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AMWA JOURNAL MISSION STATEMENT
The AMWA Journal expresses the interests, concerns, and expertise of members. Its purpose is to inspire, motivate, inform, and educate them. The Journal furthers dialog among all members and communicates the purposes, goals, advantages, and benefits of the American Medical Writers Association as a professional organization.
All living things have a metabolism, which is a set of chemical reactions. For these chemical reactions to happen, some chemicals must enter the organism and others must leave it. The first article in this series explained why it matters whether a substance dissolves in water or fat. This article describes the role of various proteins in the transport of oxygen and carbon dioxide in the bloodstream.

Blood is thicker than water. Blood is also far better than water at transporting oxygen and carbon dioxide. Oxygen (O$_2$) and carbon dioxide (CO$_2$) are nonpolar molecules. For this reason, these gases dissolve well in lipids (fats and oily substances) but poorly in water. Thus, they give us a good example of the dilemma of transport, which I described in the first article in this series:$^1$

- Lipid-soluble substances can easily pass through the cell membrane to enter or leave a cell, but they are hard to transport in the blood.
- Water-soluble substances can be easily transported in the blood, but it is hard for them to enter or leave cells.

Oxygen and carbon dioxide can easily enter or leave your cells; but how can oxygen get to your cells, and how can carbon dioxide get taken away from your cells? To solve the problems raised by the dilemma of transport, the body makes proteins. Red blood cells have 3 important proteins that make it possible for the blood to transport enough oxygen and carbon dioxide to serve the body’s needs:

- The red pigment hemoglobin
- An enzyme called carbonic anhydrase 1$^2$
- A membrane transport protein called solute carrier family 4 member 1 (SLC4A1)$^3$

The heart works hard to pump blood so that the blood circulates through the body. This energy-consuming process is an example of active transport. The flow of gases into and out of the bloodstream—and into and out of red blood cells—is an example of passive transport. Passive transport means a net flow of a substance from an area of higher concentration to an area of lower concentration, or a net flow that is “downhill” relative to a voltage gradient.

In this article, I will explain 3 important things:
- Why red blood cells play such an important role in transporting oxygen and carbon dioxide
- How your blood pH affects your respiratory rate
- Why carbon dioxide plays an important role in maintaining a stable pH within the body

OXYGEN AND CARBON DIOXIDE DISSOLVE POORLY IN WATER

As I explained in the first article in this series,$^1$ water is a polar molecule. Polarity means that the molecule has a lopsided distribution of electrical charge (ie, it has a dipole or multipole moment). A negative pole of one polar molecule will be attracted to a positive pole of a nearby polar molecule. For this reason, water molecules are strongly attracted to one another. That is why water is liquid at room temperature, even though its molecular weight is only about 18 atomic mass units.

Oxygen and carbon dioxide are gases at room temperature, even though their molecular weights are higher than water’s (roughly 32 and 44 atomic mass units, respectively). Water’s polarity also explains why water is such a good solvent for ions (eg, salt) and polar molecules (eg, sugar). However, water is a poor solvent for nonpolar molecules, including oxygen and carbon dioxide. For this reason, the watery portion of the blood can hold only a small amount of oxygen and carbon dioxide—not enough to meet the body’s needs for gas transport.

Nevertheless, blood can carry a lot of oxygen because red blood cells contain hemoglobin, which serves as a transport protein for oxygen. Blood can carry a lot of carbon dioxide partly because some carbon dioxide binds to hemoglobin but mainly because the carbonic anhydrase enzyme in red blood
cells speeds up the conversion of carbon dioxide to bicarbonate anion (\(\text{HCO}_3^-\)), which dissolves easily in water.

**WHAT IS HEMOGLOBIN?**

Hemoglobin is the red pigment in our red blood cells (erythrocytes). Hemoglobin is a metalloprotein, meaning it contains metal ions. Each hemoglobin molecule consists of 4 protein subunits and 4 molecules of heme (Figure 1). Heme consists of a porphyrin ring that surrounds an electrically charged atom of iron (\(\text{Fe}^{2+}\)).

When the hemoglobin molecule encounters a molecule of oxygen, a reduction-oxidation (redox) reaction takes place. The \(\text{Fe}^{2+}\) atom is oxidized (ie, loses an electron) to become \(\text{Fe}^{3+}\). The oxygen molecule is reduced (ie, gains an electron) to become a superoxide anion (\(\text{O}_2^-\)). The superoxide anion then forms a complex with the \(\text{Fe}^{3+}\). As each hemoglobin molecule contains 4 iron atoms, it can carry up to 4 molecules of oxygen. The oxygenated form of hemoglobin is called oxyhemoglobin. The hemoglobin in the red blood cells increases the blood's ability to carry oxygen by about 70-fold. Hemoglobin can also carry some carbon dioxide and some nitric oxide.

---

**WHY HEMOGLOBIN IS A TRANSPORT PROTEIN**

Hemoglobin is useful as an oxygen-transport protein because it can pick up oxygen in areas where oxygen is plentiful (ie, where the partial pressure of oxygen [\(\text{P}_\text{O}_2\)] is high) and release the oxygen in areas where oxygen is scarce (where the \(\text{P}_\text{O}_2\) is low). You can see this effect if you look at a graph of the oxygen saturation curve for hemoglobin (Figure 2).

Although hemoglobin binds a lot of oxygen when it is in an area of high oxygen tension (high \(\text{PO}_2\)), hemoglobin cannot hold as much oxygen in an area of low oxygen tension (low \(\text{PO}_2\)). As a result, the hemoglobin can pick up oxygen in the lungs and release it in other parts of the body, such as the skeletal muscles.

![Figure 2](https://commons.wikimedia.org/wiki/File:Oxygen_saturation_curve.png)

*Figure 2.* This graph shows the oxygen saturation curve for normal hemoglobin, as tested in vitro at a pH of 7.6 (top curve), 7.4, and 7.2 (bottom curve). Normal pH is very close to 7.4. The oxygen saturation curve for hemoglobin in vitro is sigmoidal (S-shaped) because the first molecule of oxygen that binds to hemoglobin alters the conformation (3-dimensional shape) of the hemoglobin molecule. This conformational change makes it easier for the hemoglobin molecule to bind the other 3 oxygen molecules. Note that hemoglobin has a higher affinity for oxygen at a higher pH. Thus, it would pick up even more oxygen in the high-pH environment of the lungs and release more oxygen in the low-pH environment of the rest of the body. People with sickle-cell anemia have abnormal hemoglobin. The oxygen saturation curve for their hemoglobin would be shifted to the right (lower affinity for oxygen).

Hemoglobin molecules exist in 2 basic conformations (3-dimensional shapes). Deoxygenated hemoglobin is in a “taut” or “tense” (T) state. Once the hemoglobin molecule has picked up at least 2 oxygen molecules, it can transition to...
the “relaxed” (R) state, which makes it easier for the hemoglobin molecule to absorb the other 2 oxygen molecules.6 (This explains why hemoglobin’s oxygen-dissociation curve is sigmoidal [S-shaped]). The binding of hydrogen ions (H⁺), chloride anions (Cl⁻), carbon dioxide, and organic and inorganic phosphates to sites other than the heme groups can affect the transition between the T and R states. As a result, they can help to regulate the function of hemoglobin. Note that hemoglobin’s oxygen-dissociation curve gets shifted to the right by conditions found in exercising muscles (eg, low pH and high temperature). This right shift allows the hemoglobin to deliver oxygen most efficiently where it is needed the most.

People with sickle-cell disease have abnormal hemoglobin that has a lower affinity for oxygen. As a result, the oxygen saturation curve is shifted to the right. On the plus side, this rightward shift allows the blood to unload more oxygen in poorly vascularized tissue. As a result, the patient’s heart will not have to work harder to compensate for the low oxygen-carrying capacity of the blood. The downside is that the venous blood in these patients can become severely deoxygenated. As a result, the abnormal hemoglobin molecules will be more prone to bind together into stiff polymers, causing the red blood cells to become abnormally stiff and sickle-shaped. These stiff, abnormally shaped red blood cells can clog tiny blood vessels and cause severe organ damage.6 Because of the short life span of their red blood cells, these patients often have a shortage of red blood cells (anemia).

Unfortunately, hemoglobin has a higher affinity for carbon monoxide (CO) than for oxygen. When carbon monoxide binds to hemoglobin, it forms a stable complex called carboxyhemoglobin. As a result, the hemoglobin cannot bind to oxygen. This is why carbon monoxide poisoning can be deadly. Hyperbaric oxygen (pure oxygen supplied at more than atmospheric pressure) is often used to treat carbon monoxide poisoning.6

**WHY DISSOLVED CARBON DIOXIDE LOWERS pH**

Hydrogen ions (H⁺) have an important effect on the oxygen saturation curve of hemoglobin. Some of these hydrogen ions are generated by the carbon dioxide that is dissolved in the bodily fluids. When carbon dioxide dissolves in water, some of the carbon dioxide molecules react with a water molecule to form a bicarbonate anion (HCO₃⁻) and a hydrogen ion (H⁺).

\[
\text{CO}_2 + \text{H}_2\text{O} \rightarrow \text{HCO}_3^- + \text{H}^+ 
\]

The double-ended arrow indicates that this reaction is reversible. Hydrogen ions are sometimes called protons. Most hydrogen ions consist of a single proton. However, some hydrogen ions have 1 or even 2 neutrons attached to the proton.

Normally, you would expect the pH of pure water to be 7.0, which is neutral (see sidebar). But if you expose pure water to atmospheric air, the pH will drop to approximately 5.8 because of the hydrogen ions released by this reaction. This pH is actually a bit higher than you might expect, given the amount of carbon dioxide that has reacted with the water. That’s because some of the hydrogen ions bind to bicarbonate anions to form carbonic acid.

\[
\text{HCO}_3^- + \text{H}^+ \xrightleftharpoons{\text{carbonic anhydrase}} \rightarrow \text{H}_2\text{CO}_3 
\]

Again, the double-ended arrow indicates that the reaction is reversible. Carbonic acid is a diprotic acid, meaning it can give up as many as 2 hydrogen ions. However, it is a weak acid. Only a small percentage of the carbonic acid molecules in a water solution will give up even 1 proton, to yield a bicarbonate ion (HCO₃⁻). An even smaller percentage of carbonic acid molecules will give up both protons, to become a carbonate anion (CO₃²⁻). The bicarbonate and carbonate anions can act as a buffer. If you add additional hydrogen ions to a bicarbonate solution, many of those hydrogen ions will react with the bicarbonate to yield water and carbon dioxide, which may leave the solution as a gas. This is why you get bubbles of carbon dioxide when you add an acid, such as vinegar, to baking soda (sodium bicarbonate).

**CARBON DIOXIDE MAKES HEMOGLOBIN RELEASE MORE OXYGEN**

This conversion of dissolved carbon dioxide to bicarbonate is normally so slow that it would have no useful effect on gas transport in the body. However, red blood cells contain an enzyme called carbonic anhydrase 1, which speeds up the reaction about a millionfold. This reaction has several effects.

- It decreases the carbon dioxide concentration within the red blood cells. As a result, it creates a concentration gradient that allows more carbon dioxide to flow “downhill” from the surrounding tissue into the red blood cells.8
- It generates hydrogen ions, which can then bind to hemoglobin. The hydrogen ions help to convert the hemoglobin to the tense state, so that it releases more oxygen.5
- It generates bicarbonate ions. As the concentration of bicarbonate ions inside the red blood cell rises, the bicarbonate ions start to flow out of the red blood cell through the

**What is pH?**

The pH (“power of hydrogen”) of a water-based solution is a measure of how many hydrogen ions (H⁺) are in the solution. In pure water, with no dissolved substances, there are just as many H⁺ ions as OH⁻ ions. The concentration of H⁺ ions in that situation would be 1 x 10⁻⁷ M, which is expressed as a pH of 7. If you increased the concentration of H⁺ ions 10-fold, you would have a concentration of 1 x 10⁻⁶ M, which is a pH of 6.

- It generates bicarbonate ions. As the concentration of bicarbonate ions inside the red blood cell rises, the bicarbonate ions start to flow out of the red blood cell through the
SLC4A1 transporter. SLC4A1 is an antiporter; it passively allows bicarbonate anions to leave the cell, but it uses the resulting energy to import a chloride anion. The chloride anions then bind to the hemoglobin, contributing to the tense state, so that the hemoglobin releases more oxygen. 

These effects explain a phenomenon called the Bohr effect, which is that low pH and high PCO2 both cause the oxygen saturation curve of hemoglobin to shift to the right (Figure 2). 

Thus, the blood can release even more oxygen in low-oxygen areas where there is a lot of carbon dioxide and/or a lot of lactic acid (eg, in exercising skeletal muscle).

CARBON DIOXIDE TRANSPORT

Because carbon dioxide is poorly soluble in water, only a tiny amount of the carbon dioxide in the blood that is being returned from the rest of the body to the lungs is in the form of dissolved carbon dioxide. About 80% of it is in the form of bicarbonate ions that are produced in the red blood cells and released into the plasma. A small amount of carbon dioxide is bound directly to the protein portion of hemoglobin, to form carbaminohemoglobin.

When the deoxygenated, carbon dioxide–rich blood returns to the lungs, it releases carbon dioxide and absorbs oxygen. Some of this gas exchange is the result of simple diffusion. As there is more carbon dioxide in the returning blood than in the air in the lungs, there will be a net flow of carbon dioxide from the blood to the air spaces of the lungs. As there is more oxygen in the air spaces in the lungs than in the blood returning from the rest of the body, there also will be a net flow of oxygen from the atmosphere to the blood.

In addition, this gas exchange is increased because of chemical changes in the blood. These chemical changes are basically a reversal of the changes I described above.

• Carbonic anhydrase 1 will speed up the reaction of bicarbonate anions and hydrogen ions to yield water and carbon dioxide; the carbon dioxide can then diffuse out of the red blood cell and out of the bloodstream.

• As the bicarbonate level inside the red blood cell drops, there will be a net flow of bicarbonate back into the red blood cell and a net flow of chloride out of the red blood cell, through the SLC4A1 antiporter.

• As the concentration of hydrogen ions and chloride ions in the red blood cell decreases, the hemoglobin is able to transition to the relaxed state so that it can pick up more oxygen (Bohr effect).

• As oxygen diffuses into red blood cells, it tends to displace the carbon dioxide that was bound to the hemoglobin (Haldane effect). This carbon dioxide can then diffuse out of the cell and out of the bloodstream.

CARBON DIOXIDE AND pH BALANCE

If oxygen stopped entering your bloodstream, you would quickly die. Yet low oxygen levels, as detected by oxygen sensors in your body, have only a small effect on your drive to breathe. This is why pilots flying at high altitudes in an unpressurized airplane would often pass out before they felt respiratory distress. (For this reason, federal aviation regulations require pilots to use supplemental oxygen during high-altitude flights.) Instead, your breathing rate is controlled mainly by the pH of your bodily fluids, which in turn is controlled mainly by the amount of carbon dioxide in your tissue. High PCO2 in bodily fluids would result in low blood pH and thus a high drive to breathe. In people who have abnormally low blood pH because of excess acids produced by metabolism (metabolic acidosis), such as in cases of diabetic ketoacidosis or kidney failure, the strong drive to breathe can produce deep and labored breathing, which is called Kussmaul respiration.

If you cannot get rid of enough carbon dioxide, your blood pH will be low. If your blood pH drops below 7.35 because of suppressed or impaired ventilation, the condition is called respiratory acidosis. On the other hand, if you hyperventilate, you can end up with abnormally low levels of carbon dioxide in the blood. This would raise the blood pH. If you hyperventilate to the point that your blood pH rises above 7.45, you would be in respiratory alkalosis.

During the course of a normal day, large amounts of acidic and alkaline substances enter the bloodstream. Yet the pH of the blood is supposed to remain steady at almost exactly 7.4. To maintain this steady pH, the body relies on a buffer. A buffer is a solution that resists changes in pH when acids or alkalis are added to it. Buffers are usually made out of a combination of a weak acid (eg, carbonic acid [H2CO3]) and its conjugate base (ie, bicarbonate anion [HCO3−]). Look at what would happen if you added some strong acid (eg, hydrochloric acid) or a strong base (eg, sodium hydroxide) to the blood:

• Add hydrochloric acid: HCl + HCO3− →H2CO3 + Cl−; the bicarbonate ions will mop up hydrogen ions from the hydrochloric acid. As a result, there would be little or no drop in pH.

• Add sodium hydroxide: 2NaOH + H2CO3 →Na2CO3 + 2H2O; the carbonic acid will dissociate to release protons to bind with the hydroxide ions (OH−). As a result, there will be an increase in bicarbonate and carbonate anions but little or no rise in pH.

Thus, the buffering capacity of your blood can keep your blood pH stable, despite the acids and alkalis that enter and leave your bloodstream during the course of a normal day. Adding even a strong acid or a strong base to a buffered solution will cause little change in pH until the solution’s buffering capacity is exhausted. If, however, you exceed the buffering
capacity of your blood and start to have an abnormal rise or fall in pH, your autonomic nervous system will adjust your breathing rate down or up to compensate.

ANEMIA IMPAIRS OXYGEN TRANSPORT

Your hemoglobin clearly plays an important role in transporting oxygen and carbon dioxide in your bloodstream. However, your red blood cells are responsible for carrying the hemoglobin. Hemoglobin is so reactive that it would cause problems if it were loose in the bloodstream. That’s why diseases that cause hemolysis (destruction of red blood cells) can cause serious problems, such as clotting and inflammation. Hemolysis can also lead to anemia. Anemia is a general term for any problem that involves a shortage of red blood cells or a shortage of hemoglobin within the red blood cells.

Hemoglobin clearly plays an important role in carrying oxygen and carbon dioxide. Future articles in this series will give more details about gas exchange and circulation, as well as how the blood carries other substances, including lipids such as cholesterol.

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Laurie Endicott Thomas is the author of 5 books. Her book Thin Diabetes, Fat Diabetes: Prevent Type 1, Cure Type 2 (www.thindiabetes.com) explains how a severe shortage of insulin leads to problems with blood pH (diabetic ketoacidosis).

References
Sex is the biological classification of female or male individuals, which is determined by genetics. Gender is more than sex, and it refers to the socially constructed roles, behaviors, and identities of individuals.1

What is gender bias? In theory, it can be defined as “the inclination toward or prejudice against one gender.”2 Gender bias can span a wide range of experiences, from pay inequity to inadequate parental leave policies to discriminatory funding/promotion/award practices and more.3-5

In the #MeToo era, women’s experiences in life and work have become a more regular part of the cultural conversation. In light of these developments, we wanted to examine gender bias in science and medicine (Figure 1),6 with a particular focus on how it occurs in fields related to medical writing and on how medical writers can address it. More than 60% of women in science, technology, engineering, and medicine (STEM) claim they have to provide more evidence of competence than men to prove themselves.3

WHY IS IT IMPORTANT TO HAVE ENOUGH FEMALE REPRESENTATIVES/VOICES?

There are certain experiences that are significantly different for women than for men: for example, childbirth. Thus, women may bring a perspective to the table that is different from that of men, which can have important ramifications for design and decisions. For example, when female engineers were left out of the design team for cars, early versions of airbags and voice-recognition systems didn’t perform well when used by women.7 Teams that have diversity in their experiences and ideas often produce better outputs than teams that are composed of people with similar backgrounds and experiences (eg, a team of only male doctors may design a delivery room around interventions rather than the normal physiology of birth).7,8

Sex and gender can influence health and disease across many body systems, including different responses to medicine, rates of developing certain diseases, and even symptoms of disease. For example, women have smaller-diameter blood vessels that are more intricately branched than men, which may explain the different coronary artery blockage patterns seen in women with heart disease.9 In 2013, the US Food and Drug Administration revised the dosing recommendations for products containing zolpidem (a sedative–hypnotic indicated for the short-term treatment of insomnia) to a lower dose for females, based on pharmacokinetic data that showed women eliminate zolpidem more slowly from their bodies than do men.10,11

WOMEN IN SCIENCE AND MEDICINE

In the United States, women make up 51.5% of the population of adults over the age of 18 years, and they occupy approximately 47% of all jobs.12 In STEM fields in the United States, women hold 24% of jobs (Figure 2).13

Individuals with PhDs and tenure-track faculty positions are often authors on peer-reviewed manuscripts and are often sought out as thought leaders in STEM fields, so it is important to understand women’s representation in these 2 pools.

---

**Figure 1.** More than half of women in STEM report experiencing gender biases, in contrast to 2% of men in STEM experiencing them. Data were compiled from survey responses of 1,301 scientists with doctoral degrees in the United States in 2010.6
Women’s share of science and engineering doctorates has increased substantially over the last several decades but has hovered at around 40% since 2009. In US colleges and universities, women make up an estimated 25% to 35% of tenure-track faculty (who are almost always PhD holders).

Medical journals have very few women on the editorial board or serving as editor-in-chief. Several studies show the share of women in editorial positions to be 10% to 15%. In 2018, the prestigious journal *Nature* appointed the first female editor-in-chief in its 149-year history.

The medical writing profession is one in which women are represented heavily. In 2018, AMWA leadership (Board of Directors and staff) is almost exclusively female, with 20 women and 1 man. Results from the 2015 AMWA Salary Survey show that 84% of respondents were female, which provides an estimate of the gender split for AMWA membership. Consequently, women are likely not in the minority when attending AMWA events.

**WHERE GENDER BIAS CAN OCCUR**

**Pay Inequality by Gender**

Health care and biomedical and life sciences demonstrate trends of gender pay disparities in stagnation over last decade. According to the US National Science Foundation, pay disparities exist between female and male PhD holders in science and engineering. A 2016 report indicated that the median salary for women was 24% lower than that for men. Similar observations are noted in medical academicians and providers in the United States, which can be reflected as pay inequalities and reduced reimbursements.

According to the 2015 AMWA Salary Survey, male full-time-employed medical writers earned 4.4% more than females, a difference that was not statistically significant (pay by gender for freelance medical writers was not reported).

**Funding and Awards**

Female scientists face systematic gender bias during the peer review of grants, making them less likely to be funded and less likely to be published than their male counterparts. Female physicians who report financial relationships to pharmaceutical and biotech companies receive significantly fewer research dollars (−$15,000; P = .05) than do men, after adjusting for confounding factors.

This discrepancy extends to some federal research funding as well. There is a systematic trend in National Institutes of Health R01 grant awards for women to be less likely to get awards and, if they are awarded, receive awards in lower amounts.

