, or even organize an event yourself! One of my favorite experiences to relay is that, as a regional coordinator for my chapter, I had just 2 people attend an event that I had organized—but even that small event led to securing a key

client. I’ve also gained work at nearly every AMWA conference I’ve attended, including the national conferences, so definitely go to them.

3. Also network within non-work groups. My talking to another mother in our mom’s group about how I’d like to combine my love of writing and my science background led me to learn about AMWA.
4. Before you write something, confirm the references you plan to cite with your client. It’s much harder to revise work with other references if you choose the wrong ones at the beginning.
5. If you discuss a raise or price point with a client, state those numbers in a follow-up email so that you can refer to it. Twice, I’ve had clients say they didn’t recall promising a raise, so proof is needed.
6. Consistently follow up with clients when you’re trying to “get in the door.” They may not have work the first or second time you talk to them, but checking in with them every 4 months or so will allow you to tell them what you’ve been working on in the meantime, and eventually they may have a match for you.
7. Set a comfortable timeline for your due dates, and check in with your client to ensure that they’ll meet their deadlines in delivering materials to you.
8. Don’t rush when emailing a client, especially if you are upset about something. Write an email and then take some time off before reviewing and sending it.
9. When editing someone’s work, be ever so gentle in track changes or emails.
10. Volunteer to write health- or medical-based articles for your local newspaper to generate writing samples. When I was starting out, I covered a healthy heart seminar at my library and had it published in the local paper.

—Cherie Dewar

Q As a medical writer, what are your favorite online resources?

A As a medical editor rather than a writer, I rely on sites that help me check work of medical writers. Here is my list of go-to websites that I use every day or nearly every day:

- **PubMed Single Citation Matcher (<https://www.ncbi.nlm.nih.gov/pubmed/citmatch>):** Because I use PubMed Single Citation Matcher every day, this site is my home page. This site has search boxes for journal name; year (month and day are optional); volume, issue, and first page; author name (with options to limit the author search to the first- or last-

named author); and title words. I can therefore verify references based on limited information.

- **MediLexicon (<http://www.medilexicon.com>):** This site provides links to definitions of medical abbreviations; a medical dictionary; drugs; medical equipment and devices; hospitals (by location or name); International Statistical Classification of Diseases and Related Health Problems (ICD) codes; and Medical News (from Medical News Today). This site is a great first place to search for basic information.
- **Merriam-Webster dictionary (<https://www.merriam-webster.com>):** These days I rarely look up words in a hardcopy dictionary. I have Stedman's Medical Spellchecker loaded on my computer and use <http://www.m-w.com> for verifying spelling and hyphenation of everyday terms. This site also has a thesaurus.
- **Oxford English dictionary (<https://en.oxforddictionaries.com/usage/british-and-american-terms>):** This site, from Oxford University Press, is helpful for looking up British and American English terms.
- **AMA Manual of Style, 10th ed. (<http://www.amamanualofstyle.com>):** Need to keep up to date on the latest terminology? This subscription site, from the AMA and Oxford University Press, the publisher of the hardcopy manual, is excellent for searching terms on the fly. I have an electronic subscription but I also keep the hardcopy manual on my desk when I want to flip pages or consult one of my dog-eared Post-it notes in the book.
- **PDF Unlock (<https://www.pdfunlock.com>):** This site removes passwords and restrictions from secured PDF files. The site also has a link to convert a web page into a PDF file for free (<https://www.htmlpdf.com>).

—Melissa L. Bogen

As a medical writer, I frequently consult several websites as I complete my projects. Here is a list of some of the more frequently consulted sites:

- **<https://www.ncbi.nlm.nih.gov/pmc>:** Most medical writers should know this resource. This is a free archive of peer-reviewed medical articles that are maintained by the National Institutes of Health (NIH) Library of Medicine. The website is fully searchable using several parameters. Free full-text links to articles are cited when available.
- **<https://www.drugs.com>:** This independent medicine information website has information on prescription drugs, over-the-counter medicines, and natural products. They source their data from validated sources such as Micromedex, Cerner Multum, Wolters Kluwer, the American Society of Health System Pharmacists, and others. It is a great source of information on the latest drugs.

- **<https://clinicaltrials.gov>:** This NIH website is a registry of publicly and privately supported international clinical studies. You can search for clinical trials based on topics or study names. ClinicalTrials.gov currently lists clinical studies with locations in all 50 states and 195 countries. It also lists the publications for the trials, although I have not found those to be comprehensive.
- **<https://guideline.gov>:** This is a website created by the Department of Health and Human Services and The Agency for Healthcare Research and Quality (AHRQ). It is a public resource for summaries of evidence-based clinical practice guidelines. The guidelines are categorized by clinical specialties, and the website is fully searchable. However, it includes international guidelines, so make sure you keep that in mind. You can filter results for US-based organizations only.
- **<http://www.uptodate.com/home>:** This is an evidence-based, physician-authored clinical decision and support resource that is used by many physicians. However, you need a subscription to access the full articles. It gives current and up-to-date info on the disease, treatment, and available guidelines.

