

Improving Your Scientific Writing

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left handed, incorrect



right handed, correct

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1. Forward

Your job as a scientist involves more writing with each promotion. By the time you become a lab director, you spend most of your day writing papers, grant applications, recommendation letters, texts and emails. Despite the importance, many of us received little formal training, and write ineffective prose.

Few recognize how much work it is to write well.

In grant proposals, it is common to see sentences underlined or highlighted in bold letters. The Gates Foundation even requires underlining to mark the hypothesis of the proposal. This is only necessary because typical scientific prose is so wandering and wordy that it is difficult to extract the meaning. Underlining is a desperate last effort to communicate through the clutter. Millions of dollars are on the line with large grant proposals. Inept writing creates needless obstacles for many applicants.

We scientists need to create interest in our work. In 2017, according to one measure, the United States spent \$500 billion on science. The public has a right to know where their money is going, and a right to be grumpy if scientists can't justify the expense.

Scientists are uniquely qualified to educate the public on the most important issues of our day—think of global warming, human population growth, and global pandemics. To be successful, this requires effective communication.

Here I present suggestions for improving your scientific writing. Over the years I have given the same advice to young scientists again and again, and some have told me it was useful. Write in short sentences. Cut out every unnecessary word. Start paragraphs with strong topic sentences. One idea per paragraph. Simplify wherever possible. Let the facts carry the story.

My training came from writing classes, tough critiques from early mentors, firm guidance from professional editors, and feedback from readers. Much of the best advice I received parallels three classic works on expository writing: "Politics and the English Language" by George Orwell, "The Elements of Style" by Strunk and White, and "On Writing Well" by William Zinsser. Each of these is well worth reading today, though none are specific to scientific writing. There are guides to scientific writing (several are listed at the end), but I haven't found them as useful as the three classics. Furthermore, scientific writing has been changing, for example with the new focus on bioinformatics, Big Data, and AI, resulting in new challenges that are not covered well in published guides.

Here I update the three classics and apply their advice to contemporary scientific writing. In places this guide is tough going, working through examples of weak

prose or muddy figures and how to fix them. I've tried to make the text more inviting by mixing in examples from really great scientific writing. In a few places I've also added extreme or even outlandish examples from other sources to amplify the main points and add interest--Chapter 2 features a run-on sentence of 126 words that is actually good; Chapter 8 presents what may be the worst explanatory diagram ever made; and Chapter 8 further features several DNA tattoos that are unfortunately the mirror image of the correct structure.

This booklet starts with the elements of editing, emphasizing removing clutter to highlight your content (Chapter 2). Chapters 3-6 discuss the specifics of writing research papers, grant applications, graduate preliminary exams, and emails. Chapter 7 reviews usage of words and phrases that are commonly problematic in scientific writing. Chapter 8 deals with the visual display of quantitative data--here the aesthetic is the same--removing clutter emphasizes the main points and allows addition of more content. Chapter 9 presents a few points on writing and thinking. Chapter 10, newly added in January 2023, discuss the challenges presented by ChatGPT, an artificial intelligence program that can write clear prose and edit effectively. Additional material includes suggested reading (Chapter 11), editing exercises (Chapter 12), and samples of letters important in managing scientific publication that may be unfamiliar to young scientists (Chapter 13).

2. Editing

The simpler the better.

Simplify. Every dispensable word you remove highlights your content. In Zinsser's words:

"Few people realize how badly they write. Nobody has shown them how much excess or murkiness has crept into their style and how it obstructs what they are trying to say. If you give me an eight page article and I tell you to cut it to four pages, you'll howl and say it can't be done. Then you'll go home and do it, and it will be much better. After that comes the hard part: cutting it to three".

William Zinsser, in "On Writing Well".

Even for experienced writers, it is remarkable how much of a first draft can be cut out with hard work, and how much the shortening improves the final product.

In the next sections of this chapter we first go over writing effective sentences, then merging sentences into paragraphs. The chapter ends with some general points on editing.

WRITING AND EDITING SENTENCES

Write in short sentences

Keep sentences short. Short sentences are easier to read than long sentences, and they help keep your own thoughts in order. Wandering muddy sentences reflect wandering muddy thinking. All the great scientists I've known wrote in short declarative sentences.

For example, here is the first sentence of Crick and Watson's paper on the double helical structure of DNA.