Since the National Institutes of Health Early Independence Award was established in 2011, men have disproportionately won the award. According to the most recent data from the 2017 awards, men made up approximately 45% of the applicant pool and were awarded more than 70% of the Early Independence Awards (gender was undisclosed in 29% of the applications). Women are less likely to collaborate internationally on research papers and are generally less internationally mobile than men. Studies have also shown that women lose out when reviewers assess the researcher and not the research. Success rates for applicants to conventional grant programs from the Canadian Institutes of Health Research were 0.9% higher for men than for women when program reviewers focused on the applicant’s research proposal, as compared with 4% higher when reviewers focused on the applicant’s experience and qualifications. These actions have unfavorable repercussions for the career paths of female scientists, resulting in delays or failures in the tenure-track progression or dropping out of academia altogether. Funding gaps along with leadership gaps and salary gaps are identified as core issues that must be countered to tackle the issue of women’s underrepresentation in academia.
Publication

Although there is a trend indicating that the gap is closing, women are still underrepresented in publications as both authors and editors. Gaps in mentorship result in junior women seldom coauthoring with senior men, which in turn creates the gender disparities evident in leadership roles and other opportunities such as promotion. Additionally, women are underrepresented as authors of “perspectives”-type articles, which offer opinions and may influence the field in ways differing from those of research publications. Often, male editorial members invite male reviewers for manuscript review, and these men are prone to reject papers authored by researchers of the opposite gender, leading to far too few women being involved in peer review. Cumulatively, there is a strong downstream impediment to female careers in academia, membership on editorial boards, receipt of grant money, invitations to conferences, hiring and promotion, and collaborations.

One can better understand the past, present, and (estimated) future gender ratios of authors on academic publications listed on PubMed by visiting https://lukeholman.github.io/genderGap/. On the flip side, there is evidence of a positive influence on gender diversity in scientific research. A recent study showed that publications with a male first author and a female last author most often reported adequate statistical power of the clinical trial being presented, compared with other gender combinations of authors (first/last authors: both female, both male, female/male).

Invited Talks/Symposia

As the hierarchy of power and prestige rises, the topics discussed above become increasingly influential to position the candidates for invited talks and symposia. Thus, scientific eminence through awards, funding, mentorship support, publications as first or senior authors, h-index, scientific productivity, and citations plays a very crucial role. Yet the proportion of women on invited panels is generally low.

Omitting prominent and qualified female scientists from important conferences fuels the existing gap. One study regarding a neuroimmunology meeting without gender balance on an invited speaker panel discussed the various reasons for such omissions. Conversely, it is clear that female organizers invite female speakers and that they enhance the diversity of the panel through balanced representation.

Additional Areas of Bias

Gender plays a role in obtaining and maintaining patent rights. A study of databases from the US Patent and Trademark Office showed that, after adjusting for confounding factors, women were less likely to have a favorable outcome across many measures for patent applications than did men, including for life sciences or technology patents. For example, a team of all women inventors in the life sciences was 11% less likely to have a patent application accepted than was a team of all men.

Female faculty members receive fewer scholarly awards than expected. In many scientific disciplines, the proportion of scholarly awards going to women is lower than the proportion of women who are full professors. Some possible explanations for this discrepancy are the adjectives (or lack of them) used to describe the female applicants in the application support letters (eg, fewer descriptors of exceptionality and more female-typical adjectives, such as “cooperative” and “dependable”), the language in the request for nominations (eg, language that implies male associations, such as “decisive” or “confident”), and the gender composition of the awarding committee.

When faculty members are promoted along the tenure track and researchers obtain grants and notable publications, these achievements naturally convey that the individual is an expert in the field of study, leading to further achievement and greater credibility. With more credibility comes notoriety and possibly financial benefits, in the form of career promotions, awards, and new opportunities. If women receive less recognition and publish less, they may also miss out on some of the associated financial benefits, which can obviously influence their life experiences and opportunities.

WHAT CAN AMWA MEMBERS DO?

AMWA members can influence the perception and exposure of women in science through their medical communications.
Here are a few suggestions:

- **Realize that we all have inherent biases about gender.**
  Awareness is the first step to change.

- **Use female and male examples of health care providers (HCPs) or experts.**
  - Write using both female and male pronouns. Suggest stock photos of both female and male providers for artwork, when necessary. Try to use these as equally as possible.
  - Include more nurses as interviewees and in photos, when possible. Nursing positions are predominantly occupied by women (90% of nurses in the United States are women), and they play a vital role in health care, but nurses are rarely quoted in articles and seldom even acknowledged.45-47
  - Ensure you are using the same level of language to refer to male and female HCPs. For example, use Dr [Michael] Nichols and Dr [Emily] Johnson, and be on the lookout for less formal referrals to female HCPs, such as “Dr Emily” or “Emily.”48

- **Find female thought leaders to add to lists or invite to events.**
  - A Web search for “female [therapeutic area] specialist” or “women’s [therapeutic area]” may help uncover individuals you may not have found otherwise.
  - Look at women’s subcommittees of professional organizations for members or officers.
  - Ask experts for a referral to a female colleague.

- **Point out to colleagues or clients when there’s an imbalance in the female/male ratio of authors or experts.**
  In your own work, make a conscious effort to balance the citations of papers written by female and male authors. You can use a similar search as suggested above to find these papers if you don’t already have them.

- **Interview female experts for conference reports or news articles.** Ask similar questions and give equal weight to answers from all parties.

- **Educate your peers and clients about gender bias and create awareness through various methods regarding the ways in which it can be countered.** Use social media, blog posts, publications, in-person meetings, or seminars to discuss the imbalance.

- **Use resources to source women scientists.**
  - 500 Women Scientists: https://500womenscientists.org/request-a-scientist/
  - Anne’s List: https://anneslist.net/
  - AcademiaNet: http://www.academia-net.org/

- **If applicable, use blinded review for papers or reviews.**

- **Provide mentorship and role modeling for junior and upcoming medical writers.** Guidance from senior and experienced AMWA members is crucial to develop confidence and set goals during the early years of those new to the field. Although most medical writers are female, many have come to writing/editing other careers in which they were not mentored.

- **Look out for updated Sex and Gender Equity in Research Guidelines that should incorporate a framework for gender balance in publishing.**49

With awareness and conscious effort, AMWA members can counteract some of the gender bias in science and medicine, with the hope of presenting a wider spectrum of ideas and promoting individuals who may previously have been left out of the spotlight.

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ARTICLE 3: HOW HEALTH DISPARITIES TOUCH YOUR WORK

“The inherent vice of capitalism is the unequal sharing of blessings.”
—Winston Churchill

This series of articles has been shaped expressly to the needs and concerns of AMWA medical writers and editors. Health disparities (HDs) and social determinants of health (SDHs) are of direct relevance to educational materials for physicians and all allied medical professionals, including community health workers, lay health advisors, and patient navigators; to hospital publications for providers, patients, families, and neighborhood residents; to the websites of hospitals, government health agencies, and pharmaceutical and medical device companies; to publications of research that formerly might not have clearly discussed disadvantaged subgroups; to review articles, in relation to whether the relevant literature encompasses HDs/SDHs or whether the literature is limited in having largely ignored crucial populations; to public health publications, as interest in population health is great at present and, therefore, opportunities for medical writers are considerable; to journalistic articles for magazines, books, and Internet sites; to training materials for pharmaceutical representatives; to websites for an array of audiences; to consumer-oriented publications by professional organizations and foundations (for example, the American Heart Association, the American Nurses Association, and the Kaiser Family Foundation); and to newspapers, news sites, and similar publications, both those for a general readership and those for a focused audience.

Thus, all medical communicators may find a way to participate in the widespread efforts to reduce the HDs and reconfigure the SDHs.

WHY ACT NOW?

In 2011, leading researchers wrote, “A critical mass of relevant knowledge has accumulated, documenting associations, exploring pathways and biological mechanisms, and providing a previously unavailable scientific foundation for appreciating the role of social factors in health.” As these authors state, the SDHs have come of age; the scientific foundation is solid.

The data suggest that approximately 245,000 deaths in the United States in 2000 were attributable to low education, 176,000 to racial segregation, 162,000 to low social support, 133,000 to individual-level poverty, 119,000 to income inequality, and 39,000 to area-level poverty. According to a National Academy of Medicine (NAM) Initiative, “educational level is the most powerful determinant of lifelong health prospects.”

“The US health system ranked in a World Health Organization assessment only 37th in performance among 191 member nations” and “in a recent study of 11 highly industrialized Organization for Economic Co-operation and Development (OECD) nations, the United States ranked last.”

Of the roughly $3 trillion the US spends on health, approximately 30% goes to waste, inefficiencies, and excessive prices

People Who Cannot Afford Boots Cannot Pull Themselves Up by the Bootstraps:
An Evidence-Based Exploration of Health Disparities, Social Determinants of Health, and How Medical Writers Can Help

Bob Kirsch, MA and Tamara Ball, MD / Freelance Medical Writers

In the first article in our series, we presented evidence relevant to the current state of health disparities (HDs) and social determinants of health (SDHs) in the United States. Our second article discussed some of the peer-reviewed publications describing interventions that have reduced HDs and reports on efforts currently underway by thought leaders, the Centers for Disease Control and Prevention, and medical foundations to further address the issues. This third and final article offers practical and concrete actions that medical communicators can take to support these efforts in the name of better health for all Americans. We present both tips on how to write about these problems and specific topics about which you might choose to write.
and to expenditures not aimed at the factors most important to the nation’s health profile. A Position Paper of The American College of Physicians speaks of “a small share of health expenditures (9%) being directed toward prevention and low levels of investment in social services.” The developed nations in the OECD, spend, on average, $2 on social services for every dollar spent on health care. In contrast, the United States spends only 50 cents per dollar on health care.

As pointed out by a NAM Initiative, “The traditional focus on disease screening and treatment reinforces a focus on health problems at a relatively late stage in the process and is not cost effective. It discourages accountability for overall community and population health and engagement in the large-scale community-based health-promotion and disease-prevention activities of which medical encounters are only one aspect.”

“Despite an increasingly strong and specific understanding of the preventable elements in the development of many of our health challenges — social, behavioral, environmental — our investments are primarily directed to their biomedical manifestations, well after the problems have taken root.” Thus, for example, “screening rates for health-related social problems are low despite the effectiveness of such screening in identifying health-related needs associated with social determinants of health,” according to an American College of Physicians committee.

Investing in prevention “has a greater proven return than does other health care investment.” Yet, in implementing newer approaches to population health, “local health departments continue to face resource challenges from local financing streams, and proposals to reduce federal public health spending are likely to have a major impact at the local level.” Indeed, “social justice or health equity arguments are often less persuasive than economic arguments. So, it is critical to have research showing that addressing the social determinants of health will actually save money over the long term, preventing hospitalizations and the costs of managing chronic illnesses,” explains Jennifer Alvidrez, PhD, Scientific Program Officer, National Institute on Minority Health and Health Disparities (NIMHD) (telephone interview, August 2018).

The NAM, the Centers for Disease Control and Prevention (CDC), the National Institutes of Health (NIH), the US Food and Drug Administration (FDA), private foundations, and a multitude of medical researchers are pouring great quantities of energy and funding into changing this situation. “Achieving the highest possible level of health in communities and populations requires a rebalancing of our overall investment in ways that enhance disease prevention and wellness strategies throughout the lifespan and builds the strength and resilience of communities,” the NAM Initiative advises. Poor community transportation (to and from medical facilities, grocery stores situated outside of neighborhoods with food deserts, etc), and food insecurity are all too common. As a 2018 Position Paper of the American College of Physicians states, “A review of 61 studies found lack of transportation to be a major obstacle to health care access, particularly for low-income, uninsured, or underinsured persons.” When the Nashville Area Metropolitan Planning Organization explored demographic characteristics correlated with poor health, one characteristic identified was not owning a car. “Evidence suggests that increased social services can help to mitigate health disparities.” Further, an “analysis of states between 2000 and 2009 found that those states with higher ratios of social services spending to medical spending had better health outcomes.”

Yet, in implementing newer approaches to population health, “local health departments continue to face resource challenges from local financing streams, and proposals to reduce federal public health spending are likely to have a major impact at the local level.” Medical writers and editors cannot ignore policy and funding decisions at all levels of government.

The magnitude of HDs and SDHs is not fixed. This should be encouraging for us medical and health writers and editors, as it indicates that things can indeed improve. The second article of this series described an array of different types of interventions that have succeeded in improving the health of vulnerable populations. In addition, notable medical and public health achievements have benefitted the health of these populations, and these include reductions in motor vehicle fatalities, in the US infant mortality rate, in the prevalence of elevated blood lead levels in children, in the number of adults smoking cigarettes, in the number of children exposed to secondhand smoke, and in the number of adolescents using alcohol or illicit drugs. Further, the number of adults achieving their physical activity targets has increased. Thus, progress in reducing HDs is already being made. Now would seem the time for AMWA members to take advantage of this growing momentum to help address some of the key issues involved in perpetuating HDs and SDHs.
WHAT OTHER GROUPS ARE ALREADY DOING TO RESOLVE HDS

The response to existing HDs encompasses the programs and initiatives of government agencies, professional societies, foundations, pharmaceutical companies, the media of various sorts, and other organizations. Yet it is not clear that influential persons and groups—from physicians to community members—are fully aware, or even slightly aware, that this activity is occurring. Medical communicators can have an impact here by informing readers, both professionals and the public, about what is already happening.

The integration of medicine and public health is increasing. In an official Policy Statement, the American Academy of Pediatrics asserts, “Although pediatricians and public health professionals interact frequently to the benefit of children and their families, increased integration of the 2 disciplines is critical to improving child health at the individual and population levels.”10 Similarly, a perspective published in *The New England Journal of Medicine* on “healthy eating behavior,” considers diet, obesity, cardiovascular disease, and type 2 diabetes and discusses harmonizing a “medical model (where the focus is on one patient at a time)” and “a public health model (where the focus is on entire populations).” Thus, the author asserts that “a road map for sustainable behavior change will succeed only if efforts are harmonized across various settings (eg, child care, school, work, and hospitals), at multiple levels (eg, individual, household, and community), and among a diverse set of stakeholders (eg, health care providers, lawmakers, and social workers)” and with support from “strategic advocacy by stakeholders, including direct contact with key policymakers or position statements by medical organizations” plus “design approaches that prevent the adoption of unhealthy dietary behaviors (rather than trying to modify existing unhealthy behaviors).”11 The closer integration of medicine and population health will surely have impact upon segments of medical writing.

NAM is powerful and influences the actions of the CDC and additional agencies. The final summary statement of the NAM Vital Directions Initiative involves more than 150 US experts and concludes that addressing disparities is a vital priority. When a powerful and influential organization that has the support of a large number of the most powerful and influential leaders in the US health care landscape speaks, there is a very good chance that actions will follow, whether or not those actions match precisely what the original recommendations were. And there is a very good chance that funding will follow the lines projected by the NAM.12

HDs are being incorporated into continuing medical education (CME) programs: The Accreditation Council for Graduate Medical Education has incorporated reducing HDs into its Clinical Learning Environment Review program.13 The American College of Physicians recommends that SDHs and the underlying individual, community, and systemic issues related to health inequities be integrated into medical education at all levels. “Health care professionals should be knowledgeable about screening and identifying social determinants of health and approaches to treating patients whose health is affected by social determinants throughout their training and medical career.”14 The NAM’s 2016 “A Framework for Educating Health Professionals to Address the Social Determinants of Health” recommends “making the social determinants of health a core component of all health professionals’ lifelong learning pathways.”14 Further, government agencies that possess the power to affect medical education at all levels are also moving in this direction. For example, in 2012 alone, public tax dollars contributed more than $15 billion to support residency training, with more than 90 percent coming from the Medicare and Medicaid programs, while The Centers for Medicare & Medicaid Services is currently supporting its Transforming Clinical Practice Initiative.15

Local Hospitals Are Changing How They Work with the Community

The Patient Protection and Affordable Care Act includes an amendment to the Internal Revenue Code requiring local hospitals and additional nonprofit health care organizations to assess and work toward responding to community needs and encouraging a transformative community health culture. Via community benefit programs, “hospitals can advance community-wide strategies for health improvement and have an economic incentive to do so.”4 This can integrate clinical, social service, educational, voluntary, commercial, and related stakeholders.4

WHAT CAN MEDICAL COMMUNICATORS DO TO HELP?

“Communication is arguably the most important consideration in interventions to change individual behaviors that may be influenced by social determinants.”

—2018 position paper, the American College of Physicians

Speaking at an *NEJM Catalyst* event, Russell L. Rothman, MD, MPP, Vice President for Population Health Research at Vanderbilt University Medical Center, explained, “One factor that we think is particularly important that physicians, clinics, and health systems can address is health communication and how we use health communication to engage our patients and the community to improve individual and population health. We need approaches that can reach out to our patients and their communities.”16

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“Even though many of us went into medicine because we like science and math, our patients do not,” said Rothman.16 Well, many of us medical writers and editors like, on the one hand, both science and math and, on the other hand, clearly communicating these concepts. In communicating about medicine and health, we can potentially do much to improve HDs.

We Can Change the Way We Write about HDs and the SDHs

**Improve Patient–Clinician Communication**

In an in-press review article titled “Communicating with Diverse Patients: How Patient and Clinician Factors Affect Disparities,”17 Eliseo J. Pérez-Stable, MD, Director, NIMHD, and colleagues explain that patient factors associated with poor patient–clinician communication (PCC) include membership in a racial/ethnic minority, having limited English proficiency, or having low health and digital literacy. Clinician factors include being less culturally competent, lacking communication skills in shared decision-making, and holding unconscious biases. The authors recommend offering patient- and/or clinician-targeted interventions to guard against unconscious biases and improve PCC, screening patients for health literacy and English proficiency, integrating PCC in performance processes, and leveraging health information technologies to address unconscious biases.17 We medical communicators can bear these concepts in mind when writing patient-directed communications to be provided by clinicians.

**Encourage Genuine Listening**

“If you ask most clinicians, they will tell you they are excellent at communication,” said Rothman. “They think they are really good at it. They will say, ‘Oh, my patients sit there and nod. My patients understand exactly what I am saying.’ However, when you actually observe the communication and when you talk to patients right after they leave the hospital or right after they leave the room, you find our communication skills are not actually as good as we think we are.”16

The physician-author of this article adds that a foundational truth learned early in her training was that sick people do not behave like well people and that family members may be dealing with competing stressors, be coming off a night shift, or have another legitimate explanation for their behavior. We were told to leave our judgments outside the door.

I found that genuine listening can help build relationships, solve problems, ensure understanding, resolve conflict, and improve accuracy. As medical communicators, we can communicate with hospital staff how—in a system that often fails the underserved and their families or views them as “difficult patients”—each employee has the potential to make a very big difference by embracing this technique/mindset.

**Enable Physicians to Assist Patients in Managing Health Information**

Patients, especially those with access to the Internet, may be overwhelmed with the amount of available health information—good and bad, reliable and unreliable. “The primary care physician needs to step in as the first point of reference for the patient—coordinating what to do with all the information,” said Dr Pérez-Stable (telephone interview, August 2018). We can provide patient-directed health communications to physicians who are increasingly being required to help patients manage the information overflow.

**Cite Expert Recommendations to Help Clinicians Improve Their PCC**

➲ See Online Only content:

An Interview with Eliseo J. Pérez-Stable, MD.

Dr Pérez-Stable presents key points on the communication between providers and patients, on “communication gaps,” on factors relevant to communicating with minorities, and on the role of medical writers and editors in helping to overcome health disparities.

**Encourage Appropriate Referrals from Physicians to Experts with More Time for Patients**

As the NAM Initiative “Vital Directions for Health and Health Care Priorities” states, “Policies must not only encourage more judicious use of health care services, but also ensure supports for better health behavior and facilitate integration of health-related social service interventions.”12 We can let physicians know it is now very acceptable to refer a patient to a social worker or community organization, but if and only if structures are in place to guarantee the patient will not end up in limbo or bureaucratic quicksand.

**Help Physicians Manage Information Overflow**

“We need to figure out what to do with all the information now becoming available, as physicians are more and more overwhelmed. This includes genetic and biological information, much of it generated with no clear goal in mind,” said Dr Pérez-Stable (telephone interview, August 2018). We can provide medical communications and/or strategies to help physicians manage the information overflow.
Influence the Way People Talk about Health

“As we work to shift perception and culture, we must likewise work to influence the way people talk about health, changing—literally—the terms of the debate, as we move toward the ultimate goal of changing minds and societies,” explains Sandro Galea, MD.5 “Consider our efforts to curb the gun violence epidemic. That the word ‘epidemic’ is now used prominently in reference to this ongoing tragedy is itself a sign of progress…. This shift demonstrates the power of words to both define a problem and create a context in which it might be solved,” Dr Galea explains.5 Further, as members of vulnerable populations may not only be defined as vulnerable by academics but may actually feel vulnerable, the terms of the debate may be of particular importance for these populations. We can craft our medical communications accordingly.

Make the Acceptable Unacceptable

“It does matter—very much so—if we articulate that the most common cause of death is heart disease, or being overweight, or lacking education, because the formulation of the causes of death contributes to changing how these causes are viewed by society and whether or not they are considered unacceptable and, ultimately, worth changing,” Dr Galea points out. An underlying assumption that the poor may not live long lives may undermine the perceived need to apply research findings to the improvement of the health of the poor and to appropriate adequate funds for that purpose. For “action arises when a condition we considered a ‘given’ becomes, indeed, ‘intolerable.’” And “the expression must be central to our work” if we wish to create social momentum. We can help to make “the acceptable unacceptable” so that change will follow.5

Battle Stereotypes

At an AMWA-NY meeting last May, Rachel C. Shelton, SCD, MPH, of Columbia University’s Mailman School of Public Health said that “frames help shape perceptions and parameters of health issues.”18 In this context, “frames” refers to how we sketch context, which facts we choose to bring to bear, and how we juxtapose fact with fact, knowing that facts may evoke emotions and feelings. Facts themselves need not be cold, hard facts. In presenting information about HDs/SDHs, we can avoid damaging, and frequently inaccurate, stereotypes in medical communications.

When You Write about a Study, Bear in Mind HDs

According to Pérez-Stable EJ, et al, “When you write about a study, consider who is included. Did ethnic and racial minorities participate in the study? If not, why not? If the study population is overwhelmingly White, you should be skeptical. If the researchers found differences between people of different populations, did they consider all the reasons why such differences can occur, or just jump to a conclusion that it must be because the races are biologically different? By asking these questions, we can help improve clinical research and ultimately help end health disparities.”17


Biology does matter; SDHs are a big part but not the whole story. “We know that African Americans who smoke have 2 or 3 times greater chance of developing lung cancer than Whites or Latinos. We know diabetes manifests differently in different populations. And while Whites are more likely than minorities to develop heart attacks, twice as many minorities end up on dialysis. A gene has been identified that protects some indigenous Latino women, reducing their likelihood of developing breast cancer; this shows there are different pathways at work in the development of disease. So, while it is true that the poor receive less care—and that the poor who are also minorities get worse care—not all health disparities can be explained by looking at the social determinants of health. Biology does matter. Genetics does matter,” Dr Pérez-Stable said (telephone interview, August 2018).