Other websites

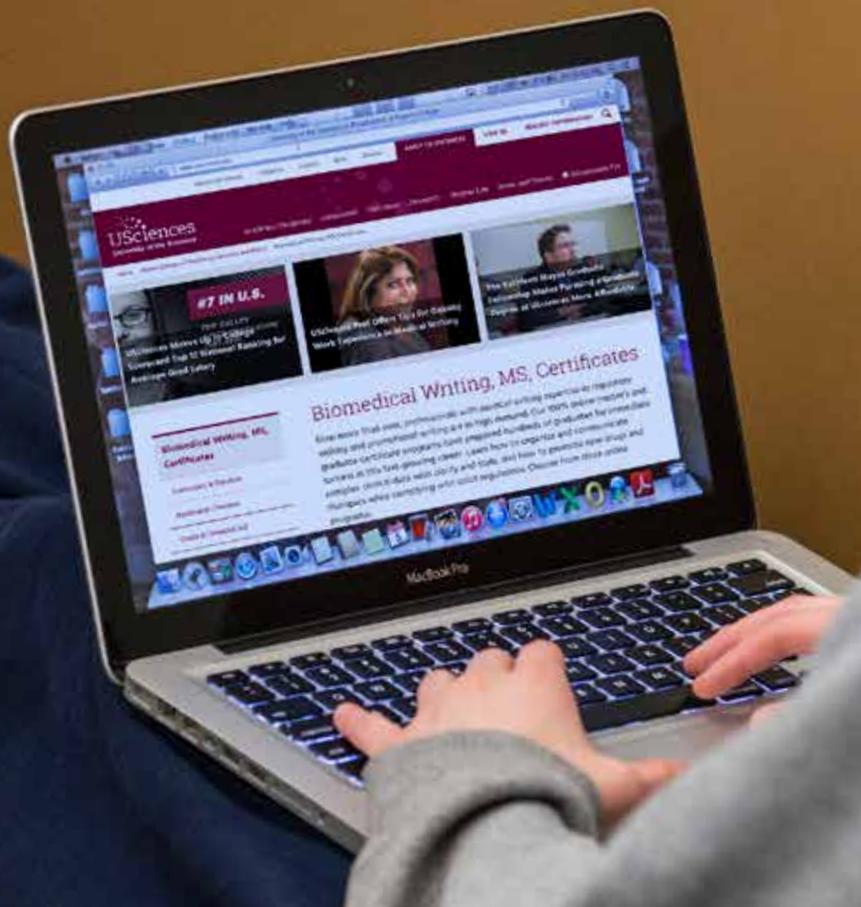
Depending on the disease state that I am writing for, I also look at disease-specific organization's websites, such as the American Diabetes Association (diabetes.org) or National Cancer Institute (cancer.gov). The Centers for Disease Control (cdc.gov) is also helpful for statistical information on various disease states. Medscape.com is also a great resource on multiple levels.

—Ruwaida Vakil

Wanted: Reporters!

Will you be attending any Open Sessions at this year's Medical Writing & Communication Conference in Orlando? Would you be interested in reporting on a session for the *AMWA Journal*?

Please contact journaleditor@amwa.org



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FROM THE PRESIDENT

AMWA From Coast to Coast

By Lori L. Alexander, MTPW, ELS, MWC® / 2016–2017 AMWA President



Do you remember the first chapter event you went to? I do. I was living in the Boston area at the time, and I went to a dinner event with a speaker. I was alone and sat at a table of strangers, all of whom immediately welcomed me into their conversations, even though I was a new medical writer (actually, editor at the time). That was nearly 30 years ago, and since then, I've been to several chapter events—in a variety of areas—and my experience is always the same: a warm, collegial feeling. A sense of connection.

AMWA wants all its members to feel that connection. Sure, we can connect virtually on *AMWA Engage*, which is great, because we can do it from the comfort of our own homes (perhaps in our PJs) and reach medical writers we might not otherwise know. And I love the energy of the annual conference, where I can connect with and learn from medical writers from all across the country. But the local experience is what members recall—and value—the most about AMWA. That experience is the heart of AMWA.

One of my goals as president was to tap into that experience by visiting with AMWA members at the local level by attending as many chapter events or informal meetings as possible. I didn't get to as many chapters as I'd hoped so far this year, but I was able to attend 2 chapter events and 2 informal meetings. (By the time you read this, I will have attended a third chapter event.) It's been wonderful, and I hope to continue visiting with members at local events next year as well.