"We wish to suggest a structure for the salt of deoxyribose nucleic acid (DNA)".

Crick and Watson¹.

DNA is a polyanion, so a cation is commonly added to neutralize the charge in water, thus "salt" is the precise description. They also use the first sentence to define the abbreviation "DNA". Just 14 words suffice to introduce the advance in the paper and address two technical points needed in what follows.

It is possible to write well in run-on sentences, but it's rare. David Foster Wallace was famous for run-on sentences. In the below, "Ennet House" is a halfway house for recovering addicts; "AA" is "Alcoholics Anonymous".

"Gately's biggest asset as an Ennet House live-in Staffer—besides the size thing, which is not to be discounted when order has to be maintained in a place where guys come in fresh from detox still in Withdrawal with their eyes rolling like palsied cattle and an earring in their eyelid and a tattoo that says BORN TO BE UNPLEASANT—besides the fact that his upper arms are the size of cuts of beef you rarely see off hooks, his big plus is he has this ability to convey his own experience about at first hating AA to new House residents who hate AA and resent being forced to go and sit up in nose-pore-range and listen to such limply improbably cliched drivel night after night".

David Foster Wallace "Infinite Jest".

Run on sentences can make for intriguing post-modern fiction, but are usually confusing in scientific writing. If you are just getting started, use short sentences only. As you become more experienced, it can add interest to vary the length of your sentences. David Foster Wallace's prose, for example, often involved short sentences—he just cut lose once in a while with a really long one. Sometimes you can make a point in one longish sentence instead of two shorter ones, and use fewer words in the process.

Variety can add interest, but mostly keep sentences short.

As a last example, consider the start of Martin Luther King's famous speech from the March on Washington in 1963:

"I have a dream."

Martin Luther King, from the steps of the Lincoln Memorial.

Just four words, each of a single syllable, were enough for a riveting start.

Weak intensifiers always hurt you.

Avoid using "very, interestingly, strikingly, new, novel, excitingly..." Only the content itself can be interesting, striking, or novel. Editorializing—proclaiming your opinion that something is interesting or whatever—only invites skepticism. Many scientists go their whole careers without catching on to this. The only route forward is to provide interesting content, and let readers conclude for themselves that it is interesting.

Annoying intensifiers can also have an emotional coloration, as in "I deeply believe in the importance of cancer research". Imposing your emotions on others

in a professional context is manipulative, and in me elicits the opposite of the hoped-for effect—quit jerking me around and explain why cancer research is important or I'll find something else to read.

Some words are always dispensable

Here is a sentence from a paper on the growth of carbon nanotubes.

“These results suggest that it would be fundamentally difficult to achieve a fast growth with a long lifetime.”

Here is the sentence without “fundamentally”?

“These results suggest that it would be difficult to achieve a fast growth with a long lifetime.”

There is no difference in meaning between “difficult” and “fundamentally difficult”. The two sentences differ in that the first contains a useless word of five syllables. The sentence also has other problems—the authors should have written “fast growth rate” instead of “a fast growth”, or still better something more specific.

Always delete “fundamentally” from your writing. Similarly, delete “certainly” and “basically”. “Basic” is fine when it means high pH, but not when interchangeable with “fundamentally”. Scrutinize your prose for additional words that add nothing and can be deleted.

Verb tense

Be careful to keep verb tense consistent within sections of a paper or written piece. For example, the Results section of a paper is usually in the past tense, because the experiments have already been done. General principals disclosed by experimentation can be described in the present tense, since the conclusion is ongoing. Be consistent.

Don't start sentences with long modifying clauses.

Here is a painful example:

“Using phosphorescence imaging as a form of biological oximetry, we confirm the oxygen poor environment of the gut lumen and demonstrate the existence of a dynamic equilibrium with an established gradient whereby the mammalian gut releases oxygen into the gut lumen”.

Anonymous, early paper draft

A reader will likely need to read the sentence several times to get the meaning.

The much shorter revision below, which lacks the modifying clause, captures most of the content:

“We used phosphorescence imaging to characterize oxygen gradients in the gut lumen and found higher levels near the gut wall”.

Here is a simple declarative sentence from a published paper:

“Escherichia coli IHF protein is a prominent component of bacteriophage lambda integration and excision that binds specifically to DNA”.

Goodman, Nicholson, and Nash⁵

The Nash sentence introduces several points but is clear in one reading.