Hold to the Distinction Between HDs and Health Inequities

This distinction matters, explained Julie Wood, MD, MPH, American Academy of Family Physicians (AAFP), Senior Vice President, Health of the Public and Interprofessional Activities. “Health disparities describe the disproportionate difference in health outcomes between groups of people. Health inequities are differences in the health of a population as the result of the way in which systems (health care, legal, social, etc.) and policies are developed and implemented.” Further, “health equity” may be defined as everyone having a fair and just opportunity to be healthier.19 She also noted that “focusing on health equity requires the participation of individuals from all industries, healthcare, banking, education, etc, to make an impact” (personal communication, August 2018). We might also encourage providers to speak about equity to influential members of the community.

Focus on the Community

We can inform everyone about community efforts and community support, from providers, to policy makers, to the public. Spread the word and build on the momentum. The
document of the NAM Vital Directions Initiative focused on chronic disease prevention provides information and insights on programs addressing nutrition, physical activity, obesity, tobacco, and coordination with the US Department of Agriculture and additional agencies—all from the perspective of communities.

It is a solid resource for writers and editors, including those working on CME, continuing education, websites, and newsletters.

**“Perceptions** matter—perceptions of income inequality, perceptions of limited choices, perceptions of community cohesion. Stress ‘gets under the skin’ and exerts an effect that can grow over the life course.”

**Consider the Range of “Communities” for Whom You Might Write**

To write about or for a given community, consider that the community likely encompasses varying sets or groups or categories of people. Geographic area is not the only way to define the boundaries of a community. There are communities of people with diabetes, those who care for relatives with a disability, those who shop at a local farmers market, those who look to the leadership of a particular government or religious leader, those who gather at a senior center or a playground or nursery school, those who regularly look at a local bulletin board, and so forth. A single topic may require writing 5 or 6 variations of the same article, each distinct. In preparation it may be useful to explore the CDC site “Gateway to Health Communication & Social Marketing Practice” ([https://www.cdc.gov/healthcommunication/index.html](https://www.cdc.gov/healthcommunication/index.html)).

**Perceptions Matter. Explain That.**

As the NAM Vital Priorities Initiative points out, “Perceptions matter—perceptions of income inequality, perceptions of limited choices, perceptions of community cohesion. Stress ‘gets under the skin’ and exerts an effect that can grow over the life course.”

**In Selecting Images for Patient-Directed Posters/Flyers, Consider Audience Perceptions**

When a person from a minority population walks into a clinic waiting room and sees a poster promoting yearly mammograms showing a healthy white woman and a poster for prevention of STDs showing a healthy black woman, what is the message conveyed?

**Tailor Communications to People with Low Health Literacy**

In appropriate ways, inform both clinicians and patients and families that a great deal of excellent, impartial information about low health literacy is available free of charge. Both the CDC and NIH websites offer free guidance for providers on working with patients with low health literacy, instructions that can serve as a resource for medical writers and editors as well (eg, [https://www.cdc.gov/healthliteracy/index.html](https://www.cdc.gov/healthliteracy/index.html)).

Further, where it is possible to explain without engendering or encouraging stereotypes, caution clinicians to be sensitive to the fact that Blacks and Latinos disproportionately have higher rates of poor literacy and numeracy skills.

**Highlight Preventing Illness**

As the nonpartisan NAM Vital Directions initiative stated in the *Journal of the American Medical Association* in March 2017, decades of research have shown that “the leading determinants are outside of healthcare.” Yet, not addressed, those same matters lead to illness, frequently life-threatening illnesses. We can be alert to these issues and weave them into our medical communications where appropriate.

**See Online Only content:**

**Table.**

This table presents a total of 29 important topics you might write on, ranging from violence as a health issue to partnering with local public schools and from social epigenomics to health impacts from exposure to chronic stress, poverty, and racism.

**Collaborate with Physicians and Other Professionals**

“I’m very passionate about our addressing the social determinants of health. So, it’s very rewarding to hear that medical writers are interested in collaborating and working on this, together,” said Julie Wood, MD, MPH, AAFP, Senior Vice President, Health of the Public and Interprofessional Activities. “It involves everything we do, including CME and recruiting residents and students into primary care and family medicine” (telephone interview, June 2018).

**The Efforts of Professional Organizations**

Professional organizations are recognizing HDs and SDHs as important to the practice of medicine. The AAFP has released
several components of its EveryONE project. Multiple audiences should be informed about the AAFP's EveryONE Project, which aims to address "diversity and the social determinants of health as they impact individuals, families and communities." The EveryONE project is detailed at several AAFP sites, including https://www.aafp.org/everyone25 and https://www.aafp.org/patient-care/social-determinants-of-health/everyone-project/cdhe.html.26

**SDHs and Face-to-Face Physician–Patient Interaction**
According to Jack Ende, MD, MACP, President, American College of Physicians, "Taking a closer look at social determinants of health can help us better understand and address the social factors that have an impact on patient health. It's important that physicians and other medical professionals recognize and account for social determinants of health to create a more comprehensive approach with our patients. Moreover, such an approach can help eliminate significant health inequalities often associated with social determinants of health, such as homelessness, food insecurity, and mental health stressors such as domestic violence or social isolation."27

**Physicians Advocating for Patients While Breaking Traditional Molds**
Whether in your local newspaper or on a feature page of a medical journal, there are few things more inspiring than the personal stories of caring individuals. "Physicians not only identify, address, and connect their patients with resources regarding social determinants of health, but they are also strong advocates and are mobilizing to improve the health of the communities in which they serve by influencing elected officials, policy makers, administrators, etc," explained Julie Wood, MD, MPH, AAFP Senior Vice President, Health of the Public and Interprofessional Activities (telephone interview, August 2018). Similarly, Dr Ende of the American College of Physicians stated, "A greater focus on social determinants of health can enable physicians to become stronger advocates for patients and to help reduce negative health outcomes that are often associated with social determinants of health."27

**Physicians Advocating on Local School Boards**
Some caring physicians have secured seats on local school boards, according to Alice Kuo, MD, PhD, MBA, Professor and Chief, University of California, Los Angeles, Medicine–Pediatrics, and President of the American Academy of Pediatrics California Chapter 2 in an interview (personal communication, June 2018). As writers, we can encourage physicians, and perhaps especially retired physicians, to participate actively in improving the health of communities.

**SDHs, Providers, and Medical Communications**
We might subtly remind providers that knowing about the SDHs with which their patients struggle can change conversations entirely. We should also explain to various readers that, for example, even where excellent medical services and interventions are available, pairing these resources with public health capabilities may offer vehicles for addressing significant distribution problems. "A patient with diabetes who lives in substandard housing recently lost their job, or lives in a food desert will face greater challenges in managing their illness than a patient who is not facing these obstacles. However, it might not be readily apparent to a physician that a patient living in substandard housing may have trouble keeping their insulin refrigerated due to poor wiring and spotty electricity or that a patient living in a food desert might also lack reliable transportation options to get to a grocery store with nutritious food."27

**Disease Management and SDHs**
Appreciation for the importance of SDHs in management of chronic illness will likely extend beyond the provider. "A clinical team attempting to help a person manage diabetes will be substantially hindered if the focus is limited to the presenting vital signs and blood chemistry profiles, when the most basic success factors reside in patient distinctions as to medication cost and access, literacy, family circumstances, mobility, digital accessibility, dietary patterns, employment status, and neighborhood character."25,6

**Physician Understanding of Structural Racism and Discrimination**
Writing by AMWA members can help providers better understand how patients belonging to an underserved population can impact health, and how those differences can limit communication. Do most physicians comprehend the impact of structural racism and discrimination on physical and mental health? "Social stigma and discrimination are a lot more pervasive than is acknowledged. As the system is in a way really stacked against certain groups, this will have a pervasive impact. Racism and discrimination themselves should be seen as social determinants of health. Providers should understand that these are important predictors and risk factors for chronic health conditions. Our society gravitates toward individual experiences and individual explanations and is less sensitive to the accumulating impact of social and structural phenomena. The medical establishment has not really embraced how the experience of racism and discrimination gets into the body," said Jennifer Alvidrez, PhD, Scientific Program Officer, NIMHD (telephone interview, August 2018).
The Provider–Patient Power Differential
Likewise, a well-written article could help to name the unacknowledged differences in authority that can limit joint decision-making in the examination room. “There is going to be a power differential between provider and patient and between researcher and participant. It might be a concern only if effective communication is lacking. At the same time, addressing it and being cognizant of it might enhance communication. For ultimately, we all want providers and researchers to be able to make recommendations we can trust,” said Nathan Stinson, Jr., MD, PhD, Director, Division of Scientific Programs, NIMHD. “We want providers to use their power to benefit us and other people” (telephone interview, August 2018).

Community Engagement
Resistance to change by those most likely to benefit is an impediment that medical writers may be able to diminish. Sometimes false steps may interfere with or discourage the “engagement of communities, especially marginalized communities with low-income populations who have previously been used by academic institutions for research that has not benefitted them or their communities. At times, students and health professionals with extremely limited experience and exposure to community engagement and the social determinants of health may push for interventions in a way that is counterproductive to building community relations. … Proper leadership support and adequate training also are necessary, or the quality of the programs offered may fulfill the requirements but fail to inspire a desire for lifelong learning in how to mitigate the root causes of ill health and disease.”14

Residency in the Community
There are numerous advances in the arena of medical education and training that are impacted by the recently increased appreciation of HDs/SDHs, and these are also areas where medical writers can likely contribute. For example, the Health Resources and Services Administration’s (HRSA’s) Teaching Health Center Graduate Medical Education Program (THCGME) helps improve access to care by providing funding to support new and expanded primary care medical and dental residency programs. Although other residency programs base training out of hospitals, the THCGME program focuses training in community-based primary care settings. Since 2011, the THCGME program has supported the training of over 630 new primary care physicians and dentists that have graduated and entered the workforce, according to Scott Kodish of the Office of Communications of the HRSA (telephone interview, August 2018).

Nurses
In medicine, like often attracts like. Gastroenterologists talk with gastroenterologists, social workers talk with social workers, and the like. Yet population health works optimally when team members with different roles and responsibilities are communicating openly. Medical writers and editors can help open lines of communication by increasing the level of understanding among categories of providers. Nurses frequently provide the indispensable service of bridging the gap between providers and members of the public, and we should encourage this. As “good communication and compassion have been the cornerstone of nursing,” Rothman said, “they play a tremendous role in helping us engage the community.”16

“The earliest planning stages of a clinical trial, it is important to think about the inclusion of disproportionately affected populations.”

Carl V. Hill, PhD, MPH, Director of the National Institute on Aging Office of Special Populations

Informing Both Professionals and the Community about Community Health Workers
Another centerpiece of community health involves community health workers, lay health workers educated and trained at community colleges and vocational training institutes, as well as relevant activities of nonhealth sectors, such as education, the workplace, housing, transportation, urban planning, community development, and public policy.2,14

The Graduate Medical Education System
Medical writers and editors can also address the challenges facing graduate medical education (GME). “A gap between new physicians’ knowledge and skills and the competencies required for current medical practice. …The overarching question in this report is, To what extent is the current GME system producing an appropriately balanced physician workforce ready to provide high-quality, patient-centered, and affordable health care?”28

The Pipelines to the Health Professions
Perhaps most importantly, communicators can make the public aware of the lack of diversity in our physician pipeline and the effects that will have on future health care. Such a wake-up call would lead to a more robust financial and strategic approach. “The clinician workforce is not as diverse as
the patient populations. And the ethnicity of the workforce is an area that needs attention,” Dr Pérez-Stable explained. “It is very important that the pipelines to medical school and other health professional schools are created earlier and enhanced” (telephone interview, August 2018).

For this, “we cannot wait until students are in college. For many students of color, the playing field is unequal and has been unequal all of their lives and all of their parents’ lives,” said Marilyn A. Fraser, MD, Chief Executive Officer, Arthur Ashe Institute for Urban Health (telephone interview, November 2016). A NAM Initiative points to the further importance of retaining minority students in the medical professions, in addition to recruiting and retaining faculty who themselves have experienced being from underserved communities. Much should be written on this subject, and for multiple audiences.

Disparities and Clinical Study Populations
“Starting at the earliest planning stages of a clinical trial, it is important to think about the inclusion of disproportionately affected populations. For example, we know African Americans are at elevated risk of developing Alzheimer’s Disease, so a plan should be in place to enroll and retain this population from early in a study’s development,” said Carl V. Hill, PhD, MPH, Director of the National Institute on Aging Office of Special Populations (telephone interview, August 2018).

Regulatory Guidance for Clinical Trials and Other Categories of Research
The FDA has issued a guidance on its “expectations for and recommendations on use of a standardized approach for collecting and reporting race and ethnicity data in submissions for clinical trials for FDA regulated medical products conducted in the United States and abroad.” Clinical trials of diabetes medication should include Mexican Americans and Puerto Ricans—populations with high rates of diabetes. Prostate cancer trials would be remiss if they fail to enroll African American men, who are twice as likely as White men to be affected by and die from the disease,” explains Dr Pérez-Stable.

NIH Focusing on Underserved Populations
The National Cancer Institute (NCI) and NIMHD are addressing the need for information on diseases prevalent in certain populations, both with ongoing trials and with reanalysis of data from recent trials, explained Jennifer Lowkissas of NCI (telephone interview, August 2018). NCI has established 12 Minority/Underserved Community Sites, which focus on research involving racial/ethnic minorities or rural residents (https://ncorp.cancer.gov/findasite/).

More Diverse Participation in Clinical Trials
This is even more important than research dollars. Writers can make clear the benefit of a more diverse research population. “It is critical that we have more diverse participation in clinical trials. That is the only way we will really know whether or not a particular treatment or medical advice has broad applicability,” explained Nathan Stinson, Jr., MD, PhD, Director, Division of Scientific Programs, NIMHD (telephone interview, August 2018).

Establishing Trust in Minority Communities
“Numerous studies have shown that racial and ethnic groups are as interested as anybody else in participating in clinical trials. The problem is the history of the Tuskegee Experiment and additional events. Minority groups really want to have a full and comprehensive discussion and know if anything might be harmful to them or their family. People want to feel comfortable trusting the researcher or the doctor. This highlights the importance of communication. At the same time, this situation shows that securing a more diverse pool of participants in research studies is not an insurmountable task,” said Nathan Stinson, Jr., MD, PhD, Director, Division of Scientific Programs, NIMHD (telephone interview, August 2018).

Funding HD and SDH Research
Medical writers and editors can help alert researchers regarding the transition of scientific interest and research dollars toward public health. A Position Paper from the American College of Physicians notes that until now, “research funding has been primarily targeted toward specific diseases or risk factors for certain diseases, focusing many available research dollars on a ‘clinical, individual approach to disease.’” As the phrase “until now” implies, it seems likely that in the future a greater proportion of research funding will be directed toward matters central to the health of populations.

How Much Do Disparities Matter to Researchers?
Addressing disparities should be “among the highest of research priorities. This not is not ‘set-aside’ science or a goodwill project,” Carl V. Hill, PhD, MPH, Director of the National Institute on Aging Office of Special Populations (telephone interview, August 2018). Medical writers and editors can help establish climates and terrains that encourage researchers to focus on some of the issues discussed in this article.

Hire Locally
Health care professionals can shape the health outcomes of the communities in which they serve by hiring their staff from the community, procuring goods and services from local vendors, and reinvesting resources locally in a manner that
aligns with their social mission, explained Julie Wood, MD, MPH, AAFP, Senior Vice President, Health of the Public and Interprofessional Activities (personal communication, August 2018).

**In Guidelines, Include Population-Specific Sections**

“We need to work harder to ensure that the evidence base for clinical guidelines and policy recommendations includes clinical trials that involve sizable numbers of populations with the highest disease burden and mortality rates. For example, current guidelines on prostate-specific antigen screening are based primarily on large US and UK trials that enrolled very few African Americans, yet African American men are twice as likely to die from prostate cancer than men in the general US population,” explained Rina Das, PhD, Scientific Program Officer, NIMHD (telephone interview, August 2018). For medical writers and editors, this means making discussions of the fundamental weakness of the US health system so abundant and so clear that experts would consider it irresponsible not to include matters related to HDs and SDHs.

**Screening for SDHs**

In the clinic, the first steps in accounting for SDHs involves identifying where they may be relevant for the patient. “Screening for patients’ health-related social circumstances is fundamentally different from screening for traditional medical problems for which screening tools, diagnostic methods (eg, laboratory testing, imaging), and interventions are accessed within the health services sector. In contrast, screening for social determinants can detect adverse exposures and conditions that typically require resources well beyond the scope of clinical care. Screening for any condition in isolation without the capacity to ensure referral and linkage to appropriate treatment is ineffective and, arguably, unethical,” a recent *Journal of the American Medical Association* article explains. For example, screening might be linked to referral and community-based resources and to the strengths of families and communities. Further, screening should not be limited to patients most obviously in need of assistance, given “societal trends such as the shrinking middle class.”7,31 Writers may be involved in developing screening tools.

**Cultural Competency**

When working with populations unlike our own, it’s important to have basic skills of cultural competency. “We need to ensure that cultural competency is included in health curricula at all stages along the pipeline” for all physicians and all providers, explained Marilyn A. Fraser, MD, Chief Executive Officer, Arthur Ashe Institute for Urban Health (telephone interview, November 2016). Cultural competency extends beyond knowing the language spoken by a population, their health beliefs, and their body language. For example, providers should be aware that the words and body language of people in minority populations may not conform to what is described in textbooks.

**The Language and Body Language of Depression**

Physicians should be aware of the language and body language some minorities may use to signal the presence of depression. “Racial and ethnic minorities are often not being offered help with mental conditions, often because they are less likely to come in with mental health as their main complaint, saying something like, ‘Doctor, I’m feeling depressed.’ If, instead, they say they are feeling tired and not having much energy that should be sufficient for the provider. Actually, this is a quality improvement matter for primary care. Universal screening for depression is important. Further, it is important for disadvantaged populations to have one-stop shopping, particularly if mental health care involves paying out-of-pocket. So this is matter of a quality of care,” said Jennifer Alvidrez, PhD, Scientific Program Officer, NIMHD (telephone interview, August 2018).

**The Changed Relationship Between Medicine and Public Health**

The partial integration of primary care medicine and public health is a major development. Why this is happening might be explained to multiple audiences. Furthermore, certain readers might value knowing that resources on how to structure links between primary care and public health are available from the Duke University Medical Center at the Practical Playbook. Subjects covered include building a partnership, securing funding, and prioritizing and evaluating. In addition,
Advantages of Hospital–Community Partnerships

Hospitals are predicted to one day meet community needs outside of health. “While there is now greater understanding among professionals that the social determinants of health exist, often that does not translate into action. Greater hospital–community partnerships would help. For example, there might be a food bank operating within a hospital setting; and so, if a physician identifies food insecurity, food is immediately available downstairs rather than referring the patient to a food bank where the patient has to take 3 buses to get there,” explained Jennifer Alvidrez, PhD, Scientific Program Officer, NIMHD (telephone interview, August 2018).

Health Centers and 27 Million Americans

Few people are aware that today, the HRSA provides funding to support nearly 1,400 health centers operating more than 11,000 service delivery sites. More than 27 million people—1 in 12 nationwide—in every US state, the District of Columbia, Puerto Rico, the US Virgin Islands, and the Pacific Basin rely on HRSA-funded health centers for care. The health centers provide primary care nationwide for 1 in 9 children 17 years or younger, 1 in 3 people living in poverty, 1 in 5 people living in rural communities, and more than 355,000 veterans (https://bphc.hrsa.gov/about/). The health centers are not run by HRSA. Rather, HRSA-supported health centers are community-based, according to Scott Kodish of the Office of Communications of the HRSA (telephone interview, August 2018). Medical communicators could help the public understand that our government has systems in place to ensure that many Americans have access to health care, no matter where they live or who they are.

Hospitals Focusing on SDHs to Reduce Readmissions

Medicare & Medicaid Services Office of Minority Health has focused on SDHs as a means of reducing hospital readmissions and avoiding associated fees, including ways to connect patients with nonmedical resources.

Continuous Learning From the Processes of Care

Improving investments and support for continuous learning from the processes of care, rather than relying on randomized clinical trials, is an approach the NAM Vital Priorities Initiative is emphasizing. Additional key NAM documents discuss deriving “evidence from each care experience” and making use of “real-world evidence.” This subject is complex, and a great range of professional audiences should be learning about it. We can help.

EHRs

The American College of Physicians “recommends development of best practices for using EHR systems as a tool to improve individual and population health without adding to the administrative burden on physicians.” “Collaboration among physicians, social workers, care coordinators, nurse practitioners, and others could support screening and data collection without adding burden” to physicians. Medical writers and editors can do much to explain to professionals both how and why this would be beneficial, while pointing out potential problems that EHRs may bring.

CONCLUSION

Martin Luther King Jr said, “Injustice anywhere is a threat to justice everywhere. We are caught in an inescapable network of mutuality, tied in a single garment of destiny.”

If equality matters here and now to you and to the people you associate with, then each of us individually and together should be trying to do something positive to remedy the current HDs. We should seek to play a role not only because it is the right thing to do but also because what we do matters. The work we do as medical communicators has weight and merit and bolsters the body of valid medical communications for all stakeholders: individual patients and families, communities, clinical researchers, health care providers, and the health care industry. We medical writers are an integral part of the health system—a system that is undergoing positive change now driven by powerful organizations and forces. We must help that change, change with it ourselves, and tell our audiences about the changes being made to eliminate HDs and the SDHs.

Much remains to be done to bring physicians, allied health personnel, associated public health and social workers, and the public to see what research findings have shown. We medical writers and editors possess skills that enable us to make solid contributions. In a joint statement, the American Hospital Association and the Association of American Medical Colleges has explained that “addressing disparities is no longer just about morality, ethics, and social justice: it is essential for performance excellence and improved community health.”