The first event I attended was the Pacific Southwest (PacSW) Chapter Conference in San Diego, California. The conference ran like a well-oiled machine. About 45 AMWA members—a mix of long-time and new members—gathered for workshops and educational sessions. Approximately 25 members came out the night before to meet for a networking happy hour—around a pool, even! It was great to meet AMWA members on the opposite coast from where I live and work.

The next event was much closer to home: the Carolinas Chapter conference in Chapel Hill, North Carolina. I had dinner with about 12 members the night before the event and was invited to speak briefly and answer questions.

Approximately 40 members attended the next day's conference, and I enjoyed networking with many of them over a casual breakfast, learning new things in an educational session on branding, and leading a roundtable on becoming more involved with AMWA. One of the things that impressed me the most is that an AMWA member saw me walking from the hotel to the conference venue and offered me a ride. It wasn't a long walk or even raining. We didn't know each other. But that doesn't matter when you're in AMWA!

My summer travels "up north" allowed me to meet informally with members in the northern Virginia and Boston areas. In Arlington, Virginia, I had dinner with 4 AMWA Mid-Atlantic Chapter members, only 1 of whom had ever been to an AMWA annual conference. The local experience was all they knew, and they embraced it. We talked about opportunities in medical writing, the challenges of freelancing, and even the trials of juggling work and motherhood. One member had traveled—by the Metro—for 40 minutes from work and traveled about an hour to get home. The local experience matters!

In Boston, Massachusetts, I had the pleasure of sharing lunch with 6 members of the New England Chapter. I was grateful to this chapter's leaders for coordinating a lunch only a week after they had held their annual meeting brunch. Of the 6 members in attendance, 2 were chapter leaders and the other 4 were fairly new members. In fact, 1 woman had just joined a few days earlier, when she registered for the annual conference! Our discussions focused on how to transition into medical writing, whether education or experience was the more important stepping stone, and the skills needed for success in our profession.

My experience at all of these local events reflected what my instinct has told me all along: chapter conferences are great, but even small, informal meetings are vital. Chapter volunteers worry that their event won't be big enough, won't draw enough people, won't be a success. But success isn't measured by the size of the event—it's measured by meaningful interactions.

Continuing the opportunities for a positive member experience and meaningful interactions is a priority for AMWA. We are working with chapter leaders to help enhance their chapter conferences. The Chapter Transition Task Force is working with volunteers in the areas of 4 former chapters (Pacific Southwest, Northwest, Michigan, and Canada) to guide them in organizing local networking events. These AMWA volunteers are known as local networking coordinators (LNCs, pronounced “links”), and they have already held some events that have been very suc-

cessful. I appreciate the time and efforts these volunteers are committing to help maintain local connections among AMWA members.

My experience visiting chapters the past few months also further confirmed what I learned at that first chapter event in Boston nearly 30 years ago. From coast to coast, AMWA members are a warm, welcoming group of people—a group of people for whom it has been a privilege and honor to serve.

AMWA Fellows for 2017

By **Karen Potvin Klein** / 2014–2015 AMWA President and Chair, Fellowship Committee

Fellowships are among the highest honors that AMWA members can achieve, and they are awarded only to those who have significantly contributed both to AMWA and to the profession at large. Candidates must have been active members in good standing for at least 5 consecutive years immediately before Fellowship nomination.

This year's Fellowship Committee reviewed the activities of qualified candidates based on information provided by AMWA HQ. Scores for each activity at the chapter and/or national level were allotted by using a standardized scoring scheme as established by last year's committee, led by Brian Bass. Each committee member scored 3 candidates; then the overall results were tabulated and shared with the entire committee. The committee then convened by email to arrive at a consensus for the nominee slate.

In the spring of 2017, the Board of Directors accepted this slate of nominees as Fellows of AMWA. They received their awards at the Medical Writing & Communication Conference in Orlando. Congratulations to the following individuals, who are our newest AMWA Fellows!

Noelle Demas

Noelle has served 5 times as the delegate to the Board of Directors and twice as president of the former Pacific Southwest chapter. She was a member of the Asilomar Conference Committee for 2 terms. At the national level, Noelle has contributed significantly to a number of successful annual conferences. She has served as Open Session Chair for 5 conferences and chaired the Annual Conference Committee, serving in that role on the national Executive Committee. She has also served as a roundtable leader at 2 annual conferences. In addition, Noelle has contributed several articles to the *AMWA Journal* and most recently was a member of the Nominating Committee. Noelle brings



creative ideas, zest, and enthusiasm for AMWA and its members to all her activities.

Vicki Foerster

Vicki has had a long and distinguished record as a leader of the former Canada chapter and served as its treasurer for 9 terms. Most recently, she was president-elect of the chapter. She has also served 8 times as chapter delegate to the Board of Directors. At the national level, Vicki has served twice on the Eric W. Martin Award Committee (once as chair). She was a coordinator of the posters session for the annual conference, and has contributed to the *AMWA Journal*. Vicki's leadership illustrates her consistent and remarkable commitment to our organization.



Julie Phelan

Julie is a member of the Greater Chicago chapter. She has held multiple leadership roles in that chapter, including 3 terms as president, and has served 13 times as chapter delegate to the Board of Directors. At the national level, Julie has contributed 4 articles to the *AMWA Journal*. She also has been a member of several national committees, including the Online Community Social Media Committee, the salary survey task force, and the Communications Committee. She served for 2 years on the Budget and Finance Committee, and she currently chairs that committee as part of her service as AMWA's Treasurer. Julie “hit the ground running” as the national treasurer and, in a short period of time, has taken on those responsibilities with grace and ease.



This year's Fellowship Committee members were Lori DeMillo, Karen Potvin Klein (chair), Joanne McAndrews, Donna Miceli, and Christine Wogan. Becky Phillips from AMWA HQ provided excellent support.

Stephan Grupp, MD, PhD, Children's Hospital of Philadelphia



By James R. Cozzarin, ELS, MWC® / Senior Editor, ProEd Communications, Inc., Beachwood, Ohio
Editor-in-Chief, *AMWA Journal*

Stephan Grupp, MD, PhD, is Section Chief, Cell Therapy and Transplant; Director, Cancer Immunotherapy Frontier Program; and CCCR Director of Translational Research at Children's Hospital of Philadelphia (CHOP). He is also a Professor of Pediatrics in the Perelman School of Medicine at the University of Pennsylvania (U Penn). I had the opportunity to speak with Dr Grupp about the recent favorable vote by the US FDA's Oncologic Drugs Advisory Committee (ODAC) for approval of an innovative new therapy—the first of its kind in the United States.

Journal: *Thank you for speaking with me today, Dr Grupp, and congratulations on the recent ODAC recommendation for approval of tisagenlecleucel (CTL019) for the treatment of pediatric and young adult patients with relapsed/refractory B-cell acute lymphoblastic leukemia (r/r B-cell ALL). Before we turn to your new therapy, would you take a moment, please, to set the stage by briefly describing the current standard of care for r/r B-cell ALL? What is the prognosis for these patients?*

Dr Grupp: It's a tough situation for those patients. If you take a step back, the current standard of care for newly diagnosed patients does a great job for the majority of pediatric ALL patients. The flip side of that is for patients who have refractory ALL or who relapse—these kids are in really bad shape. You treat them with very intensive chemotherapy to try to get them into a remission, so that they might be eligible for a bone marrow transplant, but transplant itself only works half the time. And the amount of chemotherapy, and the amount of time in the hospital, and the amount of risk associated with that very intensive treatment is significant. The overall outcome for these patients with second or greater relapse in recent registration studies is that 20% to 40% reach initial remission, and less than 10% remain in remission at a year or two.

Journal: *Now let's turn to your investigation and development of Chimeric Antigen Receptor T-cell (CAR T) as a potential treatment for r/r B-cell ALL. Why did data in the form of durable antitumor efficacy generated in a single-center phase-1/2a trial conducted at CHOP prompt further investigation?*

Dr Grupp: We treated the first of our pediatric patients a little over 5 years ago, and the first thing that became very apparent was that we were seeing very high complete remission rates. That initial remission rate has been steady at about 90% to 95% through the entire conduct of the single-institution trial, and approximately 80% of these patients are still alive at a year or more out. I would say that was the early indication that we might be onto something.

The second indication was that a number of these patients not only went into remission but retained the engineered T cells in their bodies and were able to stay in remission without further treatment—especially transplant! So, CAR T cells do a beautiful job of putting patients into the kind of remission you would dream of for a transplant. But the question is, at that point, do you even need the transplant? And for a large number of these patients, the answer is no. About 10% of the patients that we've treated at CHOP have gone on to transplant after their CAR T-cell therapy, but most of them haven't. And, for me, as a pediatric transplant, the thought that we might actually be replacing transplant with this approach was enormously exciting.

Another key factor was that U Penn licensed this therapy to Novartis, who was willing to try to develop it initially for pediatric and young adult patients with ALL.