Acknowledgment

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1. Kirsch B, Ball T. People who cannot afford boots cannot pull themselves up by the bootstraps: an evidence-based exploration of health


From our perspective as medical research scientists who write, we have found the process of writing to be a further means of scientific discovery. We and our fellow scientists generate data using scientific methods in vitro ("within the glass" of test tubes and tissue culture dishes), in vivo ("within the living" animal models), and even in silico ("within the silicon" chips that facilitate computer calculations, modeling, and simulations). These experimental data, frequently supplemented with clinical data from patients and psychosocial data from target populations, are the raw material from which we produce grant proposals, manuscripts, and regulatory and public relations materials. In some instances, the content of our writing has been predetermined by the nature of the document: methods papers and regulatory documents hold few surprises for the scientists who initiate or write them. However, we have found that as we write reviews, original research papers, and grant proposals, our work involves an additional element beyond organizing, formatting, and clarifying content. As we attempt to craft intriguing and compelling stories from the data that we are given, we frequently find ourselves searching beyond the resources that inspired and directed the studies we have been asked to communicate. Similar to solving a jigsaw puzzle, as we assemble pieces (eg, individual concepts based on data, logic, or accepted views), scientific writing sometimes allows us to clarify the specific “shape(s)” of pieces that remain missing from the picture. In this manner (subject to time limitations and access to published and privileged data and databases), our scientific training and natural curiosity compel us to attempt to fill in these missing pieces and to communicate our discoveries with our collaborators in order to assist their efforts. Thus, we have coined the term in scriptio to describe this discovery process that takes place “within the writing.”

Although we believe in scriptio to be a high-yield form of scientific discovery, we are aware of the stark contrast between it and the traditional forms of experimental discovery. On the one hand, technically driven in vitro, in vivo, and in silico forms of discovery lend themselves to mechanization with the potential to improve the quality, quantity, and speed of data production. These technical advances have fueled the current deluge of “-omics” data, much of it yet to be fully processed and integrated into new and/or existing bodies of knowledge (jigsaw puzzles). In contrast, in scriptio discovery goes beyond technical skills and machine intelligence (both of which, in theory, can be programmed) and involves a combination of creative (original) and scientific (rational) thought. Generally, new concepts generated in scriptio are consistent with existing data. However, occasional challenges to reconcile conflicting data involve attempting to define discrepancies in experimental conditions (such as design, technique, and materials) and searching publications and databases for clues that allow us to work toward confirming, enhancing, or modifying current viewpoints and/or introducing entirely new ones.

Science and medical writers with strong science backgrounds are in a strategic position to leverage their expertise to integrate big and small data into the broader context of the existing literature, filling in pieces of the bigger picture and identifying the “shape” of puzzle pieces still missing. By employing in scriptio tools of discovery, writing scientists augment the efforts of their peers and help to expand and expedite the research enterprise as a whole. To date, funding sources have invested heavily in generating massive quantities of big and small data and in training and cross-training a productive scientific workforce. Unfortunately, the volume of discovery has not matched the volume of data, even though large data acquisition continues to be heavily funded. We propose integrating in scriptio discovery personnel as project team members who are proficient in mining databases and the literature and in performing secondary analysis as a means of supplementing traditional and emerging routes of discovery. In scriptio “writing scientists” have the potential to add value to the research enterprise and enhance scientific, medical, and financial gains.

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Put simply, a clinical study protocol must accurately describe the proposed conduct of a clinical trial to generate valuable therapeutic-specific data. The guidance for industry in preparation of the clinical protocol (International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use [ICH] E6; Guideline for Good Clinical Practice) was initially published in 1996 and updated in 2016. Although this guidance document provides a general overview of the expected protocol content, it does not suggest format considerations, nor does it directly map to the anticipated presentation of the data, detailed in the ICH E3 guidance “Structure and Content of Clinical Study Reports.” Thus, ICH E6 and ICH E3 inform a medical writer in how the writing of the conduct and output of clinical trials should be aligned to provide the clearest story of those trials. However, following ICH E6 alone is rarely sufficient to write a clinical protocol.

Factors such as multi-investigator trials, multinational trials, and increased public scrutiny create pressure to produce succinct, unambiguous, high-quality, and readable clinical study protocols. Another consideration of complexity is the level of burden created for the patient participants and the investigators. Yet, authoring of protocols remains a challenge for many trial sponsors. In fact, 66% of all protocols are amended, and 10% of those amendments are reported to be necessary due to human error. The need for template-driven protocol development has been well established and is documented in clinical literature. Advocates for specific diseases/conditions encourage standardized trial design to allow data comparability across trials and to allow earlier, more thorough understanding of safety signals. For example, disease-specific protocol templates have been published for vaccines and for alopecia areata. Although these disease-specific templates have been used to align researchers across organizations, such as the National Institutes of Allergy and Infectious Diseases, Bridge et al suggest that a single template for all clinical trials may not adequately serve the investigator community. Despite this observation, the quest to develop a single standard protocol template continues.

In the past year, the need for alignment of protocol writing was recognized by both a nonprofit and several US governmental entities and funding bodies. The National Institutes of Health (NIH) and the US Food and Drug Administration (FDA) protocol template and e-protocol writing tool, released in 2017, provides NIH-funded researchers with a structured guidance for trial design and protocol development for phase II and III clinical trials and is characterized in detail. With a mission to expand this template with instructional text for other types of studies, the NIH will expand the template to cover phase I trials and behavioral studies in the future. A comparison of this protocol template to ICH E3 and ICH E6 was recently published.

TransCelerate Biopharma and the TransCelerate Common Protocol Template

Formed in 2012, TransCelerate BioPharma is a nonprofit organization with a mission to collaborate across the biopharmaceutical research and development community. The organization issued Release 5 of its common protocol template (CPT) in December 2017 with the stated goals of aligning with the Guideline for Good Clinical Practice, ICH, and European Union requirements and following clinical data standards. The CPT is a Microsoft (MS) Word document template with headings, instructions for authors, and sample text. It specifies 3 components: core backbone headings (level 1 headings that are intended to always be used), libraries (repositories for specific content), and appendices (headings/locations for information that may be deleted if not used). The CPT also provides terminology, formatting, and text conventions. In addition to the MS Word output, it...
includes an e-protocol writing tool that uses a series of questions to guide population of the template. Thus, it can generate an MS Word document or be used to create a technology-enabled deliverable in XML format (in anticipation of FDA electronic submission gateway requirements). The CPT also has an implementation tool kit to use with therapeutic area-specific libraries to foster common wording to facilitate review. This tool kit is consistent with the Clinical Data Interchange Standards Consortium therapeutic area standards.13,14

Comparison of the CPT with ICH E6 and ICH E3 Guidance Documents

The CPT includes detailed instructional text to guide in document completion. Perhaps, because ICH E3 is more detailed, the CPT aligns most closely with the content of this guidance document. ICH E6 in some ways lacks specificity, leaving the interpretation open. In those instances, the CPT has provided its own direction. Table 1 on the next page shows how each heading in the CPT compares with subsections of both the ICH E3 and the ICH E6 guidance documents. Notably, a number of sections within the CPT are not represented in either guideline. Sections such as 5.3.2, 8.3.5, and 8.9 may reflect changes in clinical trial development processes that have occurred since ICH E3 and ICH E6 were written (in the 1990s) or alignment of the CPT to the interests of the TransCelerate BioPharma members.

Sections 1 through 4 of the CPT include the introduction, overall design, objectives, and rationale for the study. These sections are well defined in both the ICH E6 and ICH E3. Section 5 of the CPT describes the study population. Although most of the CPT content for Section 5 maps to both ICH E3 and ICH E6, specific subsections for information on lifestyle considerations were added to encourage the reporting of restrictions to lifestyle or diet recommended during a clinical trial. For example, the CPT includes a statement on exposure to sunlight in the suggested text for interventions with a potential for photosensitivity. Although ICH E3 includes a section on selection and timing of doses for each patient (Section 9.4.5), the CPT includes the delineation of food and drink restrictions and encourages more detail on the timing of meals relative to dosing. In a departure from ICH guidance documents, restrictions on the consumption of water, alcohol, tobacco, caffeine, and xanthine-containing products are also specified. Limitations on physical activity, especially strenuous physical exertion, are a new consideration.

Section 6 (Study Intervention) is largely consistent with ICH E3 and ICH E6. A notable addition to the CPT is an optional subsection on medical devices. In the context of the CPT, this section highlights companion diagnostic tests used for participant stratification or sponsor-provided medical devices used in product dosing and administration. The CPT template notes that the wording in this section can be modified to reflect region-specific definitions of medical devices, as not all countries use the FDA definition of diagnostics as medical devices. Lastly, intervention after the end of study (CPT Section 6.7) is specified in Section 6.4.5 of ICH E6 and is implied, although not specified, in ICH E3.

Although Section 7 of the CPT closely hews to guidance, Section 8 (Study Assessments and Procedures) has several subsections that are specific to the CPT, likely reflecting the development programs of TransCelerate BioPharma members. One section on suicidal ideation and behavioral risk monitoring for the assessment of compounds known to be active in the human central nervous system (CPT Section 8.2.5) is unique to the CPT. In addition, medical device incidents, including malfunctions (Section 8.3.8), are not found in either guidance document. Optional subsections on immunogenicity, ribonucleic acid (RNA) transcriptome research, RNA expression research, proteomics research, and metabolomics research may reflect the advances in clinical analysis of novel treatment modalities that have been developed over the past 2 decades. These precede the ICH E3 and ICH E6 guidance documents.

Some of the CPT appendices represent a departure from ICH E3 and ICH E6. Appendix 4 (Contraceptive Guidance and Collection of Pregnancy Information), Appendix 5 (Genetics), Appendix 6 (Liver Safety: Suggested Actions and Follow-up Assessments and Study Intervention Rechallenge Guidelines), Appendix 7 (Medical Device Incidents: Definition and Procedures for Recording, Evaluating, Follow-up, and Reporting), and Appendix 8 (Country-Specific Requirements) do not directly map to either ICH E3 or ICH E6. However, some of these do correspond to newer guidance documents and/or region-specific position statements. For example, Appendix 6 aligns closely with FDA guidance (Guidance for Industry Drug-Induced Liver Injury: Premarking Clinical Evaluation).15 The inclusion of Appendix 8 is an acknowledgment of the global nature of clinical development. It also helps reduce the “country-specific” amendments that bog down the study and are confounding for the statistical analysis and when developing the clinical study report. Instead, you can maintain 1 global protocol with subsections in Appendix 8 for each country that requires special procedures.

Considerations for the Application of the CPT

The CPT is intended for all phases of drug development. The core backbone of the CPT establishes a common heading structure and recommends content applicable to all protocols. Many redefined headings in the template map to ICH E6, ICH E3, and more recent guidance documents. Several new headings encourage the inclusion of more detailed and updated information in the protocol. When needed, subheadings...
### Table 1. Comparison of CPT Sections with ICH E3 and ICH E6 Headings

<table>
<thead>
<tr>
<th>Section of CPT</th>
<th>Corresponding Heading from ICH E6</th>
<th>Corresponding Heading from ICH E3</th>
</tr>
</thead>
<tbody>
<tr>
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<td>Heading 6.2</td>
<td>Section 1: Title Page and Section 2: Introduction</td>
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<td>Section 8: Study Objectives³</td>
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<td>Overall Design</td>
<td>Heading 6.4</td>
<td>Section 8.1: Overall Study Design and Plan-Description</td>
</tr>
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<td>Section 1: Title Page</td>
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<tr>
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<td>Section 8.1: Overall Study Design and Plan-Description and Annex 1 (Planned and Analyzed)</td>
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<td>Section 7: Introduction</td>
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<td>Section 7: Introduction</td>
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<td>2.3. Benefit/Risk Assessment</td>
<td>Heading 6.2.3</td>
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<td>3. Objectives and Endpoints</td>
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<td>4.4. End of Study Definition</td>
<td>Headings 6.4.5 and 6.9.4</td>
<td>Section 9.4.1: Treatments Administered and Section 9.5.1: Efficacy and Safety Measurements Assessed and Flow Chart³</td>
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<td>restrictions may be needed. no water is</td>
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<td>allowed until 2 hours after dosing, after</td>
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<td>which time, water is allowed ad libitum.</td>
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<td>6. Study Intervention</td>
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<td>Headings 6.4.4 and 6.6.1</td>
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<tr>
<td>6.2. Preparation/Handling/ Storage/Accountability</td>
<td>Heading 6.4.4</td>
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<td>Section 9.4.3: Methods of Assigning Patients to Treatment Groups and Section 9.4.6: Blinding</td>
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<td>Section 9.4.8: Treatment Compliance</td>
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<td>Heading 6.6.2</td>
<td>Section 9.4.7: Prior and Concomitant Therapy</td>
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AE, adverse event; CPT, Common Protocol Template; CSR, clinical study report; ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals in Human Use; N/A, not applicable; RNA, ribonucleic acid; SAE, serious adverse event.

*The term “Endpoints” is not included as a heading in ICH E3.

*Although "End of Study" is not clearly defined in ICH E3, the timing of End of Study (withdrawal of study drug and completion of End of Study visit) is addressed in Sections 9.4.1 and 9.5.1.

*Information guiding the definition of screen failures resides in Sections 9.3.1 and 9.3.2 of ICH E3, but the rationale behind why screen failures were identified is included in Section 10.1.

*Describes the use of tests such as electrocardiogram to define efficacy.

*Describes the use of tests such as electrocardiogram to define safety.
may be added. One of the benefits of the CPT is the detailed instructional text, which attempts to reduce misinterpretation by the study sites and global regulatory authorities while enabling downstream automation. In addition, TransCelerate has stated in Release 5 that the CPT is intended to support the requirement for disclosure data upload commitments to clinical trial registries.

**Limitations of the CPT**

Although the CPT invites inclusion of more detailed information within clinical trial protocols, some “core backbone” sections do not fit the needs of all users. Like the ICH E6 guidance, the CPT is aligned with pharmaceutical development. The utility of the CPT for medical devices is likely limited and would result in much of the core backbone being noted as “not applicable.” Conversely, the subheading for medical devices (CPT Section 6.1.1) would need to be deleted for therapeutic interventions that do not require a medical device. Sections on contraception and genetics may not be applicable to all trials.

The CPT was developed by a consortium of global pharmaceutical companies to suit their needs and may not be broadly applicable to smaller companies, more novel modalities such as gene therapy and RNA modulation, or medical device firms. It also does not contain language specific to pediatric or geriatric studies. Food effect studies are well supported by the CPT but are not universally required, particularly for therapies that use a nonoral route of administration. In addition, although it aims to ease interpretation by study sites and global regulatory authorities, and enables downstream automation, its terminology and adoption have not yet been broadly established.

**Discussion**

For the most part, the body of the CPT fits well within the framework created by ICH E3 and ICH E6. The CPT’s most notable exceptions are found within the appendices, most likely to make it more accessible across the life science industry, to address emerging therapeutics, to recognize newer guidance documents,16,19-21 and to create thought leadership in an evolving landscape. For example, international regulatory authorities may not agree on standards for birth control; thus, there are no specific, harmonized, international regulatory guidelines on birth control requirements and pregnancy prevention within clinical trials. The CPT’s inclusion of Appendix 4 may be how the industry acknowledges the need to clarify the contribution and complexity of these data considerations. Notably, contraceptive use is outlined in the US-specific 1993 document 58FR39406: “Guideline for the Study and Evaluation of Gender Differences in the Clinical Evaluation of Drugs.”17 Similarly, a recent publication by the Health and Environmental Sciences Institute’s Developmental and Reproductive Toxicology Technical Committee displayed results of a pharmaceutical industry survey on current industry practices for contraception use during clinical trials. This survey attempted to compile and promote consistency and/or compliance with contraception requirements and detailed the effectiveness of current contraception practices in preventing pregnancies during clinical trials.18

Perhaps more so than any other aspect of the CPT, Appendix 5 (Genetics) speaks to the emerging technologies of biopharmaceutical development and the more recent guidance documents on pharmacogenomics, genomic biomarkers and genomic sampling, and data management.19-21 These guidance documents reflect trends that encourage genetic profiling within clinical trials22,23 and provide direction on how to manage and report these data.

**Conclusions**

The CPT includes a common structure, common text, and regulation-oriented definitions to be used across a clinical development program while leaving usage to the discretion of the user. This approach supports the use of Clinical Data Interchange Standards Consortium therapeutic area standards for unifying data representation and statistical endpoints for specific diseases. The section headings highlight a paradigm shift in pharmaceutical development toward precision medicine. As the CPT is implemented by the TransCelerate member companies, it may establish a new standard in protocol development and become familiar to all members of the pharmaceutical industry and global health authorities, ultimately helping speed new therapeutics to the patients who need them. Certainly, the standardization of protocol development procedures will facilitate collaboration, encourage information sharing and disclosure, and, hopefully, increase efficiency in clinical development.

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**References**


A pronoun is a word that stands in for a noun or noun phrase. Pronouns have no meaning of their own. Instead, they take their meaning from context. In the movie *Tarzan of the Apes*, Tarzan had difficulty in understanding this concept. When Jane pointed to herself and said “me,” Tarzan assumed that Jane’s name was “Me.” Tarzan was baffled by the concept that when someone says “I” or “me,” that person is referring to him- or herself. In other words, the words *I* and *me* always denote the speaker or writer. Thus, the person whom the words *I* and *me* denote depends on who is speaking or writing.

In linguistics, words that have a fixed semantic meaning (dictionary definition) but whose denotational meaning varies according to extralinguistic context (such as time, place, or person) are called “deictic” (Figure 1). Pronouns and possessive adjectives (such as *my* or *their*) are deictic. So are words such as *this* and *that*, *soon* and *recently*, and *here* and *there*. The function or use of deictic words, forms, or expressions is called “deixis.” Most deictic words are simple, common English words whose semantic meaning (ie, their dictionary definition) is clear. Yet if you use them carelessly, your reader may not know what person, thing, time, or place that you wanted those words to denote.

**Types of Deixis**

**Person Deixis**

**First Person.** Person deixis deals with the grammatical person. The first-person singular pronouns *I* and *me* always denote the speaker or writer. However, the meaning of the first-person plural pronouns can be unclear. Unless you are a monarch using the royal “we” to refer to yourself, or an editor using the editorial “we,” the first-person plural pronouns refer to a set that includes more than 1 person. When you use the words *we*, *us*, or *our*, you need to clarify who belongs to that set and who does not. Careful writers clarify the denotation of *we* and *us* by stating exactly who they mean.

- As medical writers, we play an important role in medical research.
- We medical writers play an important role in medical research.

**Second Person.** Second-person pronouns refer to the intended listener (of speech) or to the reader (of text). Note that whenever you issue a command or request, the implied subject of that sentence is in the second person.

- (You) please pass the salt.

In modern English, we use the same second-person pronoun *(you)* for both singular and plural. Thus, you would use the same second-person pronoun if you are addressing one person or more than one person. However, English speakers also use you to refer to an unspecified person. This usage is called the “indefinite you,” the “generic you,” or the “impersonal you.” Good writers often use the “indefinite you” because it helps them engage their readers personally. However, the “indefinite you” is sometimes regarded as inappropriately informal, and it can sometimes come across as bossy or preachy.
There are 3 alternatives to using the “indefinite you”:

😊 One can use the indefinite pronoun one, which often sounds stuffy.

😊 The writer can use the third person, which often sounds impersonal.

😊 The passive voice can be used, which may sound even more impersonal.

Even in informal writing, the “indefinite you” can pose problems. For example, if you are addressing an audience of people with diabetes, your audience will probably include a lot of people with type 2 diabetes, some pregnant women with gestational diabetes, a few people with type 1 diabetes, and perhaps someone with one of the rare genetic forms of diabetes, such as maturity-onset diabetes of the young (MODY)—as well as many healthy parents and spouses of someone with diabetes. In that situation, the things you write about “you” or “your pancreas” may not apply to all of your readers. To clarify the scope of the statements you are making, you may need to use adjectival and adverbial hedges (words or phrases that limit meaning) or use the third person:

😊 If you have type 1 diabetes, your pancreas is not making enough insulin to keep you alive.

😊 For people with type 1 diabetes, insulin therapy is essential.

Third Person. The third-person personal pronouns include he/him, she/her, it, and they/them/their. There are also possessive adjectives that express the third person (his, hers, its, and their). As with the first-person plural pronouns, a careful writer must ensure that the reader can tell what these words are intended to denote. Before I edit a piece of text, I run a macro that highlights all of the pronouns and possessive adjectives. I remove the highlighting from a word only after I am satisfied that its denotation is clear. Often, I find that I must replace the pronoun with its noun referent for clarity.

😊 He said that he didn’t understand what he was talking about.

😊 Sam said that Patrick did not understand what Clem was talking about.

They and them are plural pronouns. Unlike the singular pronouns (he, she, and it), they and them are not marked for gender (masculine, feminine, or neuter). For centuries, good writers of English have been using they/them as a pronoun of indefinite number (singular or plural) and sometimes as a singular pronoun of indefinite gender. Saying “they” is far more convenient than continually saying “he or she.” Lately, some people have been using the words they/them to refer to a definitely identified individual who objects to the use of a gender-specific pronoun because that individual does not self-identify as male or female. English does have a neuter singular pronoun (it), which has traditionally been used to refer only to things, animals, and occasionally infants. Thus, referring to a person as “it” would be dehumanizing or at least infantilizing. Unfortunately, the use of the plural form of the verb with they is confusing. I suggest that if you do insist on referring to a particular person as they instead of as he or as she, you should use the singular form of the verb (they is, they does, they has). Otherwise, your audience would have no way of knowing that you are talking about only one particular identified person.

Time Deixis
Time deixis or temporal deixis is a reference to time relative to some timepoint, which is typically the moment of utterance. For example, the denotations of the words yesterday, today, and tomorrow depend on the date of utterance. The same goes for phrases such as this week, last year, or next Monday. Other words that refer to relative time include now, then, ago, later, soon, before, and after. The goal should be to ensure that the time referent is correct and clear.

Be particularly cautious about the word recently, especially if you are editing a textbook that will go through later editions. In the first edition, the word recently could have meant the year before the word was written. By the time the book goes into the fifth edition, the timepoint described as “recently” could be 20 years in the past, which is ancient history in some fields.

Place Deixis
Place deixis or spatial deixis deals with the relative location of persons and things being discussed. The words here and this refer to things that are near the speaker or writer, whereas there and that refer to things that are distant. Words and phrases such as left, right, up, down, above, below, in front of, and behind are deictic. So are verbs such as go, come, and bring.

Discourse Deixis
Discourse deixis is deictic reference to a portion of a discourse relative to the speaker’s or writer’s current location within the discourse. In text, the words above, below, last, previous, proceeding, next, or following are often used to express discourse deixis. In speech, the words this, that, there, next, and last are often used to express discourse deixis.

Writing Versus Speech
Tarzan had no idea what “me” meant, even though Jane was pointing at herself when she said it. When we write, many of the other clues about the denotation of a word like “me” or “there” or “recently” may be lost. For this reason, writers and editors must be sure that the meaning of person, place, and time referents would be obvious to the reader.