Journal: *Well those are the benefits, but what are the risks involved with this therapy? We know the serious downsides for intensive chemotherapy and for bone marrow transplant; what are the downsides for CAR T therapy?*

Dr Grupp: There are absolutely toxicities associated with the therapy, and the most significant is cytokine release syndrome (CRS). So, we've learned A) how to treat it, and B) what to expect in terms of who is at risk. And we learned this really in our very first patient, a little girl named Emily. She came to CHOP with completely refractory disease, and we were never able to get her into remission for transplant. She went into CAR T therapy with two-thirds of her bone marrow replaced by leukemia, and she had really significant, life-threatening CRS. Through a combination of intensive research/analysis and quite a bit of luck, we came upon the approach that we would use for all of our CAR T patients, which is to block a particular inflammatory cytokine, interleukin-6 (IL-6), using a drug that was originally developed for rheumatoid arthritis. Without the ability to block IL-6, there would be no CAR T therapy; the toxicities would be too great.

So, now we've learned that a high tumor burden is a real risk factor for more significant CRS. Why? The CAR T cells go into the body, and they grow in response to leukemia cells—the more leukemia cells they see, the more they grow. Now that is very good news, because we can take patients with even very high disease burden into remission—which is fantastic. But the flip side of that is that the more T cells you have, the more inflammatory proteins they make, and the more clinically unstable the patients can become, especially in regard to CRS. The key, of course, is IL-6, and the fact that we can specifically block IL-6—sometimes within hours. It's amazing how well the CAR T cells work, and how well this toxicity control works (not 100% of the time, but most of the time), and that makes it much safer to treat these patients.

Of course, if we can identify patients earlier, before they have refractory disease, before they have a high disease burden, then CAR T doesn't produce these potentially dangerous significant side effects. They get fevers, some muscle aches, might be in the hospital for up to a week or so, but there's no dramatic toxicity in these patients. And that kind of toxicity compared to transplant or intensive chemotherapy? There's just no comparison.

Journal: *How is CAR T different from current therapeutic modalities for r/r B-cell ALL? How does this adoptive immunocellular cancer therapy work?*

Dr Grupp: We're looking for remission, and for maintenance of remission. Remission comes from the initial, very significant proliferative burst of T cells that lets you get on top of the leukemia; that's what puts you in a complete remission within about a month in 85% to 95% of patients. What *keeps* you in remission is the small number of CAR T cells that remain in the body and remain on the hunt for leukemia cells.

Now there are 2 ways to activate T cells: there's an activation domain (which all CAR T cells have), and there's a

costimulatory domain that provides a second signal for T-cell activation. That costimulatory domain differs from product to product, and the particular U Penn/Novartis product, CTL019, uses 4-1BB, which is associated with a nice initial proliferative burst, does a nice job of getting patients into remission, but then has the ability to maintain the T cells in the patients literally for years. The first 2 adult patients treated at U Penn more than 6 years ago remain in remission and still retain engineered T cells (at least at the time they last checked), and the first pediatric patient that we treated at CHOP still had engineered T cells the last time we looked at that in her. And it was that longevity of the engineered T cells that first led us to believe that we could use this therapy transplant free.

And because you're not treating them with anything after they reach remission, these kids bounce back really quickly. They're just waiting for the opportunity to heal from all the treatments, and as soon as you leave them alone for a while they're out on the soccer field, they're back at school, they're just doing their own thing, because they just want to keep going on with life. So that has been the most gratifying thing from our perspective.

Journal: *There is quite a bit of buzz in the media around the FDA Advisory Committee's vote for approval of your CAR T product. What makes this such an innovation?*

Dr Grupp: One big part of it is that this is the first treatment ever like this presented for FDA approval in medical history. From another perspective, there's a lot of interest in immunoncology. Now there are 2 ways to approach this: you can use drugs to reactivate natural T cells in the patient's body that might have the potential to recognize tumors, which works nicely for certain patients across a variety of tumor types. Or, using the CAR T-cell approach, Novartis is making a personalized product that is manufactured for each individual patient. We take their own T cells out of their body, genetically reprogram them to go after tumor cells, and then reintroduce them into the patient. And that genetic engineering, that reprogramming approach, is brand new. So, it is gene therapy, it is an engineered cell therapy, and nothing like this has ever reached the point of FDA approval.

The genetic modification of the cells involves viral technology, specifically a lentivirus, which also has regulatory and safety implications. Indeed, the FDA Advisory Committee was very interested in the long-term safety of using that viral technology. Our ability to show the safety data and show that this was safe over the long term was very important to the Agency. And now Novartis has taken it out of the academic setting and transferred the simple manufacturing to the pharmaceutical company setting, so they can make it for hospitals all across the country. So, if you're a doctor at one of those hospitals, you

will be able to write a prescription for this therapy, which would have been unimaginable even just 5 years ago.

And then there was our ability to bring this to the FDA for consideration, showing that we could do this in the Novartis registration trial with a global reach—25 centers in 11 countries (Canada, Japan, the United States, multiple countries in the European Union). You can make the cells from patients all over the world, you can ship the cells all over the globe, successfully, and that whole idea was brand new and had never been done before.