Writers, educators, scientists, and journal editors have been lamenting poor writing in the scientific literature for more than a century.\textsuperscript{1,2} A recent analysis of scientific abstracts published between 1881 and 2015 has justified those laments by showing that scientific texts have become harder to read over time.\textsuperscript{3} The authors found that the scientific literature has developed a “general scientific jargon”—distinct from “subject-specific words” (eg, “tumor”) that increase in number and frequency as science advances—that is accessible only to an “in-group.” Using this “science-ese,” as the authors call it, is one of many bad habits that contribute to poor writing. These bad habits, which extend beyond language and style to include practicalities like time management, are transmitted from older to younger generations of scientists (eg, a senior scientist who throws together grant proposals at the last minute sets that example for mentees). The transmission of bad writing habits through generations of scientists may explain the continuous decline in the readability of scientific writing.\textsuperscript{1}

In academia, the specialized language that defines an in-group and the bad habits passed down from senior to junior scientists form a culture of poor writing within a department or institution. Department leaders, senior investigators, and mentors shape this culture by the extent to which they invest in and advocate for good scientific writing.

As scientific editors at an academic research institution, we are uniquely positioned to address poor scientific writing as a problem of departmental or institutional culture. We work with faculty on a continuous basis, editing their manuscripts and grant proposals, so we can change their writing habits over time. Also, we have developed educational programs, including workshops and seminars, to provide direct instruction to a wider departmental audience. By employing a variety of strategies that incorporate writing education into the everyday life of the department through continuous interaction with faculty and trainees, we seek to gradually change our department’s writing culture from within.

### Three Strategies for Educational Programs Aimed at Improving Academic Writing

We firmly believe that writing can only be improved by forming good habits and practicing continuously. Accordingly, we interact with faculty and trainees as frequently and in as many contexts as possible. Because we work with writers with different levels of experience, different needs, and different language backgrounds, and because we receive documents at various stages in the writing process, we use a variety of educational strategies to address the specific needs of each writer and each document.

Our primary strategy to improve academic writing is **didactic editing**, which uses the editor’s query to educate writers.\textsuperscript{4,5} Didactic editors query not only to request clarification, but to explain editorial changes pertaining to grammar, style, structure, and data presentation, and to show how these specific interventions enhance overall clarity and cohesion. Editors can also link to resources, such as the...
AMA Manual of Style, that explain the rules, standards, conventions, or best practices that underlie these editorial changes. Through didactic editing, we can precisely target a specific issue in the writer’s work and address it in context and at a level appropriate to the writer’s position and experience, whether she is a postdoctoral fellow or an associate professor. Didactic editing is also cost-effective, as editors can practice it without developing additional programs. This may be particularly important for editors whose departments don’t support scientific writing education.

Also, we have developed workshops and seminars that provide broader instruction on common document types, such as grant proposals, scientific manuscripts, abstracts, and posters. These multisession series combine didactic content delivery in an interactive lecture-discussion format with hands-on writing exercises (in seminars) or guided revision of participants’ research documents (in workshops). The hands-on components of these sessions are at least as important as the didactic content, because improving writing requires forming habits and practicing continuously more than mastering the content.

Finally, we provide one-on-one coaching to supplement the other strategies. Faculty or trainees meet with us individually to discuss our editorial suggestions for their documents or the lecture content of a recent workshop or seminar. Some investigators ask for our help with research development and strategic planning for grant proposals, including identifying appropriate funding sources, writing or soliciting institutional letters of support, and establishing timelines and checklists to ensure that all grant components are completed on time. Faculty and trainees benefit from personalized attention to specific needs, and we as editors benefit from establishing good working relationships with them, as they are then more likely to attend a workshop, send us documents for editing, or recommend us to others.

Combine and Choose the Right Strategy for Your Audience

We developed a Grantsmanship Education Program for junior and intermediate faculty that coordinates the 3 strategies described above to instill new habits and change the way the faculty develop and write grant proposals (Figure 1):

- **Workshops on writing grants**: Interactive lectures provide information on specific grant components and best practices for writing (eg, active voices, parallel structure). Each session also includes time for participants to work on their own writing samples, which they prepare in advance. After each session, participants email us their samples for feedback.
- **Didactic editing**: Throughout and after the workshop series, we provide continuous editing support and practice didactic editing to improve grant proposals, reinforce lecture content, and instill good writing habits for future proposals.
- **One-on-one coaching**: After the workshop series ends, we meet with each participant to gauge their progress, offer suggestions for revision, help them plan the next steps, and solicit feedback to improve the next iteration of the series.

Both didactic editing and one-on-one coaching help investigators improve their writing, regardless of seniority or language background. In our experience, didactic editing works especially well with investigators who send their manuscripts for multiple rounds of editing and engage in active discussion through comments. We recommend in-person meetings for new investigators or those whose documents need substantive editing. As an example, we encourage junior faculty who are new to grant writing to develop a personalized editing plan, to include both one-on-one coaching and several rounds of didactic editing.

![Figure 1. Grantsmanship Education Program for junior and intermediate faculty.](image-url)
We have designed educational programs that address different needs for different academic levels (eg, faculty, trainees) by talking with mentors, division chiefs, and directors of residency programs. Because the workshop component distinguishes our grantsmanship series from other communication seminars, faculty members with working drafts and concrete plans to submit a grant proposal benefit most from participating. Those with no working drafts may learn useful information from the lecture component of the series but will find more value in our interactive lecture-based seminars, where no working documents are needed. Our seminars on “Manuscripts” and “Abstracts and Posters” are attended primarily by residents, postdoctoral fellows, and instructors, but they would also be suitable as refreshers for midcareer and senior faculty.

Achieve Better Teaching and Learning
Because clear and concise writing takes continuous practice and commitment, we strive to improve effectiveness and overcome difficulties in all 3 teaching strategies to ensure that all faculty and trainees can benefit.

Didactic Editing
The success of didactic editing through tracked changes and queries depends on how much authors pay attention and how willing they are to accept the editor’s suggestions. Because investigators’ commitment to reading queries and checking edits carefully varies considerably, we encourage forming and maintaining a relationship of trust with them as a first step. We often recommend multiple rounds of editing, both to ensure the document’s quality and to create an ongoing conversation with the investigators, which will encourage them to read comments more intently and remember the suggested changes. Although it is not the editor’s job to praise an investigator’s work in a manuscript or grant, paying occasional compliments for well-written paragraphs and sentences can boost the author’s confidence and provide a welcome break from the tracked changes. Queries should be simple, to the point, and written in a friendly, conversational, noncommanding tone.

Workshops and Seminars
In addition to excellent content, useful exercises, and effective organization, teaching successful writing workshops and seminars depends largely on the support of mentors and department leaders to promote active participation by faculty and trainees. For our Grantsmanship Education Program, the division chiefs nominate or approve faculty to attend the series. Besides teaching workshops and seminars, editors should continuously encourage mentors to advocate for good writing and to model good habits.

We constantly work on overcoming practical difficulties in facilitating workshops and seminars:
• We address scheduling issues by sending surveys to faculty members to solicit preferred days of the week and time slots. Also, we ask mentors for help in securing junior investigators’ time to attend the sessions, especially for those with clinic duties.
• We promote attendance by sending reminders and calendar invitations, and we also offer incentives, such as refreshments.
• We collect grant and manuscript examples to present in workshops and seminars by asking senior faculty to share their work, especially funded proposals. This further highlights the importance of partnering with department leaders and senior investigators.

One-on-One Coaching
Investigators have not pursued this strategy as actively as we had hoped. One possible explanation is that many investigators who seek our help are nonnative speakers of English, and the language barrier can interfere with productive face-to-face discussion. Despite this difficulty, we still encourage these investigators to meet with us in person. A feasible alternative to overcome the language barrier could be to establish a correspondence over email or through queries within documents, which can help improve their writing skills. Another explanation is that some investigators find it difficult to set time aside during busy clinic times. Although incorporating one-on-one coaching into our Grantsmanship Education Program has helped, setting up in-person meetings still requires time and patience, particularly with investigators who may not respond to us. Approaches to address this problem include soliciting one-on-one sessions more proactively and seeking the help of mentors.

Evaluating Progress
Assessing our strategies’ success is somewhat difficult. Our investigators attend workshops or seminars and request editing or coaching on a voluntary basis, so we may interact with individual authors only once. Thus, we still need to develop ways to measure the improvement of writers who work with us infrequently. Also, collecting data across the department is difficult because not all investigators use our services. At the program level, however, we currently track faculty and trainee participation in our editing services by recording the documents we receive for editing each week, and we assess participant satisfaction in workshops and seminars by distributing surveys to identify the strengths and weaknesses of our programs so we can improve them on a regular basis. So far, we have received consistent positive feedback from satisfaction surveys.
surveys, and requests for our editing services have increased steadily over the 3 years that we have provided writing education programs. These observations suggest that we have made progress in incorporating writing education into the life and culture of the department.

Conclusion
The main goal of our educational programs is to teach academic writers how to communicate ideas clearly, concisely, and cohesively in research documents. This relies on the writers’ awareness of and commitment to forming good writing habits, which can go much beyond mastering proper grammar, style, and spelling. For this reason, both faculty and trainees from our and other departments will benefit from the education strategies we described, which aim to instill good writing habits on a continuous basis to help change departmental writing cultures over time.

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“This kind of research experience should be a requisite part of the career of any science journalist.”
The Advent of Preprint Servers for Scientific Publications

The idea of a written information exchange (preprint server) to augment yearly conferences among scientists is not new. Trials of such information exchange occurred in the early 1960s. One trial was supported by the National Institutes of Health (NIH) and established Information Exchange Groups (IEGs), the members of which periodically received hard copies of research “memos” via US mail. These summaries of current data were circulated among members of the IEGs for review and comment before publication.1

By the early 1990s, technology finally caught up to the need for scientific communication more than annual conferences. Theoretical high-energy physicists were the first to adapt; the first preprint server was developed at Los Alamos National Laboratory. This server (arXiv.org) has grown since its inception and now archives more than 1.4 million preprints in the fields of physics, mathematics, computer science, quantitative biology, quantitative finance, statistics, electrical engineering and systems science, and economics. It is supported by Cornell University.2

However, information exchange within the biological sciences had been hampered by fears—fear of journals losing paid circulation, fear of copyright infringement, fear of unrefereed papers getting into general circulation.1 A second attempt to establish a preprint server was made when Harold Varmus was head of the NIH; however, this time it was doomed to failure because of the Federation of American Societies of Experimental Biology, which threatened to lobby Congress to affect the NIH budget should the proposal come to fruition.3

In 2013, Drs John Inglis and Richard Server founded bioRxiv.org. This third attempt to establish a biological preprint server appears to have been better received than the 2 previous attempts, which may be due to the advent of open-access journals, the established history of the arXiv model, and continued delays in the time from acceptance to publication in print journals.3

Cold Spring Harbor Laboratory and the Chan Zuckerberg Initiative are supporting the current preprint server, which accepts manuscripts from scientists in 26 different biological fields.4 In the beginning, the most popular fields to use bioRxiv were evolutionary biology and bioinformatics, but as of June 2018, the submissions from neuroscience have surpassed both of those (J. R. Inglis, PhD, written communication, June 2018).

As of the end of September, 193,000 authors from 12,000 institutions in more than 100 countries have contributed to nearly 33,500 manuscripts posted on the bioRxiv server. According to Dr Inglis, submissions have been increasing each month; more than 1,900 new papers are being submitted each month with 3.5 million page views and 750,000 downloads of PDFs (J. R. Inglis, PhD, written communication, June 2018 and October 2018).

Several factors are contributing to the increase in usage of bioRxiv, including a willingness of most biology research journals to consider manuscripts that have been posted to preprint servers, recommendations from the server users to other scientists, readers discovering the quality of work, and scientists from the most prolific research institutions posting

Scientific Publications Ethics Meet Main Street, USA

The New York Times in collaboration with ProPublica reported on September 8 that Dr Jose Baselga, chief medical officer at Memorial Sloan Kettering Cancer Center, failed to properly disclose his industry affiliations and payments in peer-reviewed publications in journals including The Lancet and The New England Journal of Medicine.1 According to this investigative report, Baselga received nearly $3.5 million from 9 companies between 2013 and 2017 as reported by the Open Payments federal database; however, no industry relationship was disclosed for more than 100 of his publications during this same period.2 On September 13, the New York Times and ProPublica reported that Dr Baselga had resigned from Memorial Sloan Kettering Cancer Center and is working to update his conflict of interest forms for those publications that are lacking the proper disclosure.2

For information on recommendations for best practices and ethical standards for publishing research and other material within medical journals, visit The International Committee of Medical Journal Editors (ICJME) website (icjme.org).

References
Loneliness and the Long-Distance Worker: Is Social Media the Remedy?

Megan Garlapow, PhD / Freelance Medical Writer, Phoenix, AZ

Where people work has rapidly changed, with increasing numbers of workers doing business from home offices and coffee shops at least some of the time. Although remote work can be a boon for workers requiring flexibility and can increase productivity, loneliness and isolation pose difficult obstacles to working from home. Engagement via various social media platforms can offer an important route through such obstacles.

At a recent springtime gathering of medical writers, editors, and communicators in Phoenix, Arizona, the conversation quickly turned from one of admiration for the gorgeous sunset over Camelback Mountain to the various approaches people take to battle the loneliness that accompanies working remotely. This gathering comprised both freelancers and employees, yet the majority of attendees work remotely, as this work setting is no longer the exclusive domain of the “solo-preneur.”

With good reason, remote work is becoming more common. Mounting research indicates improved productivity for remote workers, due at least in part to the removal of distractions workers face in offices. According to one study, from 2008 to 2014, the percentage of office-based workers who reported being unable to concentrate at their desks increased by 16%. In another study in China, the productivity of remote workers increased 13% compared with office workers, and attrition rates decreased.

At the conclusion of the Chinese study, remote workers were allowed to return onsite to the office, and over half of the remote workers chose to return to the office at least part of the time. Apparently, relinquishing productivity, calm, and quiet was a worthwhile trade-off to avoid the isolation that can plague remote work. This sense of isolation is not culturally limited either: A Buffer Open 2018 survey of remote workers showed loneliness tied for the top spot for the biggest struggle with working remotely.

But what is the freelance or employed worker to do when onsite office work is not an option? How do you stay connected when your only officemates are empty coffee mugs and stacks of books? As a testament to this struggle, a Google search of “loneliness remote work” yields millions of results, from advice columns to interactive forums.

Because how often we connect with other people correlates with our levels of happiness, one solution is to actively seek out a community using the technological tools that allow work to be done remotely in the first place. Social media can offer essential human connection and enable us to establish a global network of colleagues in our industry with whom we can discuss trends and concerns. Twitter, LinkedIn, and Facebook can provide forums in which to share ideas, showcase work, ask for advice, offer advice, and meet new colleagues and friends (Table 1). Workplace tools such as Slack and WhatsApp are communication platforms through which remote workers can upload and share files, exchange one-on-one direct messages, or have group conversations in topic-specific chatrooms. Collaborative tools such as IDonethis and Microsoft Teams can provide project and work management capabilities while integrating interactions across contributors.

How a remote worker uses social platforms matters, too. Because close relationships and connections are critical for happiness, mere browsing is unlikely to result in a sense of connection. Thoughtful interactions and conversations can foster a sense of purpose and belonging that could otherwise be missing. In the AMWA community, Engage provides a forum for members to connect, chat, and collaborate. Through these
### Table 1. Social Media Platforms, Apps, and Collaboration Tools

<table>
<thead>
<tr>
<th>Name</th>
<th>URL</th>
<th>Description</th>
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<tbody>
<tr>
<td>LinkedIn</td>
<td><a href="https://www.linkedin.com">https://www.linkedin.com</a></td>
<td>Linkedin is a social network specifically designed for the business community. This is an ideal platform to build professional connections, to find potential collaborators, or simply to keep job prospects open. In addition, industry news is shared between users.</td>
</tr>
<tr>
<td>Twitter</td>
<td><a href="https://twitter.com">https://twitter.com</a></td>
<td>Twitter is a social network that relies on microblogging for communication. Users communicate with their followers through short messages. This is an ideal platform to share/find real-time industry news. Moreover, users with shared interests can stay connected through a unique hashtag, aka “twitter chats.”</td>
</tr>
<tr>
<td>Facebook</td>
<td><a href="https://www.facebook.com">https://www.facebook.com</a></td>
<td>Facebook is a social network designed for personal and business use. This is an ideal business platform for market research, brand awareness, relationship building, and customer service. Users can create a business profile to promote their brand, share announcements, and engage in online networking through updates, videos, and photos.</td>
</tr>
<tr>
<td>Slack</td>
<td><a href="https://slack.com">https://slack.com</a></td>
<td>Slack is a cloud-based team collaboration tool. Users can create organized conversations (channels) and bring relevant information to each of these channels. Integrated file-sharing allows users to share PDFs, images, and other files. A real-time messaging feature allows users to stay connected throughout the workday.</td>
</tr>
<tr>
<td>Telegram</td>
<td><a href="https://telegram.org">https://telegram.org</a></td>
<td>Telegram is a free messaging app that allows users to sync messages, photos, videos, and files over all devices at the same time. Users are also able to make outgoing calls via the Internet. This is an ideal app for business users looking for fast, secure, file-sharing options.</td>
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<tr>
<td>WhatsApp</td>
<td><a href="https://www.whatsapp.com">https://www.whatsapp.com</a></td>
<td>WhatsApp is a free messaging app owned by Facebook that allows users to share photos, videos, and files. Users are also able to make outgoing calls via the Internet. This is an ideal app for business users looking for fast, secure, file-sharing options. Features include the ability to create a business profile.</td>
</tr>
<tr>
<td>I Done This</td>
<td><a href="https://idonethis.com">https://idonethis.com</a></td>
<td>I Donen This is a productivity app based on the Web and through email that automatically turns logged activity into reports. It allows users to track team tasks—akin to a shared work diary—and is an ideal tool for project management.</td>
</tr>
<tr>
<td>Pivotal Tracker</td>
<td><a href="https://www.pivotaltracker.com">https://www.pivotaltracker.com</a></td>
<td>Pivotal Tracker is a Web-based project management tool for real-time collaboration built around a shared “to-do list.” It is ideal for business users requiring cross-project tracking that can be viewed on a customizable dashboard, and is ideal for both small- and large-scale projects.</td>
</tr>
<tr>
<td>Workfront</td>
<td><a href="https://www.workfront.com">https://www.workfront.com</a></td>
<td>Workfront is a Web-based project management tool that allows users to understand their task, track progress, and measure productivity. It is ideal for medium to large businesses requiring document management, workflows, and project visibility.</td>
</tr>
<tr>
<td>Engage</td>
<td><a href="http://engage.amwa.org/home">http://engage.amwa.org/home</a></td>
<td>Engage is the AMWA online community for medical communicators. This is an ideal platform for medical communicators to network, collaborate, and share industry news and work experiences.</td>
</tr>
<tr>
<td>Microsoft Teams</td>
<td><a href="https://products.office.com/en-us/microsoft-teams/group-chat-software">https://products.office.com/en-us/microsoft-teams/group-chat-software</a></td>
<td>Microsoft Teams is a platform that combines group chat, notes, meetings, and attachments, integrating with the Office 365 suite. Members of a “team” join through a specified URL or invitation by the team administrator. It is ideal for business users requiring real-time collaboration with team members or looking to provide professional learning communities for staff/colleagues.</td>
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services and other approaches, perhaps it is more feasible now than ever to work remotely without loneliness.

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References

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manuscripts to the server (J. R. Inglis, PhD, written communication, June 2018). Dr Inglis also attributes the increase in usage to “a general increase in the use of Twitter by scientists…from the beginning bioRxiv has been prominent on Twitter: there are currently 10,000 @biorxivpreprint tweets a month.”

Although clinical trials with a registered trial identification number can be archived on the bioRxiv server,² medRxiv is being developing by Dr Inglis in collaboration with the Yale University Open Data Access (YODA) Project and other partners.³ Begun with a commitment to open science and data transparency, the YODA Project has the mission of increasing access to clinical research data and generating new knowledge.⁴ Dr Inglis notes that “the founders are fully aware of the concerns around the availability of medically relevant information that hasn’t been peer reviewed and are taking steps to mitigate the risks. The site and manuscripts on it will be clearly labeled as containing information that hasn’t been peer reviewed and shouldn’t be used alone to guide clinical practice. And the criteria for submission and acceptance of manuscripts on medRxiv will be different, requiring, for example, information about funding, competing interests, trial registration, and data sharing; reporting checklists relevant to the field of study; and information about institutional review board review and patient consent given where applicable.”

Dr Inglis also notes one of the rationales for developing medRxiv is the hope for making more clinical trial data available, including trials with conclusions that generally are not published by journals. The medRxiv.org website is due to launch in winter of 2018.

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“AMWA’s Engage is the only social media platform that I use regularly. I receive a daily email for the Engage communities that I subscribe to. I usually read these on my iPAD as I’m waking up each morning. It’s great to be connected with other medical writers who generously share their expertise and are as excited as I am about scientific writing and editing and the business side of freelancing. I do not participate in discussions as often as I would like, but I am always reading along in the wings.”

Theresa Singleton, PhD
Owner/Principal Scientific Writer
Singleton Science, LLC (www.singletonsience.com)

“LinkedIn is the primary social media platform that I use to stay connected on a business level. I typically publish professionally minded posts on various topics (freelancing, entrepreneurship, personal development) at least once a week on LinkedIn to foster discussion. I also regularly connect with other medical writers to build my network and stay connected with medical writers that are not in my geographical area. I also enjoy reading through and contributing to the AMWA Engage forums. The forums provide a great way for AMWA members to ask questions, provide advice, and occasionally vent frustrations.”

JoAnna Pendergrass, DVM
Founder, JPen Communications, LLC (http://www.jpenmc.com/)

“AMWA Engage gives me a daily connection to colleagues in my field. It is an outstanding forum for members to ask questions and exchange insights and ideas.”

Jennifer Nepo, MS
Principal, Medparency LLC (https://www.linkedin.com/in/jennifernepo)
My medical writing department is undergoing a change, and I need to transition from full-time employee to freelance; what are my first steps?

The first step is to ask/answer the following question: “Do I truly wish to be self-employed? Why?” Be sure to identify and list your expectations and think about such a step—and it is a big step: it’s not just going out and writing an article here and there from a home office while you wait to find another job! I recommend, if possible, that you spend 6 months carefully planning your business strategy. Preferably you can do this while still employed full time. During the planning stage, I suggest taking a free SCORE workshop on starting a small business. Sponsored by the Small Business Administration, these workshops are available free online (as webinars) or in classrooms in various cities throughout the United States. I have taken a few different SCORE workshops and found them to be excellent and truly helpful. SCORE teachers consider it essential to write a formal Business Plan, and they provide a template and guidelines for doing so. I agree with this direction, even if you are starting out as a solo freelance medical writer! SCORE also helps you determine the structure of your business (eg, sole proprietor, general partnership, LLC, or other corporate structure). Included in the Business Plan is the name of your company, how you intend to operate, and what your “corporate identity” will be (eg, logo and design for your website or any printed materials you may create to help market yourself and your business).

I also consulted 2 professional business consultants (one in New York that was free to women starting a small business, the other a professional individual in California whom I paid), and I suggest anyone starting out consider doing the same, as it enables one-on-one communication and opportunities to ask specific questions related to your own situation. One of the first things they advised was: be sure to have a minimum of 6 months’ living expenses in the bank before you quit your job—1 year’s living expenses would be even better!

Part of writing the Business Plan includes identifying your niche, or defining yourself and your business, as well as your market (or potential customers). For instance, are you planning to focus on a specific disease? If so, what types of organizations typically produce or publish information in that area and how will you contact them? Are you planning to focus solely on writing grant applications, regardless of topic? Identify the nonprofit corporations that might give you grant-writing business. Are you going to focus on public relations (PR) writing? Again, identify PR firms, hospitals, universities, etc—all have PR writing tasks, and many use freelance writers. Pharmaceutical/biotech industry? What aspect? Regulatory affairs? Clinical or preclinical? Medical communications? Sales training? Medical education? Advertising agencies? Are you thinking of managed care companies? You must be quite clear with exactly what service(s) you intend to offer in order to do the appropriate marketing research to identify your prospective clients.

Make a list of everyone you know who is in your prospective field, and everyone you know who might be related to or know someone in that field. These people likely will be your first contacts once you have finished your Business Plan. Let all your friends and business associates know your intentions and ask them for referrals as well as permission to call on them once you are “in business.” Ask your former employers if they have work they might give you—this is important, as they already know you and your work and are most likely to give you business. Networking is crucial, and, basically, everyone you have ever met becomes part of your network. This includes professional associations such as AMWA, the Council of Science Editors (CSE), Drug Information Association (DIA), Society for Technical Communication (STC), The Author’s Guild, American Association for the Advancement of Science (AAAS), Accreditation Council for Continuing Medical Education (ACCME), American Psychological Association (APA), American College of Clinical Pharmacy (ACCP), and other relevant communications or medical/science associations you may wish to join.

There are many other steps necessary for starting a freelance medical writing/communications business, but these are the “first steps.”

—Cathryn Evans
Although I have seen many writers freelance while they are between full-time positions, there are several things to consider before transitioning into freelancing on a full-time basis. The most important thing to keep in mind is that freelancing is a business, so your clients are not your employers. This is an important point that many newbie freelances struggle with. It is important to realize that as a freelance, you need to have a diverse portfolio of clients, and no more than 30% of your business should come from any single client. Freelances also need to learn to manage their own money, pay taxes, read contracts, negotiate with clients, and deal with software and hardware issues. You can hire professionals for various aspects of managing the business, but the freelance is ultimately responsible for it. Once you have decided that you want to be a full-time freelance, you need to network and start marketing to potential clients. Joining professional organizations like AMWA as well as using content marketing on LinkedIn are essential ways to develop a client portfolio.

—Ruwaida Vakil

As a freelance medical writer, how do you feel AMWA membership has helped your career?

AMWA has been absolutely instrumental in my success as a freelance medical writer! I’ve gotten many referrals to wonderful clients through my AMWA colleagues, and other wonderful clients have found me through the AMWA Freelance Directory. By wonderful clients, I mean clients who pay me well and treat me right. Most also give me a lot of work.

But I didn’t get the referrals simply by being a member of AMWA. I started volunteering the year I joined, for the Delaware Valley chapter and at the national level. Colleagues who saw that I was dependable and trustworthy began to refer work to me. In networking, I’ve always focused on helping other people without asking for anything in return. I do this because it’s the right thing to do, but it also resulted in referrals from the people I have helped.

—Lori De Milto

There is no question that AMWA membership—and particularly active involvement—has helped my career as a medical writer (both when I was a full-time employee and when I became self-employed). While an employee, AMWA educational workshops were fantastic in helping my career development, as well as informing my decision of the niche I would choose when I eventually became self-employed. For both employees and self-employed businesspersons, the AMWA conferences provide a fabulous opportunity to meet like-minded others and exchange ideas and experience.

As a freelance, the value of meeting other people and networking has been important, as has the listing in the Freelance Directory—but I must admit that other professional organizations (DIA, for example) may be more helpful when it comes to fruitful networking because you are meeting a larger pool of potential clients rather than a large group of peers who are also looking for medical writing opportunities/assignments. If you feel that having AMWA certificates will help you in your freelance business, then by all means go ahead and get the certificates (keeping in mind that they are not certifications).

Even if you do not undertake the formal certificates offered by AMWA, the freestanding AMWA workshops themselves are generally remarkably helpful and interesting! I never attended a workshop that I did not find helpful, even in cases when I had more experience than the teacher. Learning is a lifelong process, and AMWA provides many excellent informational workshops and publications!

—Cathryn Evans

Since joining AMWA in 1994, my freelance business has benefited immensely from membership—which, in my opinion, remains a bargain considering all the great benefits! One of those benefits is the AMWA Freelance Directory.

The Freelance Directory has come a long way technologically since I first joined AMWA. Back in the day, the search capability wasn’t nearly as powerful as it is today, and companies that wanted to search for a freelance had to pay to do so. Now companies need only to sign up for free, and they can search the directory as often as they want by a wide range of criteria. The listings themselves are much more robust now, too. The Freelance Directory has become a great resource for companies that are looking for freelances, which means it’s a great marketing tool for us!

I invested in a listing in the Freelance Directory as soon as I joined AMWA, and my listing quickly bore fruit. The profit I made on the first project was enough to pay for my listing for decades to come! I continue to get opportunities to turn potential clients into paying clients thanks to my listing in the AMWA Freelance Directory, and now it’s even easier to maintain my listing thanks to it being combined with my annual membership dues form.

But that’s just the tip of the iceberg. Opportunities rarely present themselves spontaneously out of the blue. So if you’re a member of AMWA and a freelance, and you’re sitting back waiting for something good to happen, you better get comfortable. You’re going to be sitting a very
long time. For freelances, AMWA is a tool, and tools only work when you pick them up and use them.

I became active in AMWA’s Freelance Listserve, which was an early predecessor to AMWA Engage. I got to know people and they got to know me. I went to chapter meetings and annual conferences. When I saw the opportunity to get involved with my chapter as a volunteer, I took it. As I said last November in my Swanberg address, volunteering in AMWA has made all the difference in the world to my career.

I’m not saying this to recruit people to volunteer in AMWA, although that certainly would be a nice byproduct. But just considering the career aspect, in my opinion, there isn’t a more effective way to build your freelance business than by becoming a leader in your field. You become a leader by volunteering.

Help at the registration table for a local chapter event; it’s a great way to meet people and for them to meet you. If you’re in a region without a local chapter or in a chapter that’s geographically spread out, do what we do here in southwest Florida and what people do in similar areas—take the lead in arranging a networking event, or sign up to be an LNC (Local Networking Coordinator).

Get active on Engage, so you can elevate your visibility by being a part of the professional conversation. Take the reins in your career by sharing your knowledge and experience with others. There are so many venues in which you can demonstrate your expertise—by leading roundtables and open sessions at the Medical Writing & Communication Conference, or by presenting a webinar or developing a Fast Interactive Training (FIT) presentation.

The skills I learned and honed as a volunteer serving on the chapter and then national committees led to my eventually being confident enough to take on a leadership role. Today, my clients proudly present me to their clients as an AMWA past president. Trust me, this works!

Putting yourself out there can be scary sometimes. But my experience is that when you give of yourself, you get so much in return.

—Brian Bass

**Q** What other organizations besides AMWA do you recommend a freelance medical writer join?

**A** There are many helpful, professional associations for freelance medical writers. Which are best for you depends partly on the type of work that you do and partly on what you’re looking for in professional associations.

My current and past professional associations (along with AMWA) include Society for Healthcare Strategy and Marketing Development (of the American Hospital Association), Association of Health Care Journalists (AHCI), Healthcare Businesswoman’s Association, and Editorial Freelancers Association.

The Society for Healthcare Strategy and Marketing Development and the Association of Health Care Journalists both offer lots of great free resources and have an annual conference. The Healthcare Businesswoman’s Association has national and local meetings and offers lots of resources. It’s very impressive, but it’s not a great fit for me because most members work in or with pharma (and I don’t). Likewise, the Editorial Freelancers Association, made up mostly of editors, isn’t a good fit for me. It has an active jobs list (mostly low-paying, one-time jobs) but very few meetings (and those are usually in New York).

Other helpful professional associations for freelance medical writers include Alliance for Continuing Education in the Health Professions (ACEHP) and DIA, which has interest areas such as Medical Affairs and Scientific Communication, Regulatory, and Patient Engagement. These associations aren’t relevant to my work (health and medical content and health journalism), but I know that other freelance medical writers have found them very useful.

—Lori De Milto

There are several professional associations that medical writers and editors should consider joining in addition to AMWA. The choice of association is dependent on whether you are a writer or editor and on what type of writing you do. Many AMWA editors are members of Board of Editors in the Life Sciences (BELS). If you do manuscript writing, you may want to consider the International Society for Medical Publication Professionals (ISMPP). CME writers may want to consider the Alliance for Continuing Education in the Health Sciences (ACEHP). Additional professional associations to consider include the Drug Information Association (DIA) and the Association of Health Care Journalists (AHCI).

—Ruwaida Vakil
Comparing Lori De Milto’s Books on Marketing for Freelances:

**The Mighty Marketer: Your Guide to Making More Money as a Freelance Medical Writer**

**7 Steps to High-Income Freelancing: Get the Clients You Deserve**

In 2017, the *AMWA Journal* published original research by Monica Nicosia, PhD, who surveyed freelance medical communicators to learn about the tools that they used in their work. Nearly half of her respondents (48% of 307) did not have a business website, most (82%) were on LinkedIn, and many used various other social media platforms. If it were up to Lori De Milto, every freelance would have at least a website and a LinkedIn profile, because she deems these to be 2 of the strongest marketing engines for freelances. She offered her advice on this issue and others in her 2014 book *The Mighty Marketer: Your Guide to Making More Money as a Freelance Medical Writer*. This advice appears again in her 2017 book *7 Steps to High-Income Freelancing: Get the Clients You Deserve*. Only this time, some aspects of her advice have been updated. The 3 years between publications might not appear to be significant, but in *7 Steps*, De Milto provides new strategies accounting for some of the changes in technology that have occurred. Also, one major difference is that *The Mighty Marketer* was written with freelance medical writers in mind, and *7 Steps* was written for a broad array of freelances.

In *The Mighty Marketer*, De Milto tells of her jump to a 6-figure income after 18 months of dedicated marketing. She recounts her story in *7 Steps* as well. The AMWA members who responded to the 2015 AMWA Salary Survey had income between $20,000 and $450,000 and undoubtedly varied in multiple ways—in years of experience, in years of education, in types of education, and more. One additional difference might be in marketing. De Milto does not provide a designated figure that can result from concentrated marketing efforts, but both of her books are guides to earning high incomes. With De Milto’s long-term presence as an AMWA member and volunteer, many members are familiar with *The Mighty Marketer*. Even for those who are not, the divergences and similarities between *The Mighty Marketer* and *7 Steps* will be summarized here.

In both books, De Milto discusses the components that should be considered in a marketing plan: a solid description of what the freelance offers, a description of the ideal client, methods for finding clients, developing a LinkedIn presence and strategy, and developing a website. One slight but important change is the use of the word “steps” in the second book. In *7 Steps*, De Milto drives each chapter without calling it a chapter at all. Those who find marketing to be overwhelming might appreciate the streamlining of the content in this way. Whereas *The Mighty Marketer* is organized around topics, *7 Steps* is akin to a well-annotated checklist that might be used to guide a freelance through the process of developing a marketing plan.

The benefits of LinkedIn are extolled in both books, but the suggested strategy evolves. For instance, in *The Mighty Marketer*, the author’s approach on LinkedIn is to connect only with people she knows. In *7 Steps*, she suggests that freelances should also connect with people they are “related to” in terms of common industries or being freelances. In the second book, LinkedIn gets its own chapter, with some discussion spilling into another chapter. The author explains how to develop a profile that draws potential clients, especially after the algorithm changes that were implemented when Microsoft purchased LinkedIn. Furthermore, more information on LinkedIn strategy and etiquette is included in *7 Steps*.

WYSIWYG website builders are embraced in *7 Steps* in a way that they are not in *The Mighty Marketer*. In the latter, the advice is that hiring a web designer is well worth the expense. In *7 Steps*, De Milto doesn’t retreat from this advice, but she does explain how using either a web designer or a DIY website builder might be advantageous under different circumstances. According to the author, regardless of the choice, the freelance should remember that the website is representing a freelance business and not a typical small business. As such, the freelance’s website will have some components that the small business’s website will not have and vice versa if the website is maximized for the greatest potential impact.

As noted, De Milto’s newer book lists 7 steps to achieving a high income through marketing. In this review, only 2 were
explore in depth. Taken together, all 7 steps guide the reader to complete a marketing plan. In the beginning pages of the book, there is an image of the 7 steps with a winding road as a backdrop. This image seems a fitting representation of how I De Milto's personal marketing journey as told in the book. The author also includes bonus content that she suggests will help the reader navigate the marketing process.

Of the two books, 7 Steps is more directly presented than The Mighty Marketer. Because of the “step” wording and the support built around that structure, 7 Steps can more easily serve as the guide that it is intended to be. The latter book also captures from The Mighty Marketer valuable marketing content for medical writers and presents it as valuable for freelancers in general. Lori De Milto's book 7 Steps to High-Income Freelancing: Get the Clients You Deserve is a simple guide to creating a marketing plan whether one is a medical writer or a freelance professional from a different field.

Reviewer: Sharese Terrell Willis, PhD

Sharese Terrell Willis, PhD, is a medical editor and writing instructor for her company, Doc's Editing Shop in Phoenix, Arizona.

* * *

The Ethics Police? The Struggle to Make Human Research Safe

Robert L. Klitzman
New York, NY: Oxford University Press, 2015, Hardcover, 422 pages, $36.95

The ethics and safety of clinical trials receive much attention, yet institutional review boards (IRBs) have received surprisingly little. The Ethics Police? The Struggle to Make Human Research Safe, by Robert L. Klitzman, attempts to address this gap. Although published several years ago, this book remains timely, and the issues it raises are by no means resolved.

Briefly, IRBs approve research protocols involving human subjects. They are composed of clinicians, scientists, and lay people from the community. Most IRBs are based at academic medical centers or hospitals and thus provide local perspectives on proposed research at those sites. However, some IRBs are commercial entities and may be thousands of miles away from sites of proposed research. Regardless, an IRB's approval and surveillance of ongoing human subject research is required by institutions, funders of research grants, and various accreditation bodies.

The author interviewed 46 IRB chairs, members, and staff from across the United States. Quotes from these individuals (all given pseudonyms) are scattered throughout the book, adding a welcome human-interest touch to the policy and ethics discussions that some readers may find a bit dry. These voices effectively convey the human side of research. That said, one must be cautious in drawing conclusions about a complex system based on the opinions of only 46 people.

The author, a physician, begins by describing his father's death from leukemia and how that experience affected his views about the ethics of experimental treatments, patient safety, and the rights of patients. This vignette provides a context for the rest of the book, in which IRB members discuss their perceptions of risk, the highly subjective federal guidelines that IRBs must follow, and how they try to do the right thing for participants even when they are uncertain about the effects of a proposed intervention. For example, the concept of "minimal risk" deservedly receives a lot of attention. But although risk to patients is a fundamental consideration for every protocol an IRB reviews, "minimal" does not mean the same thing to every IRB member, every IRB, or every oversight or accreditation agency.

Another concept that IRBs find difficult is appropriate payment of research participants. What amount is fair (ie, reflects invasiveness or inconvenience) and what is excessive or possibly coercive is often unclear. Coercion—the idea that people might do something not in their best interest solely for financial reasons—could undermine the bedrock concept of informed consent. A recent proposed framework for fair payments (Gelinas et al., N Engl J Med. 2018;378:766-771) illustrates the continuing lack of consensus in the research community.

The book's title is a dismissive term sometimes used for IRBs. However, the author concludes that, instead, IRB members want to work with investigators to assure—as much as possible—that people do not suffer unintended consequences from participating in research.

Even if you have frequent interactions with IRBs, much in this book will be eye-opening. Because of the complexity of the research regulatory environment, it may not be the best introduction to those new to clinical research. However, for students of biomedical ethics (and IRB members), it will be thought-provoking.

One last point: I was disappointed by typographical and editing errors in the first chapters of this book. Perhaps they can be corrected in a future edition.

Reviewer: Karen Potvin Klein, MA, ELS, GPC, MWC®

Karen (2014-2015 AMWA President) is Director of Grant Development and Medical Editing at Wake Forest University Health Sciences in Winston-Salem, North Carolina.
FROM THE PRESIDENT
Moving Forward with Open Arms and Open Minds

Cynthia L Kryder, MS / 2018–2019 AMWA President

When I attended my first AMWA chapter meeting in 1993, I never imagined that one day I would have the privilege of serving as president of this association. With Donna Miceli as my wingman, I walked into Williamson's Restaurant in Bala Cynwyd that evening without business cards and without any expectations with regard to the benefits I might receive from attending.

My first encounter was with Edie Schwager, our own Dear Edie, who welcomed me to the tribe with her trademark hug—and promptly sold me a copy of her book, *Medical English Usage and Abusage*. That paperback was the first of many resources my AMWA colleagues shared with me, and that experience with Edie and colleagues in the Delaware Valley Chapter made me eager for more. I remember thinking how friendly the people were, that they did more than shake my hand and drift on to the next person. These people asked me what type of medical writing I did (they were interested); they held out their hands for my business cards (fail on my part); they answered my questions about clients and rates and who knows what else without hesitation (they weren't worried about competition). I left that meeting thinking that this freelance gig just might work and I knew I had to tap into this network of collective medical-writing intelligence.

Twenty-five years ago, tapping into the AMWA network was not so easy. Every event was a live one, and if the date or location was inconvenient, I didn't go. What's more, I could access AMWA's educational resources only at in-person events; webinars, self-study modules, and online learning were not yet mainstream technologies.

But as most of us know, AMWA events are like a bag of potato chips; you can't stop with just one. And my, how I've indulged!

Why am I telling you this? Because I want every AMWA member to have this same experience. During my tenure I want members to feel welcomed and valued, I want them to feel excited about the benefits they receive from being part of our clan, and I want everyone to indulge in that potato chip bag of AMWA offerings.

How do we accomplish this? My positive experience began at the local level, and I believe it still does. The key ingredient is you. You must be the friendly face and the warm handshake people receive when they attend an AMWA event. You must be the expert to whom members go when they need a resource or an answer to a question. You must be the reason someone keeps coming back to AMWA again and again and again.

That being said, we don't expect you to work alone. AMWA remains committed to ensuring that members' local experiences are positive. That's why we appointed a local networking coordinator (LNC) board liaison, Melory Johnson, to serve as the point of contact for LNCs and to communicate the value of local networking both within and outside of the chapter structure. We also created an Engage discussion group exclusively for chapter officers, and we've designated a board liaison, Elise Eller, to review discussions, to respond to posts when appropriate, and to identify opportunities for AMWA to support chapter leader challenges and celebrate successes.

I'm also happy to report that the Chapter Advisory Council (CAC) successfully completed its first year of operation. The CAC is the direct connection between chapter leaders and the AMWA Board of Directors. The CAC held its inaugural face-to-face meeting at the Medical Writing & Communication Conference last month in Washington, DC. Under the leadership of Katrina Burton, the CAC will continue to advise the AMWA board on the organization's strategic direction.

AMWA has always been on the right track when it comes to education. In fact, it's one of the reasons people give for joining the organization. But as humorist Will Rogers said, "even if you are on the right track, you'll get
run over if you just sit there.” With Lori Alexander as its engi-
neer, AMWA’s Education Committee train is moving ahead full
throttle to ensure we create new educational resources to meet
members’ needs. They continue to recruit, vet, onboard, and
mentor educators for all of AMWA’s educational activities. In
response to members’ requests, the committee is developing a
series of certificates that can be earned through online learning
in various topics. The first certificate is expected to debut
over the next fiscal year. Keep your eye on the AMWA Blog
(http://engage.amwa.org/browse/blogs) for information
about our progress.

In response to members’ requests, the committee is developing a series
of certificates that can be earned through online learning in various
topics. The first certificate is expected to debut over the next fiscal year.

Did I mention blog? Yes, we have one. Yes, we want you to
read it. It’s one of several ways we communicate information to
members as well as the general public. Bookmark the page and
check it often for updates.

And speaking of member resources, one asset closely asso-
ciated with the AMWA brand is our exclusive salary survey.
I’m thrilled to report that preparatory work on the next salary
survey has commenced, with guidance from the ad hoc Salary
Survey Task Force. AMWA has partnered with a research com-
pany to implement the survey to medical communicators
within the broad medical communication community, not just
AMWA members. With this arrangement, AMWA will be able to
deliver the survey results in a timely manner.

Stepping into the presidential footwear of Kathy Spiegel,
Lori Alexander, Steve Palmer, and Brian Bass, to name a few, is a
scary experience. These recent presidents oversaw an organiza-
tion undergoing rapid changes as we brought our governance
structure into the 21st century and invested in technology to
give our members the best possible experience.

We’ve spent the last 4 years focusing tremendously on gov-
ernance and infrastructure. Where do we go next? We’ll still
be making data-driven decisions but with a focus on member
recruitment and retention. We are strengthening our relation-
ships with corporate medical communicators and department
directors to build membership and participation in AMWA pro-
grams. We are collecting data to find out what brings people to
our organization, what keeps them with us, and what makes
them leave. As you can imagine, serving thousands of mem-
bers who work in diverse medical-communication settings and
have different needs is a challenge. We are listening to you, our
members, to better understand your needs, and we’re making
strategic decisions about what we can provide. For example,
we’ve heard from many of you in the mid-to-late stages of your
careers and we are developing content for you. Nevertheless, it
takes time for subject matter experts to create accurate, peer-
reviewed resources we can deliver with pride. I ask that you be
gentle with us as we go through this process.

My dad, a bit of a visionary, worked in television sales and
service. I recall him returning from a trade show in the 1970s
and telling me about this wonderful gadget we’d use in the
future to record and view television shows on demand. I’m sure
I bestowed upon him a teenage eye roll, but it didn’t
quell his enthusiasm. His mind was open to innovations and
fresh ideas, whereas I couldn’t imagine anything beyond the
status quo.

What about you? I hope you’ll keep your minds open to the
future possibilities for AMWA. We may make some missteps as
we set priorities and implement plans, but if that happens we’ll
correct our course as soon as possible.