And so there have been a lot of “firsts.” And I will say, as a pediatric oncologist/pediatric transplanter, that seeing a pediatric indication offered first for FDA consideration was also incredibly exciting. As you know, most indications are approved in adults initially, with pediatric indications following along (or with pediatric patients being treated off label), but in this case the kids came first.

Journal: *One last question, Dr Grupp—what do you believe is important for our audience of professional medical communicators to know about CAR T so that we can write effectively about this new therapy?*

Dr Grupp: There are several aspects that would be important from that perspective. One unique aspect is the challenges involved in drug manufacturing wherein one lot goes into one patient, and you have to do all the release testing every time you make a product. Another unique aspect is the fact that we’re using viruses, the lentiviral system, for genetic modification of the T-cell genome. And then there’s the issue of cost—we don’t know how much this is going to cost, but that is an issue that people will talk about when this comes up. And when this becomes FDA approved, we’ll find out.

The future of CAR T therapy is about 2 things: First, can you reduce costs in the manufacturing procedure by making it less manual and more automated? Can it be made faster, cheaper, and with fewer people involved? This is what Pharma should be awesome at. And second, can we expand it beyond hematologic malignancies? Right now, we’re seeing good response rates across the range of leukemia, lymphoma, multiple myeloma—with ALL being by far the best. But solid tumors (like lung cancer, breast cancer, pancreatic cancer) are a different challenge. The key there is to overcome the issue of getting the CAR T cells not just into the body where they can proliferate, but into the actual tumor tissues themselves—and solid tumors are very good at excluding T cells. So, when your readers write about this, it’s important to know that this is great for blood cancers, but that we still have a ways to go before we will have the same kind of efficacy in solid tumors—that’s a tough nut to crack. One possibility, and we see this sometimes with responses to the checkpoint inhibitors, is that when you get the tumor inflamed, that bootstraps a beneficial immune response that pulls in T cells and can really blow the tumor away. Now, until it happens, it hasn’t happened, and I don’t want to over-promise, but there are so many potential approaches to cracking open the solid tumors to T cells that I’m very hopeful that there will be a way.

NOTE: As we were going to press, the US FDA announced its approval of Kymriah (tisagenlecleucel).

CALENDAR OF MEETINGS

2017
AMWA

Medical Writing & Communication Conference
NOVEMBER 1-4 | ORLANDO, FL

Trends and Opportunities for Medical Communicators

Council for Programs in Technical and Scientific Communication

October 5–7, 2017
Savannah, Georgia
<http://www.cptsc.org/annual.html>

Drug Information Association Annual Canadian Meeting

October 17–18, 2017
Ottawa, Ontario, Canada
www.diaglobal.org

World Conference of Science Journalists

October 26–30, 2017
San Francisco, California
www.nasw.org/events

European Medical Writers Association

November 2–4, 2017
Cascais, Portugal
<http://www.emwa.org>

Association of American Medical Colleges

November 3–7, 2017
Boston, Massachusetts
www.aamc.org/meetings/annual

American Public Health Association Annual Meeting & Exposition

November 4–8, 2017
Atlanta, Georgia
www.apha.org

Alliance for Continuing Education in the Health Professions 43rd Annual Conference

January 20–23, 2018
Orlando, Florida
www.acehp.org

2018 European Meeting of the International Society for Medical Publication Professionals

January 23–24, 2018
London, United Kingdom
www.ismpp.org/european-meeting

American Association for the Advancement of Science Annual Meeting

February 15–19, 2018
Austin, Texas
meetings.aaas.org

American Pharmacists Association Annual Meeting & Exposition

March 16–19, 2018
Nashville, Tennessee
aphameeting.pharmacist.com

2016 Freelance Medical Communicators Tools of the Trade Survey Instrument

Survey Q & A

What is the purpose of this survey?

The purpose of this survey is to collect data about the software, apps, and other tech tools that freelance medical communicators use in their daily work. Once analyzed, this information will help current and new freelancers expand and upgrade their own toolbox.

I got the idea for this survey earlier this year when I spent countless hours researching all the different tech tools I needed to reboot my freelance business. I realized it might have helped me narrow down my choices if I had known what software, apps, and online services my colleagues use for web hosting, accounting, time tracking, etc.

Who is running this survey?

I am Monica Nicosia, PhD, a freelance medical writer with over 20 years of experience in medical communications. To find out more about me visit my website (<http://www.nicosiamedicalwriter.com>) or my LinkedIn profile (<http://www.linkedin.com/in/monicanicosia>).

How will you use the survey data?

I will use the analyzed survey data to prepare a journal article and/or conference presentation. I will send a pdf copy of summary findings to all survey participants who, at the end of the survey, provide their email address for this purpose. If the survey is successful, I might repeat it every 1 to 2 years to monitor trends/changing patterns.