Please join me over the next year as we open our arms to
our members and open our minds to all we can achieve work-
ing together to move this wonderful organization forward. It’s
going to be an exciting ride!
Coming Soon: AMWA Salary Survey

Grab your W-2 or your profit-and-loss statement and get ready to participate in the 2019 AMWA Salary Survey! Over the past 30 years, AMWA salary surveys have served as dependable bases for setting salary ranges for employers and negotiating salaries and fees for employees and freelances/independent contractors.

This year, AMWA has contracted with Association Research, Inc. (ARI), a third-party research firm located in Gaithersburg, Maryland, to conduct its 2019 Salary Survey. ARI has produced customized survey research exclusively for associations and nonprofit organizations since 1984.

You will receive the link to the online survey in an email from ARI in the first quarter of 2019. For your convenience, the survey will include a log-in feature to provide you the opportunity to start and finish at your own pace, as well as to provide additional security. Be assured that ARI will hold all individual data in confidence. To ensure you receive the link to the survey, please add amwa@associationresearch.com (Association Research on behalf of AMWA) to your safe sender list.

Please try to answer every applicable survey question accurately. The more complete the data, the more meaningful the results will be. Summary results will be provided to all who participate in the survey, and expanded results will made available to all AMWA members.

This is the only compensation survey that focuses on you—the medical writing, editing, and communication professional. Be on the look-out for your survey invitation from ARI and make sure to complete the survey on time.

Be sure to receive the 2019 AMWA Salary Survey invitation! Add amwa@associationresearch.com to your safe sender list.

It’s time to talk money.

Get ready to participate in the most in-depth study on compensation in the field of medical communication.

Look for the AMWA Salary Survey invitation in February 2019!
After years of assessment, development, and ongoing AMWA support, the MWC Commission launched the Medical Writer Certified® (MWC®) credential in September 2015. Since that time, as of October 2018, the MWC Commission has certified 75 medical writers! The Commission continues to review new applications to sit for the MWC certification examination on a regular and growing basis.

A few key updates are worth noting.  
• The MWC Commission created an MWC Examination Study Guide available on the AMWA website. This tool includes examination preparation recommendations, example examination topic and subtopic categories, example questions, and selected examination preparation resources.  
• The MWC Commission created a Qualifying Work Experience aid you can link to from the MWC Q&A section of the AMWA website. This aid is particularly helpful for those seeking certification who are not employed professional medical writers.  
• The MWC examination has moved from a paper-based format with limited location and timing options to a computer-based format at testing centers around the world, with large time windows to take the exam.

The MWC Commission is offering the examination during two 3-week open periods in June and December of 2019. The 2019 MWC application and examination timelines are as follows:  
• Exam Dates: June 1-21, 2019  
  – Application Deadline: approximately April 2019  
  – MWC Exam Registration Deadline: approximately May 2019  
• Exam Dates: December 1-21, 2019  
  – Application Deadline: approximately October 2019  
  – MWC Exam Registration Deadline: approximately November 2019

There are testing centers in most major cities globally. Global testing locations are noted at www.isoqualitytesting.com/locations.aspx.

For further information about MWC certification and recertification, check out the certification menu on the AMWA website home page: www.amwa.org.

In the next few months, the Commission will be sharing testimonials from certificants about why they decided to get certified, how they feel it will help their careers, and their exam preparation study tips. Keep an eye out for these on the AMWA website. The following testimonial does a nice job of capturing the MWC Commission’s belief: “MWC certification is a manifestation of my expertise; it gives my work credibility and distinguishability. Moreover, credentials garner respect for our profession. People do notice.”
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People Who Cannot Afford Boots Cannot Pull Themselves Up by the Bootstraps: An Evidence-Based Exploration of Health Disparities, Social Determinants of Health, and How Medical Writers Can Help

Bob Kirsch, MA and Tamara Ball, MD / Freelance Medical Writers

An Interview with Eliseo J. Pérez-Stable, MD
Director, National Institute on Minority Health and Health Disparities

Knowing how to speak about health and things medical is not something a person is born with. The skills can be learned, and Eliseo J. Pérez-Stable, MD, Director of the National Institute on Minority Health and Health Disparities (NIMHD), helps point the way.

We medical and health writers and editors are in a position to help everyone—from the physician professor of medicine to patients with poor health literacy—improve skills around communication so as to bring people to where they will readily do what it takes to be healthy.

The authors were fortunate to speak at some length with Dr Pérez-Stable on communication between providers and patients. Below is a selection of his comments on the possible role of medical writers and editors in helping to overcome health disparities in America.

“Many physicians may take communication for granted. It is a learned skill.”

“In primary care disease management, the main skill we bring is to communicate and message over time. That is where a lot of the disparities can be addressed, managed, and reduced.”

“We were communication in the clinic improved, that in itself would make a major impact on disparities.”

“The relationship between clinician and patient is undervalued, in part, because it is hard to study and hard to quantify.”

Why is communication not accorded its proper place? The following “factors underscore the unique challenges in communicating with minorities and health disparity populations. A substantially higher proportion of minorities and health disparity populations have unmet needs that interfere with their abilities to care for themselves. For example, minorities experience food (31.5% of African Americans and 35.4% of Latinos vs 18.2% of Whites) or housing (43.7% of African Americans and 47.3% of Latinos vs 28.4% of Whites) insecurities. Similarly, 40.1% and 51.8% of persons with less than high school education (vs 11% and 21.4% of college graduates) experience food and housing insecurities, respectively. Among immigrants, religion, cultural background, English language proficiency, acculturation level, immigrant generation, and documentation status have heightened relevance. Further, health disparity populations often exhibit factors associated with poor health such as low health literacy and/or limited English proficiency.”

Yet, “most clinicians are not incorporating social determinants of health into their interactions with patients,” said Dr Pérez-Stable.

“There is no reason a person’s hypertension can’t be controlled—but people of color and especially poor people of
color are less likely to have this happen. Clinicians and health systems need to address this disparity. Similarly, people with diabetes should be able to achieve a measure of control, and what happens when clinician and patient meet can make a difference.”

“If the patient is not compliant, maybe a different message is needed.”

“The interaction between clinician and patient, the communications they share, makes a big difference in improving the lives of patients and decreasing the burden of illness,” with the understanding that PCC encompasses all forms of communication—verbal, nonverbal, written—that occurs between patients and their physicians.¹

New technologies may facilitate the interaction. “Where the technology is appropriate, electronic information may let the clinician prepare for the patient so the time with the patient is more quality time, communication time, and human touch time.”

“It is not always necessary to tell the patient to see a specialist, because an excellent primary care clinician should function as a coordinator providing comprehensive care and selecting referrals and tests—like a quarterback.”

“NIMHD is committed to supporting research and communications efforts to improve cultural competency and clinician–patient communications (see the Language Access Portal: https://www.nimhd.nih.gov/programs/edu-training/language-access/ and https://nimhd.blogs.govdelivery.com/2017/03/14/introducing-the-language-access-portal/). We need to be culturally sensitive. Not every patient understands our level of jargon. We need to respond differently to different patients.”

“How racism and structural racism relate to illness has been kicked around for decades, but we now have the tools to understand the biological mechanisms. Decades ago this topic was frequently dismissed as belonging to politics and not to science. Currently, it is well understood that chronic stress and adverse childhood events may be associated with illness later in life. The same applies to structural racism. Now we are studying how people may internalize the effects of racism and structural racism, and how it might affect a person’s health decades later.”

“When the patient is able to see the same clinician over the years, a bond of mutual trust can develop. Once trust has been established, the patient does not always need to be persuaded by scientific data, although the clinician should always use data as leverage. Often the patient really comes to a place of feeling, ‘you, the clinician, are the expert. I trust what you say. For example, about my taking 3 medications to lower my blood pressure.’”

“The primary care clinician who has a long-term sustained relationship with a patient can influence the patient’s adherence to medications, follow-ups, and appropriate use of health services. The majority of patients appreciate that and look for that in primary care. But this approach, this configuration, is too frequently not implemented in the United States.”

Here Are Some Topics You Might Choose to Write About: Some Suitable for Professionals, Some for the Public, Most for Both

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<th>Table. Here Are Some Topics You Might Choose to Write About: Some Suitable for Professionals, Some for the Public, Most for Both</th>
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<tr>
<td><strong>Health Outcomes</strong></td>
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<td>“Less than 10% of an individual’s health outcomes are influenced directly by the receipt of health care services,” explained Julie Wood, MD, MPH, Senior Vice President, Health of the Public and Interprofessional Activities, AAFP (personal communication, August 2018). Yet, as with climate change and many additional scientific findings, our nation has revealed an unwillingness to respect reliable data or expert opinion.</td>
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<td><strong>Behavior Patterns</strong></td>
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<td>“Among the influences on health, those related to behavior patterns represent the single most prominent preventable source,” according to the NAM Vital Priorities Initiative. Yet behaviors are “driven at least as much by external factors as internal, as, for example, in the access and affordability of healthy foods. Behavior patterns reflect culture, access, economics, and other factors such as the quality of early experiences and the central importance of supportive human relationships.”</td>
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<td><strong>Social Epigenomics</strong></td>
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<td>“We are promoting research on Social Epigenomics exploring the relationship between social determinants of health and epigenetics” with the goal of better understanding the mechanisms of health disparities and how the biology of people living in disadvantaged social environments is altered, Rina Das, PhD, Scientific Program Officer, NIMHD (telephone interview, August 2018).</td>
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<td><strong>The Environment Shapes Inequalities</strong></td>
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<td>“Any discussion of health inequalities needs to tangle with how the social, economic, and physical environment shapes inequalities, and gets “under the skin,” said Sandro Galea, MD, DrPH, Dean, Robert A Knox Professor, School of Public Health, Boston University (personal communication, July 23, 2018).</td>
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<tr>
<td><strong>Health Impacts from Exposure to Chronic Stress, Poverty, and Racism</strong></td>
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<td>What had not been definitively shown until recently and now has been definitively demonstrated is that accumulated stress, inadequate relaxation, personal slights, and additional insults of one sort or another lead over time for many people to illnesses manifest in the body’s organs. “One important area is how chronic stress, even at a relatively undramatic level, can damage health; and how both poverty and racism are sources of chronic stress. Understanding how stress, poverty, and racism are linked is key,” Paula Braveman, MD, MPH, Professor of Family and Community Medicine and Director of the Center on Social Disparities in Health at UCSF (personal communication; July 25, 2018).</td>
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<td><strong>Excessive Focus on Individuals May Undercut the Broader Benefits Derived from Focus on Population Health</strong></td>
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<td>According to ACP, as the focus of the “dominant health model” tends to prioritize “biology of disease and individual risk factors,” both public policy and much of our nation’s approach to health and medicine in general focuses “on treating illness and managing risk to the detriment of broader population health.” For example, lowering levels of air pollution may be a more effective and cost-effective approach to asthma than countless visits to individual providers. We should be explaining this to our readers.</td>
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<td><strong>System-Wide Strategies Have Proven Value</strong></td>
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<td>At present, the NAM Vital Directions Initiative explains, “prevailing cultures, financing, standards, accountability, accessibility, and organizational structures are largely designed to foster narrow perspectives and poorly coordinated activities.” It would help to “implement system-wide strategies for better health.” This means linked interventions, team care, and effective information system platforms plus leadership messaging on health progress, underscoring key trends. Notably, we medical writers can assist in such messaging.</td>
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<tr>
<td><strong>Align Structural Forces to Improve the Health of the Under-served</strong></td>
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<td>“The complex nature of health disparities requires complex solutions. It’s much easier to tell people ‘You need to do this’ than to see where the health system is not very welcoming or not very available if you do not own a car or the bus stop is far away. Structural forces have to be aligned” with good options if we want to get to healthy behaviors, Nathan Stinson, Jr., MD, PhD, Director, Division of Scientific Programs, NIMHD (telephone interview, August 2018).</td>
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<tr>
<td><strong>Partnerships are Moving into Prominence</strong></td>
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<td>“Partnerships are key to effectively addressing the social determinants of health. These partnerships entail close working relationships among policy makers, educators, representatives of the health and nonhealth professions, community organizations, and community members. They also involve strong linkages between nonclinical faculty and clinical faculty or preceptors so that experiences in and with communities related to the social determinants of health are reinforced during clinical rotations;” according to a NAM committee.</td>
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</table>
Partnering with Local Public Schools

Our nation’s public schools play key roles in determining the health children and adolescents will experience later in life, according to a NAM Initiative. For example, children and adolescents “consume up to 50% of their total daily calories in school.” Schools can directly increase young people’s levels of physical activity. Further, “school wellness policies are an important mechanism for engaging families and communities.” For schools to participate effectively in “helping advance the agendas of the health and social service sectors, the communication interfaces with those sectors have to be as seamless and fluid as possible, the databases interoperable, and the reward structures fully aligned.” Medical writers and editors may be able to help inform both professionals and the public about the role of schools in relation to health.

Activating Communities

“It is through shifts in power from health professionals to community members and organizations that communities share in the responsibility for developing strategies for the creation of learning opportunities that can advance health equity based on community priorities and build upon community assets.”

Explain There Is Risk of Squandering Community Trust

“The risk of eroding the trust of vulnerable communities is very real,” according to a NAM Initiative. “Thus, it is essential to understand a community’s issues before acting on the social determinants of health through well-thought-out partnerships.”

How Institutions Can Build Community Trust

“There is concern in some communities about the trustworthiness of medical institutions. It is not sufficient for an institution to say, ‘Trust me. I will respect you.’ The first thing is for institutions to do things for the community and not ask for anything in return. Organizations shouldn’t be going out into the community—organizations should already be part of the community. That’s the part that is often missing. But now some institutions ask people to participate in research or come to the organization’s clinic for care before they have demonstrated that they really are trustworthy,” Nathan Stinson, Jr, MD, PhD, Director, Division of Scientific Programs, NIMHD (telephone interview, August 2018).

Community as Partner

A reciprocal commitment ensures that the community is an equal partner in any initiative undertaken. The commitment is heavily based on community-identified priorities and real community engagement that are the second and third components of this domain.

Neighborhood Factors Contributing to Poor Health

As a 2018 position paper of the ACP states, “Neighborhoods with concentrated poverty often lack grocery stores with fresh food, adequate public transportation, access to public spaces, adequate employment prospects, and access to health care services; often have underfunded schools; and often are situated near environmental hazards. Low-income persons are disproportionately affected by major weather events.” Providers who do not comprehend the existence of such configurations may be unable to understand well what is going on with some patients. Our role as explainers can be of great value here.

Local Government Policies Impact Health

Municipal public health departments and municipal governments in general set standards for and influence not only food, sanitation, and environmental safety, but also green space, activity-friendly building designs, the placement of fast food and alcohol outlets, and employee involvement in community-wide initiatives. Here, as well, advocacy is required.

Disaster Planning

It is important to explain to all audiences that disaster planning should take into account that “there may be exacerbations of pre-existing health problems among those who survive disasters, as well as the onset of new problems,” with injuries and acute renal failure occurring early on; gastrointestinal symptoms, musculoskeletal pain, and psychiatric disorders occurring within weeks; and risk of cardiovascular disease and diabetes being elevated over the long term, Dr Galea points out. One of the authors who has lived through multiple hurricanes knows firsthand that the economically depressed don’t always have the option to evacuate during a time of impending disaster and frequently can’t access a supply of medication, or be well taken care of if the relief doctors don’t speak their language or have their medical records. All of this needs to be explained to providers during times of calm.
Violence as a Health Issue

“Violence as a public health problem merits greater attention. In this society, we often view violence as a social problem rather than as a health issue; or think it is too politically charged to be a topic for health research or for medical systems to address. Violence directly causes death and disability, and exposure to violence places people at risk for both mental and physical health problems across the lifespan. As well, we know violence disproportionately impact racial groups and minorities, particularly African Americans, Latinos, and American Indians and Alaska Natives.” Jennifer Alvidrez, PhD, Scientific Program Officer, NIMHD (telephone interview, August 2018).

The Misconception about Childhood in the US

“I think some people have the misconception that growing up in the US is great—and that’s true if your family has money. For the most part, life in this country for children is very, very hard. So, 20%-25% of US children are experiencing food insecurity. And there is gun violence. And immigrant issues at the border with separation from parents. So, advocacy and attention are required,” explained Alice Kuo, MD, PhD, MBA, Professor of Internal Medicine and Pediatrics at the David Geffen School of Medicine at UCLA, and of Health Policy and Management in the Fielding UCLA School of Public Health; and a spokesperson for AAP California (telephone interview, June 2018).

Adolescent Health

An age group that is “frequently invisible, neglected, or vilified” in discussions on health and wellbeing needs our attention. Were we medical writers and editors able to throw some light for our readers on the needs of adolescents, then greater numbers of adolescents might achieve successful adult status. In this age group, “unemployment disempowers and is strongly linked with poor mental health and increases in health-risk behaviors, such as alcohol misuse. If unemployment happens at the start of adult life, these risk factors will have long-lasting and devastating effects at a stage when excitement, enthusiasm, and creativity should prevail,”7 as the Lancet Commission on Adolescent Health and Well-being points out.

Big Tobacco Targeting Vulnerable Populations

News that smoking rates are among the lowest they’ve ever been tends to overshadow the ugly truth of those Americans disproportionately affected by cigarette smoking and tobacco use: people living in rural areas, military veterans, LGBTQ individuals who are actively targeted by tobacco companies, lower-income Americans, racial and ethnic minorities, individuals with mental health or behavioral health conditions—all with higher smoking prevalence rates. “None of them deserve to be targeted as big tobacco’s next replacement customer,” said Jennifer Hobbs Folkensroth, National Senior Director, Tobacco Programs, American Lung Association (telephone interview, August 2018).

Isolation and Older People

“Over the last 15-20 years, older people have become more isolated, and new cohorts of middle-aged adults, especially those 55-64 years old, have shown a major drop in engagement. In addition, national volunteer efforts—such as Foster Grandparents program, the Retired and Senior Volunteer Program (RSVP), and the Senior Companions program—reach only a small percentage of the eligible target audience and have long waiting lists. Programs with high impact on the volunteers and recipients, such as the Experience Corps, have an inadequate number of high-impact opportunities because of low financing.”8 As the NAM Vital Directions Initiative highlights this, we should be informing readers about it.

Health Benefits When Older People Find Work

“An impressive and growing body of evidence suggests that working is health promoting as well as economically beneficial. With overall increasing healthy-life expectancy, many Americans will be able to work longer than they do now. Working longer will be health promoting for many Americans, providing not only additional financial security but continued opportunities for social engagement and participation in society. Leave policies related to employee and family sickness are essential to enable workers to remain in the workforce until retirement and at the same time provide social support for their families.”8 We medical writers and editors may join the NAM Vital Directions Initiative in shedding light on these findings.

Transportation and Older People

“Strengthened neighborhoods through transportation and housing policies are needed that aim to keep older men and women engaged in their communities,”8 the NAM explains. Such steps can readily be taken by local governments.

Intergenerational Programs

The NAM Vital Directions Initiative encourages “broadly disseminating intergenerational volunteer programs, such as Experience Corps, which benefit youth and seniors.” In addition, “reengineering federal volunteer programs such as Foster Grandparents, RSVP, and Senior Companions to serve a much larger portion of the potential beneficiaries.”8 These are the sorts of matters community publications and hospital newsletters can advance.
**Engagement in Society**

We writers should follow the counsel of NAM and promote the social engagement of older persons. “The effect of deficient social networks and relationships on mortality is similar to that of other well-identified medical and behavioral risk factors. Conversely, social engagement—through friends, family, volunteering, or continuing to work—has many physical and mental benefits.” Yet, recent evidence suggests that older persons are becoming less engaged. Vigorous efforts to promote engagement are needed, and this might include encouraging communities to brainstorm and experiment with how best to achieve defined goals.8

**The Elderly Disabled**

“The population of the elderly disabled, not only those with dementia but especially those with dementia, just keeps growing. Yet, we know so little about those who are not in a nursing home or other facility. There is great need to look into the quality of long-term care for the elderly disabled in terms of existing disparities. Yet, because it is hard to study, researchers tend to neglect the matter and so we know little about it,” said John Haaga, PhD, Director, Division of Behavioral and Social Research, National Institute on Aging. Importantly, “nonresidential services cost less per person served than a nursing home does, so unless they attract a lot of otherwise unserved clients, they probably do save federal and state governments and private insurers money...lots of funders think so, at any rate. LTSS can be a real bargain,” but it requires research to “figure out what works for whom” (telephone interview, August 2018).

**Regionalization of Health Outcomes**

“Since around 1970 there has been regionalization of health outcomes in a way that never had existed before. Things like smoking and obesity do not fully explain this divergence. Why is smoking so much worse in Tennessee than in Minnesota? Even if you look only at people without a high school diploma, various measures of health status are worse in Arkansas than in Iowa. Why is that?” said John Haaga, PhD, Director, Division of Behavioral and Social Research, National Institute on Aging. “If you live in Oklahoma, you ought to be demanding an explanation” (telephone interview, August 2018).