Who should participate?

If you are a currently working freelance (ie, self-employed) medical communications professional (eg, writer, editor) you are eligible to participate in this survey.

How long will this survey take?

SurveyGizmo estimates that the survey will take 6 minutes to complete.

Sounds good, I am in. What do I do next?

Click on the NEXT button below to start the survey. Thank you.

Work History Questions

- How would you describe your work status as a freelance medical communicator?*
- On average, how many **hours per week** do you work as a freelance medical communicator?*
- What is your primary function (>50% of your billable hours) as a freelance medical communicator?*
- How many **total years** have you worked in medical communications (as an employee and as a freelance)?*

- Full-time
- Part-time

- <15
- 16-20
- 21-30
- 31-40
- >41

- Writer
- Editor
- Other (Fill in blank.) _____*

- <1
- 1-2
- 3-5
- 6-10
- 11-15
- 16+

5. How many **total years** were you employed as a medical communicator before going freelance?*

 - None
 - <1
 - 1-2
 - 3-5
 - 6-10
 - 11-15
 - 16+

6. How many **total years** have you worked as a **freelance** medical communicator?*

 - <1
 - 1-2
 - 3-5
 - 6-10
 - 11-15
 - 16+

7. Which of following are your **top 1-3** areas of freelance medical communications work? (Select up to 3.)*

 - Books
 - Continuing education for healthcare professionals (medical, nursing, pharmacy, allied-health)
 - Education materials for patients and their caregivers
 - Grant proposals
 - Health journalism (print/web news article on health and medicine for lay audiences)
 - Materials for payers
 - Promotional materials (for clinicians, allied health, payers, etc)
 - Regulatory documents
 - Sales training materials
 - Scientific publications for peer-reviewed publications
 - Other (Fill in blank.) _____*

8. Where do you work most (>50%) of your billable time?*

 - Home-office
 - Rented office space
 - Client's office
 - Other (Fill in blank.) _____*

9. Do you own the computer you use for your freelance medical communicator business?*

 - Yes
 - No

Tools of the Trade Questions

10. What type of computer do you use for most (>50%) of your freelance medical communication work?*

 - Laptop
 - Desktop
 - Tablet

11. Which operating system does your business computer use?*

 - Apple OS
 - Windows
 - Linux
 - Other (Fill in blank.) _____*

12. How do you back-up your work computer? (Check all that apply.)*

 - Online/Cloud-based service
 - External drive
 - Other (Fill in blank.) _____*
 - No backup

13. [If selected "Online/Cloud-based service" in question 12] Which online/cloud-based service do you use to back-up your computer?*

 - Carbonite
 - Comodo Backup
 - CrashPlan
 - Dropbox
 - Google Drive
 - Memopal
 - Mozy
 - Other (Fill in blank.) _____
 - None

14. Do you have a business website?*

 - Yes
 - No

15. [If selected "Yes" in question 14] Who designed your website?

 - I designed it myself
 - A relative/friend designed it at no charge
 - I paid someone to design it

16. [If answered "Yes" in question 14] Which Web hosting service do you use for your website?

 - A2 Hosting
 - Arvixe
 - Bluehost
 - DreamHost
 - eHost

- FatCow
- GoDaddy
- GreenGeeks
- HostGator
- InMotion
- SiteGround
- SquareSpace
- Weebly
- Wix
- Other (Fill in blank.) _____*

17. Which software/app do you use for accounting/bookkeeping?*

- FreeAgent
- Freckle
- FreshBooks
- Harpoon
- Harvest
- Paydirt
- Paymo
- QuickBooks Online
- Quicken Home & Business
- Spreadsheets (eg, Excel, Numbers, OpenOffice)
- Wave
- Xero
- Zoho
- Other (Fill in blank.) _____*
- None

18. [If selected "Spreadsheets" in question 17] Which spreadsheet software/app do you use for accounting/bookkeeping?*

- Apple Numbers
- Microsoft Excel
- Google Sheets
- OpenOffice (Apache)
- Other (Fill in blank.) _____*

19. Which software/app do you use for time tracking?

- Everhour
- FreshBooks
- Harpoon
- Harvest
- Hours
- Hubstaff
- Klok
- On The Job
- Paydirt
- Paymo
- Spreadsheet (eg, Excel, Numbers, OpenOffice)
- Timely

- Toggl
- Tyme
- Zoho Invoice
- Other (Fill in blank.) _____
- None

20. [If selected "Spreadsheets" in question 19] Which spreadsheet software/app do you use for time tracking?*

- Apple Numbers
- Microsoft Excel
- Google Sheets
- OpenOffice (Apache)
- Other (Fill in blank.) _____*

21. Which software/app do you use for email? (Check all that apply.)*

- Airmail
- Apple Mail (Mail.app)
- Gmail (free service)
- Google Apps for Work Gmail (paid service)
- MailMate
- Outlook
- Postbox
- Yahoo mail (free service)
- Other (Fill in blank.) _____*
- None

22. Which citation/reference management software do you use? (Check all that apply.)*

- EndNote
- Mendeley
- Papers
- Reference Manager
- RefWorks
- Sente
- Zotero
- Other (Fill in blank.) _____*
- None

23. To which of the following professional association do you belong? (Check all that apply.)*

- American Medical Writers Association (AMWA)
- European Medical Writers Association (EMWA)
- International Society for Medical Publication Professionals (ISMPP)
- International Science Writers Association (ISWA)
- Drug Information Association (DIA)
- National Association of Science Writers (NASW)
- Regulatory Affairs Professionals Society (RAPS)
- Other (Fill in blank.) _____*
- None

24. Which social media and online communities do you use for your freelance medical communication business? (Check all that apply.)*
- AMWA Engage
 - Facebook
 - LinkedIn
 - Twitter
 - Other (Fill in blank.) _____*
 - None
25. Which online freelance directories do you use to promote your business? (Check all that apply.)
- AMWA Freelance Directory
 - EMWA Freelancer Directory
 - Other (Fill in blank.) _____*
 - None
26. What **one essential software/app** would you recommend to your fellow freelance medical communicators? _____
27. What **one essential hardware or specialized device** would you recommend to your fellow freelance medical communicators? _____
28. Do you have any comments or suggestions on how to improve this survey? _____

Demographics Questions

You are almost done. Just a few more quick questions.

29. How do you identify yourself?*
- Man
 - Woman
 - Other
30. Which category includes your age?*
- 20-29 years
 - 30-39 years
 - 40-49 years
 - 50-59 years
 - 60 years or older

31. Where do you live? [country drop-down list]
32. What is your highest degree?*
- Associate
 - Bachelor
 - Master
 - Advanced (eg, DNP, DO, MD, PhD, PharmD)
 - Other (Fill in blank.) _____*
33. What is the general field of your highest degree?*
- Communications
 - English
 - Health sciences
 - History
 - Journalism
 - Medicine
 - Nutrition
 - Nursing
 - Pharmacy
 - Social Science
 - Other (Fill in blank.) _____*
34. If you would like a pdf copy of the survey summary findings, please provide your email below. Your email will not be used for any other purpose.
Email Address _____

Thank You for Participating in this Survey.

**Questions marked with an asterisk were mandatory (ie, an answer was required to move to the next part of the survey).*

Supplemental Table 1. Links to Ethics-Related Resources from the AMWA Website

Ethics-Related Resource	Website Link*
AMWA-EMWA-ISMP Joint Position Statement on the Role of Professional Medical Writers	https://www.amwa.org/general/custom.asp?page=Position_Statement
Code of Ethics	https://www.amwa.org/page/code_of_ethics
Education program	
Workshops	https://www.amwa.org/events/event_list.asp
Essential Skills	https://www.amwa.org/page/Essential_Skills
Online Learning	http://www.amwa.org/page/Online_Learning
Self-study Workbooks	https://www.amwa.org/store/ListProducts.aspx?catid=549813
Medical Writing Certificate outline	https://c.ymcdn.com/sites/www.amwa.org/resource/resmgr/certification/Forms/MWC_ExamContentOutline.pdf
Opportunities to highlight ethics knowledge	
Personal Profile	http://www.amwa.org/?page=ManageProfile_Custom&hhSearchTerms=%22profile%22
Freelance Directory	http://www.amwa.org/page/Freelance_Directory
<i>AMWA Journal</i>	http://www.amwa.org/page/Journal
<i>Engage</i>	http://engage.amwa.org/home

Call for Volunteers

AMWA welcomes members with all levels of expertise and experience in medical communication to help support our activities and programs.

Give back.

Connect with peers.

Gain leadership skills.

www.amwa.org/volunteer

VOLUNTEER TODAY



ENGAGE

Join the discussion.
Expand your network.
Share resources.



AMWA COMMUNITY
Connect and Collaborate

engage.amwa.org

MACROEDITING

Ensure a clear message with credibility and clarity.

Macroediting helps an author speak with credibility and clarity. The process works to ensure a clear message with congruent parts, coherent information, and a unified focus. Create high-quality scientific documents with the essential components of macroediting and gain the “bird’s eye view.”

MICROEDITING

Produce the desired effect with accuracy and intention.

Microediting dives into the details by requiring a close analysis of a text’s smallest building blocks: words, phrases, sentences, and paragraphs. This process makes the paper easier to read, factually and grammatically sound, and more likely to produce the desired effect on its audience.

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