**Poor Sleep and Its Effects on the Health of the Underserved**

“Insufficient attention is being paid to how sleep disparities affect the health of socially disadvantaged populations. Americans of racial/ethnic minorities and of low socioeconomic status have the highest prevalence of sleep deficiency (shorter duration and quality), particularly many Native Hawaiians and Pacific Islanders, while many American Indians/Alaska Natives and African Americans, as well, do not have the sleep duration of most White Americans. Poor sleep is associated with a range of consequences for a person’s health, both mental and physical, including cardiovascular disease, obesity, stroke, cancer, depression, and suicide. Further, African Americans tend to have more severe health outcomes associated with poor sleep, for example, in relation to elevated risk of both obesity and hypertension,” Rina Das, PhD, Scientific Program Officer, NIMHD (telephone interview, August 2018). In general, Native Americans represent a population much denied an adequate foundation for good health.1,6

**University-Community Partnerships Can Improve the Health of the Underserved**

“University-community partnerships that create quality primary and secondary education programs in vulnerable communities” can provide benefit to vulnerable populations.4

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Background
According to the World Health Organization (WHO), acute poisoning is the third leading cause of unintentional deaths in children up to the age of 14 years. WHO estimates that each year, these episodes of acute poisoning are fatal in approximately 3,000 children and that 90% of those poisonings take place in the home.1

According to the 2016 annual report of the American Association of Poison Control Centers’ National Poison Data System, the top 5 substance classes most frequently involved in all human exposures are analgesics (11.2%), household cleaning substances (7.54%), cosmetics/personal care products (7.20%), sedatives/hypnotics/antipsychotics (5.84%), and antidepressants (4.74%). The top 5 most common exposures in children 5 years of age or younger are cosmetics/personal care products (13.3%), household cleaning substances (11.1%), analgesics (9.21%), foreign bodies/toys/miscellaneous (6.48%), and topical preparations (5.07%). The overall rate of poison exposures is 660/100,000 population, with the highest rates in children of ages 1 year (8,083/100,000 population) and 2 years (7,675/100,000 population).2

Various regulatory requirements exist to prevent unintentional drug poisoning in children. The United States Food and Drug Administration (US FDA)’s Consumer Product Safety Commission’s special packaging standards, also known as child-resistant packaging (CRP) standards, are applicable for most oral prescription drugs, many nonprescription drugs, and various household products. Under the Poison Prevention Packaging Act (PPPA), one of the best-documented successes in preventing unintentional poisoning in children,3 any package (including blisters or pouches) containing a substance regulated under the PPPA must meet CRP standards. Otherwise, the product could be misbranded or recalled and the marketing authorization holder penalized.3 The US FDA also recommends including a labeling statement declaring the compliance of the product to the CRP standards.3 Since the PPPA has been in effect, reported deaths of children from ingestion of toxic household products, including medications, have declined remarkably.4 The International Organization for Standardization also published an internationally agreed standard test procedure for reclosable CRP.5 In Europe, several regulatory requirements have been introduced that complement the International Organization for Standardization’s standard.6,7

What Is the F Value?
For products requiring CRP, there is also a regulatory requirement to calculate the product’s F value (“failure value”).8 For unit dose packages, the F value is defined as the number of individual dose units of a drug that can cause serious illness or injury in a 25-lb (11.4-kg) child. Failure occurs when a 25-lb child can gain access to this number of tablets or capsules in 10 minutes. For example, if a substance will breach this toxicity threshold after exposure to 3 units, the substance is assigned an F value of 3. For highly toxic or harmful products, the F value is usually set at 1 (F = 1), which indicates that a child’s access to even a single unit is considered a failure. For less toxic or harmful products, the F value may be higher. A default limit of “greater than 8” is usually adopted in the US. Unless a lower failure limit is declared, a failure occurs when a child gains access to a ninth unit.

The F value is used to guide the design of product packaging and in the tests to evaluate safety. Products with a lower F value require reinforced (better) CRP such as a strip pack, a blister pack, or a container with a child-resistant closure system, which are designed or constructed to be significantly difficult to open for most children younger than 5 years.

Chinmayee Joshi, MBBS / Sciformix Technologies Private Limited, Pune, India

Beyond Child-Resistant Packaging for Drugs: F Value Determination for Added Child Safety
Determining the F Value

Although guidance is available on the conduct and reporting of packaging tests, guidance is scarce on specific methods for determining the F value. Each manufacturer needs to conduct risk assessments and decide what constitutes “serious personal injury or serious illness” for their products. Acute and chronic animal toxicology data, adult clinical dose response data scaled to children, and postmarket surveillance reports of acute overdose in children are generally evaluated for this purpose. A single method for determining the F value cannot be applied to all drugs.

A weight-of-evidence approach is usually applied for calculating the F value9 (Figure 1). Data on overdose in children, if available, are given the highest priority, followed by data on overdose and adverse events (AEs) in adults. As the F value is defined for children with a body weight no greater than 25 lb, a body weight scaling method is usually used in the calculation of this value. When pediatric or adult overdose data are scarce or unavailable, the maximum tolerated dose (MTD)—the largest dose of a drug a patient can take without unacceptable AEs—in adults or even preclinical data can be used. When none of the above evidence is available, overdose data about a similar compound can be used to calculate the F value. When determining the F value of a combination product, the F value for each drug is calculated and the lower value is assigned to the combination.

Challenges in Determining the F Value

Many oral drugs are not approved for use in pediatric patients; therefore, direct clinical dose response or pharmacokinetic (PK) data for a 25-lb child may not be available. In this case, the MTD in adults is usually used as a basis for calculating the F value. In the absence of pediatric data, a provisional F value can be assigned to a product (with assumption that the nature of toxicity is similar in adults and children) until pediatric data are available. Below are some examples of our company’s experiences using various approaches to determine the F values for oral drugs.

Bupropion XL

The safety and efficacy of bupropion XL (extended-release antidepressant drug) tablets in the pediatric population have not been established. Although the MTD of bupropion for adults has not been established, bupropion overdose, with symptoms of neurologic, cardiovascular, and gastrointestinal signs,10 has been reported in adults who have ingested up to 30 g of the product.

In a case report, an 11-month-old infant boy (weighing 12 kg) ingested 30 tablets of 300 mg bupropion SR (sustained release), resulting in a dose of 750 mg/kg. He developed generalized tonic-clonic seizures, dilated pupils, tachycardia, and severe hypotension with metabolic acidosis and became comatose (Glasgow Coma Scale score 7). He received mechanical ventilation, inotropic support, and extracorporeal membrane oxygenation along with other overdose management therapies. The infant was extubated on day 8 and discharged 2 weeks after extubation. Neurologic sequelae were not observed at the 12-month follow-up.11

In another case, a 7-year-old boy (weighing 21.8 kg) ingested 7 tablets of 150 mg bupropion XL (1,050 mg). He experienced vomiting, hallucinations, tachycardia, and a tonic-clonic seizure. He recovered and was discharged after 48 hours without any sequelae.12 A dose of 1,050 mg in a 21.8-kg child would be equivalent to 48.17 mg/kg.

Using the body weight scaling approach, the corresponding dosage in an 11.4-kg child that could cause AEs would be approximately 549.08 mg. Based on these historical data, the F value assigned to bupropion XL 150 mg tablets is 3 and to bupropion XL 300-mg tablets is 1.

Pyrimethamine

Pyrimethamine is an antiparasitic that has a good safety and tolerability profile. Adverse events observed with pyrimethamine, including anorexia, vomiting, atrophic glossitis, hematuria, megaloblastic anemia, leukopenia, agranulocytosis, thrombocytopenia, and cardiac rhythm disorders,13 are primarily due to central nervous system toxicity in acute overdose and due to folate depletion in chronic overdose. The lowest reported fatal dose of pyrimethamine is 375 mg; however, there have been case reports of pediatric patients recovering after an overdose of up to 625 mg.14

Several case reports have been published on pyrimethamine overdose in children. A 23-month-old infant girl...
ingested eight 25-mg tablets of pyrimethamine (200 mg) and experienced vomiting, irritability, jerky movements of limbs, opisthotonus, and ataxia for 2 hours, but she recovered spontaneously without any interventions.  

Because the average weight of a 23-month-old infant is 11.27 kg according to the 2006 WHO child growth standards, 16 200 mg is equivalent to 17.74 mg/kg. Using the body weight scaling approach, the corresponding dosage in an 11.4-kg child would be approximately 202.3 mg. Therefore, the recommended F value for pyrimethamine 25-mg tablets is 8.

**Documentation**

Any package of drugs regulated under the PPPA must mention the F value of the packaged substance. Evidence-based justification and calculation of the F value is described in a report (Figure 2), which requires submission to the US Consumer Product Safety Commission. The F value report titled “F Value Calculation and Justification” is intended to provide a critical analysis of the available clinical and preclinical information about the drug, along with the conclusions and implications of the information. Literature pertaining to preclinical and clinical information is identified through a targeted literature search on databases such as PubMed and Embase. Additional relevant data are also included from databases such as Poisindex and overdose case reports.

The rationale for calculating the F value based on weight of evidence is then developed and added to the F value report. If pediatric data are not available, a temporary F value is calculated on the basis of adult data and assigned to the molecule until pediatric data become available.

The F value report should also be a useful reference to the clinical safety information, especially pediatric overdose case reports, for regulatory authorities. The F value report is a succinct report of the prescribing information, AEs, overdose information, and the implications of these data for child safety. For a single product, the document is typically 30 pages long; for combination products, it could be longer. When exhaustive information about the molecule is available, tables may be used for brevity.

The F value report includes the following sections and subsections.

- **Introduction and background**
  - Physiochemical properties and pharmacologic class of the drug
  - Mechanism of action, such as receptor binding; onset and/or offset of action
  - Clinical indications
  - Approved dosage, formulation, and administration

- **Animal toxicology**
  - An overview of the pharmacologic, PK, and toxicologic evaluation of the product in animals such as rats, mice, rabbits, guinea pigs, hamsters, dogs, and monkeys
  - The onset, severity, and duration of the toxic effects; their dose-dependency and degree of reversibility; and species- or gender-related differences
  - The effect of the drug observed in nonclinical studies in relation to that expected or observed in humans
  - The MTD and no observed adverse effect level, whenever available

- **Effects in humans**
  - Brief overview of the PK and pharmacodynamics (PD) data:
    - PK data include comparative PK in healthy individuals, patients, and special populations; extent of absorption; distribution, including binding with plasma proteins; excretion; time-dependent changes in PK.
PD data include information on the mechanism of action and the relationship of favorable and unfavorable PD effects to dose or plasma concentration (ie, PK/PD relationships).

- Adverse events reported during clinical trials and post-marketing studies:
  - Nature, absolute number, and frequency of common, nonserious, and serious AEs, including deaths, and other events leading to discontinuation or dose modification are to be included in this subsection. This information is generally included from the prescribing information of the molecule substantiated by published literature.
  - Case reports of overdose in adults and children:
    - The age, weight, and health status of the patient; dose of the ingested product; and the nature, severity, and frequency of the observed AEs should be discussed in this section. Any conclusions regarding a causal relationship (or lack thereof) to the product and laboratory findings should be mentioned. The potential for dependence, rebound phenomena, and abuse should be discussed. Management and outcome of overdose cases should be included.

- Rationale for F value calculation
  - Interpretation of the data and evidence (the case report or the MTD) used as the basis for calculating the F value is included here.
  - A justification for using the chosen case report followed by the calculation of an appropriate F value is discussed in this section.

- Conclusion
  - The conclusion mentions the F values assigned for the various strengths of the drug.

**Conclusion**

Despite the regulations and standards for CRP guidelines on determining the F value of oral pharmaceutical products are unavailable. This article discusses how our company has implemented best practices to determine F values amid various challenges, especially lack of pediatric data. Further scientific discussion is necessary to critically evaluate the various approaches used. Furthermore, the use of data and the required documentation processes should be standardized to effectively fulfill this important regulatory obligation.

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**References**

Lay titles for clinical trials: A balancing act

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Abstract
With increasing transparency demands and the new legal requirements for providing clinical trial information to lay readers, clinical trials need to be given titles that patients can understand and recognise. Trial titles inform the readers what the trial is about, what substances are studied, and who the target population is. Devising a lay title is challenging as it needs to be understandable to lay readers, fully identify the trial, meet registry requirements, and also be translatable into different languages. Lay titles also need to fit different types of documents, e.g. trial protocols, trial advertisements, informed consent forms, and lay summaries. As the lay title is one of the first pieces of information that is displayed, good lay titles help patients searching clinical trial registries for trial participation. For sponsors, informative and understandable lay titles increase the chances of attracting the target patient populations for clinical trials.

Every clinical trial protocol needs a title to define and identify the trial. This title serves as a point of reference within the sponsor organisation, with ethics committees, institutional review boards, and regulatory authorities. The scientific title is developed by the trial sponsor and is primarily written for medical experts who read the protocol and may become investigators in the trial. The scientific title therefore needs to provide a considerable amount of detail. It informs investigators about the objective of the trial, its main design features, the key characteristics of the trial participants, the medical procedures to be performed, and other information considered important. This results in trial titles that are complex and highly condensed, aiming to convey a maximum of information using technical language, sometimes with abbreviations and acronyms only familiar to medical specialists. The title usually includes specific trial features (e.g. randomisation, blinding, placebo, or active controls) to help identification within electronic databases. The CONSORT 2010 statement recommends including the word “randomised” in the trial title to ensure that the trial is identified as a randomised trial. Scientific trial titles, written for the scientific community, are usually too complex to provide insightful information to patients and the general public.

Increasing transparency demands and legal requirements for the provision of clinical trial information to the public, as well as the need to demonstrate scientific integrity, have led to the mandatory registration of clinical trials in public registries. In general, all clinical trials involving human subjects need to be registered before trial start. Many major medical journals will not publish results of trials that have not been registered. In addition to the scientific title, many registries require trials to have a version of the title that is understandable for the lay public. Most importantly, ClinicalTrials.gov requires that every trial posted must have a brief title “written in language intended for the lay public”. However, the terminology used by ClinicalTrials.gov is confusing as the word brief only addresses length restrictions and does not convey the notion of lay-friendliness that is required according to ClinicalTrials.gov instructions. We will therefore use the term “lay title”. Trial registries are searchable by patients and the title is usually the first and most prominent piece of information about a trial they will encounter. Attractive and understandable titles help lay readers decide whether they should continue reading or focus on other registry entries.

Trial titles that are understandable for lay readers are needed for several trial-related documents (see Figure 1). These include informed consent forms, trial advertisements, and lay summaries of clinical trial results. For the public, the lay title is the main identifier of a trial. Therefore it is important that each trial has only a single lay title that is used across all documents.

Lay titles and patient engagement
Depending on the disease, clinical trials are an important option for patients to receive innovative treatment. Patients who are searching for clinical trials need to be able to readily determine whether any given trial is of interest to them. For sponsors, it is important to inform potential participants about available trials as this supports recruitment and hence accelerates clinical development. The lay title is often the first element of contact between the patient and the

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trial. Sponsors of clinical trials have several ways to inform patients about trials they could participate in. In addition to large registries such as ClinicalTrials.gov, information about clinical trials is available via local and national trial finders and databases of hospitals, charities, and patient advocacy groups. Most of these databases include a lay title in addition to the scientific title, while some only include a lay title without providing the scientific title at all. Many databases import their data, including the lay title, directly from ClinicalTrials.gov. The words used in the lay title will therefore determine how likely a patient is to find the trial. As a consequence, the lay title might be the single most important sentence of a trial’s public posting. By ensuring that the lay title is informative and understandable, sponsors can attract the appropriate target patient population. This can be done not only via registry entries but also in trial-specific advertisements either online, in print media, or via other channels. To help potential trial participants understand the purpose of a trial, lay titles should also be used on informed consent forms or trial information leaflets.

In addition to the many uses of lay titles at the outset of clinical trials, lay trial titles are also relevant after completion of a trial. A good lay title will help sponsors to ensure that patients and their doctors can find the results of clinical trials they participated in or of other trials that are also relevant for them. Therefore, the lay title should also be mentioned on the lay summary detailing the clinical trial results.

What are the challenges in writing lay titles?

As mentioned above, trials should have a single lay title in all documents for trial participants and the general public. The most stringent requirements for lay titles seem to be those of ClinicalTrials.gov (see Table 1). The requirements of ClinicalTrials.gov concern both technical and content aspects for lay titles. Apart from the formal requirements, our experience is that ClinicalTrials.gov reviewers may sometimes have additional requests. Examples of such requests are that titles comprise a single sentence, that they should not have a full stop at the end, and that trial acronyms are included only at the end of the title.

Lay titles on ClinicalTrials.gov need to be unique.* This is important when searching for trials in order to differentiate between similar trials. However, it is more difficult to provide unique lay titles than unique scientific titles because lay titles mention fewer distinguishing features of a trial. Especially in the early stages of clinical development, individual trials may not differ much from one another and subtle differences between trials may be difficult to convey with their lay titles. Examples include the single rising dose and multiple rising dose Phase I

<table>
<thead>
<tr>
<th>Table 1. Lay title requirements by ClinicalTrials.gov</th>
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<tr>
<td><strong>Requirements for the brief title in ClinicalTrials.gov</strong></td>
</tr>
<tr>
<td>Technical requirements</td>
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<tr>
<td>Maximum of 300 characters including spaces</td>
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<tr>
<td>Has to be biunique</td>
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*These are expectations that have occasionally been provided as feedback from ClinicalTrials.gov reviewers. As this did not happen for all lay titles, these items seem to depend on the individual ClinicalTrials.gov reviewer.
trials, where the only distinguishing feature is how often the substance is taken.

Because of length and content restrictions, as well as the need to translate medical concepts into lay language, it is inevitable that lay titles deviate from the scientific title. The translation of complex medical or technical concepts into lay terms often increases word count and is one reason why a lay title can only provide a limited amount of detail about the trial. It may be difficult to include specific details on trial design, procedures, or patient population while adhering to requirements for length and lay language. As a result, some ethics committees might find that a lay title provided on the patient information or informed consent form does not include all important information, or that it is not consistent with the scientific title. The challenge for the sponsor is to find the appropriate balance between adhering to registry requirements, making the title understandable for the lay reader, and staying as close as possible to the scientific title.

How can sponsors write a good lay title?

A well-written lay title is not only easy to read but also informs the reader what the trial is about, what interventions are studied, and who the target population is. A poorly written lay title could mean that patients miss the opportunity to participate in clinical trials that could be of benefit to them.

There are a few general considerations when it comes to writing a good title. The title should be informative to the reader and as specific as possible.\(^9,10\) It should also be concise – not only to meet formal requirements, but also because short titles are more likely to make an impression with readers and to be remembered.\(^9,10\) Titles also need to be accurate and care must be taken not to be misleading about potential benefits of the intervention being investigated.\(^11\) Including details on the research design in the title may be informative but this usually comes as the expense of conciseness.\(^9\)

To ensure consistency and quality, lay titles should ideally be written by a single function. We believe that medical writers are best suited to writing lay titles. Medical writers as language experts can balance the competing aims of providing a title that is informative, compliant with regulations and guidelines, and understandable for patients. A key role of medical writers is to develop consistent standards and messages across a range of different documents. This also applies to lay titles. A good tool to ensure consistency across lay titles is a continuously updated repository of all lay titles that have already been provided by the sponsor. Collecting information about the trial, such as the scientific title, the clinical phase, or the indication can help immensely in the development of standards and in harmonisation across trial designs and therapeutic areas.

Content of a lay title

The lay title gives patients an immediate impression of what the trial is about. At a minimum, the lay title should include the name of the substance or intervention, the target population, and ideally the aim of the trial. For the name of the substance, the choice is between the international nonproprietary name (INN), the lab code, and the tradename. The advantage of the tradename is that it is most likely to be recognised by patients. However, tradenames can differ by country and region and might also change over time. Our recommendation therefore is to use the INN, but if no INN is available, the lab code could also be used.

The description of the target population usually means including the name of a specific disease or subtype of a disease. The names of common diseases (e.g. diabetes, asthma) are often well known to the general public and are therefore likely to be understood if included in lay titles. Rarer diseases and those with complicated medical names (e.g. palmoplantar pustulosis, non-valvular atrial fibrillation) will not be understood by members of the wider public but are likely to be known to patients with that particular diagnosis. To make the lay title meaningful for the wider population but specific enough for the target population, it can be helpful that the title includes both the wider concept of the disease as well as the medical name, for example “…in patients with the skin disease palmoplantar pustulosis”. If length permits, we recommend including additional details about the patient population. Including information on sex, required age range, or required background medication can all help the title address the relevant patient population.

Describing the aim of the trial within the constraints of a lay title can be challenging. We recommend focusing the lay title on the primary objective of the trial, even if that means losing some information that is provided in the scientific title. It is also useful to define standard phrases for specific scientific terms. For example, “pharmacokinetics” in the scientific title can be written as “how [substance X] is taken up by the body” for

### Table 2. Examples for lay titles for different trials

<table>
<thead>
<tr>
<th>Type of title</th>
<th>Example trial 1</th>
<th>Example trial 2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Scientific title</strong></td>
<td>Safety, tolerability, pharmacokinetics and pharmacodynamics of single rising intravenous doses of Testdrug in healthy male subjects (single-blind, partially randomised, placebo-controlled design)</td>
<td>A randomised, double-masked, double dummy, placebo and active controlled study to evaluate the efficacy, safety and tolerability of orally administered Testdrug for 52 weeks in patients with mild visual impairment due to center-involved diabetic macular edema (DME). ACRONYM1</td>
</tr>
<tr>
<td><strong>Sentence</strong></td>
<td>This study in healthy men tests how different doses of Testdrug are taken up in the body and how well Testdrug is tolerated.</td>
<td>This study tests how well Testdrug is tolerated and how effective it is. This is studied in patients with mild eye problems because of diabetic macular edema. ACRONYM1</td>
</tr>
<tr>
<td><strong>Title format</strong></td>
<td>A study to find a suitable dose of Testdrug in healthy men and to test how different doses of Testdrug are taken up in the body</td>
<td>Effects of Testdrug in patients with mild eye problems because of diabetic macular edema – ACRONYM1</td>
</tr>
</tbody>
</table>
the lay title. Such an approach also helps to achieve harmonisation across different trials. It might also be useful to consider how frequently certain words are used in everyday language.

To keep the lay titles for similar trials unique, adding the trial acronym is recommended, provided one is available. The disadvantage is that trial acronyms might be cryptic, difficult to read, and thus likely to cause confusion for a lay reader.11

The use of abbreviations in titles has both advantages and disadvantages. Abbreviations in lay titles could be perceived as helpful by laypersons because they reduce the number of complicated, technical words and might in some cases be more common than the long form (e.g., HIV). On the other hand, ClinicalTrials.gov requires abbreviations to be explained at first occurrence,12 which is technically the lay title.

**Format and structure of a lay title**

There are several structure and format considerations that authors need to think about when writing lay titles. One is whether to use a classic title format or a sentence (see Table 2). A sentence format might be easier to read for laypersons because complex information can be divided over two short sentences. The sentence format allows adding more specific details about the trial, which may help patients identify relevant trials and also helps keep titles unique. However, titles over two sentences or more are not always accepted by ClinicalTrials.gov reviewers (see Table 1). Furthermore, readers are often not familiar with a sentence format for titles and may even not recognise it as a title. The reason for this is that we are all trained to recognise a line of text as a title because of its location and its structure. In everyday life, titles do not follow the conventional sentence structure of subject, verb, and object. Instead, they are fragments of text that anticipate the subsequent content.

As the lay title will be used on documents at any time during the conduct of the clinical trial, it should be in the present tense. Titles should be written in the active rather than the passive voice because active voice is clearer and easier to understand.13

Lay titles often need to be translated to other languages. Some words and phrases are hard to translate into certain languages. In some cases a word for word translation might lead to a misleading description of the trial. As the translator might not be familiar with the medical content, it is important to use language that is as clear as possible.

**Conclusions**

Clinical trials need to have titles that can be easily understood by laypersons. A good lay title can help patients find an appropriate trial for their condition, and sponsors in the recruitment of the relevant target population for clinical trials. The lay title is the link between different trial-related documents from trial registration to the provision of trial results. Writing a lay title is a balancing act between registry requirements, readability for lay audiences, level of detail required and permitted, and reflecting the trial design and objective.

**Conflicts of interest**

The authors are employed by Boehringer Ingelheim Pharma GmbH & Co. KG. However, the views expressed in this article are those of the authors and do not necessarily reflect those of their employer.

**References**


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