Starting with long modifying clauses will usually require the reader to go back and reread the sentence once they know from the second half what the first half was modifying.

Get to the subject and verb early

Consider the following difficult sentence:

“Here, a study of microbial communities inhabiting mangrove sediments across southeastern China, spanning mangroves in six nature reserves, was conducted.”

Rearranging to place the subject and verb early in the sentence improves clarity:

“We conducted a study of microbial communities inhabiting mangrove sediments in six nature reserves in southeastern China.”

Rephrase for brevity

Editing is hard work. Below are three before-and-after examples. The first is a wordy paragraph I wrote in a 1999 review article on retroviral integration⁶. “PIC” stands for “pre-integration complex”; “integrase” is an enzyme encoded by retroviruses.

1) Original: “Much interest has centered on the question of whether host proteins are important for the function of PICs in vivo. This article will first review proposals for important proteins arising from studies of PICs, then review studies employing reactions with purified integrase. Proteins thought to influence integration by binding target DNA will be considered in a following section”. (58 words)

Here is a version rephrased for brevity that is also more accurate.

“Are host proteins important for the function of PICs? Below I review proposals derived from in vitro studies of 1) PICs, 2) purified integrase, and 3) purified target DNA binding proteins”. (31 words)

The next two examples are contrived for this work with the goal of illustrating specific editing steps.

2) Original: “A wide variety of factors influence the success of treatment of multiple human cancers.” (14 words)

Rephrased: “The success of cancer therapy is affected by multiple factors.” (10 words)

Phrases like “A wide variety of...” can usually be replaced by reorganizing a sentence. The thick phrase “...influence the success of the treatment of...” is clumsy and again invites rewording and shortening. The rephrased declarative version is four words shorter and the meaning clearer.

3) Original: “Based on data presented here and the published literature (21-23), we propose a model in which HIV can exploit binding to multiple cell surface proteins to enter cells efficiently.” (29 words).

Rephrased: “Evidently HIV can bind multiple cell surface proteins to facilitate entry (this work and 21-23)”. (15 words).

The phrase “we propose a model in which” is a careful statement of the scientific process, keeping distinct the data and ideas about what they mean, but the phrase is also wordy. Consider “evidently” as a one-word summary for “based on evidence”. The long initial modifying clause (“Based...”) is difficult and offers an opportunity for rephrasing for brevity. Clarifying that others have made the same point as in your paper is delicate, but the parenthetical clause is shorter and adequately respectful.

Chapter 11 presents three examples that you can try to edit, then compare your edited text to revised versions that are presented on following pages.

Pompous opinionating is particularly inviting to cut. Just get rid of all of it and let the facts carry the story. Mark Twain, traveling in Europe, became heartily sick of the vague language sophisticates used to discuss famous paintings.

Commenting on one masterpiece, he wrote:

“The colours are fresh and rich, the ‘expression’, I am told, is fine, the ‘feeling’ is lively, the ‘tone’ is good, the ‘depth’ is profound, and the width is about four and a half feet, I should judge.”

“The Innocents Abroad”, Mark Twain, 1869.

In technical writing, we would cut the above to “The painting is ~4.5 feet wide”.

Minimize novel abbreviations

Inexperienced writers seem to find it exhilarating to define novel abbreviations. I’m saving words! Maybe my new abbreviation will be the next IBM!

The trouble is that each time you encounter a novel abbreviation, you need to make the effort of remembering the new coinage. This may be OK for one, maybe two new abbreviations. Beyond that readers rebel, continuing to read without remembering the abbreviation, progressively losing the thread. It doesn’t take long to until they give up.

Instead make it easy—minimize new abbreviations, or eliminate them altogether.

When to spell out numbers

Most scientific papers will include numbers. Write out all numbers less than 10 (i. e. “nine” not “9”). Write out any number at the start of a sentence. For sentences starting with long numbers, it is usually best to rearrange:

“Four hundred and sixty one samples were analyzed” can be changed to “We analyzed 461 samples”.

If you are going to reuse tired phrases, at least learn what they mean.

How often have lazy scientists written that “A is the hallmark of B”? Did they know what a hallmark actually is? Do you? In Great Britain, in the Renaissance, metal workers banded together into guilds that worked out of guildhalls. They would stamp a mark specific to their hall onto completed gold and silver pieces—the hallmark. In saying that “A is the hallmark of B”, how often do writers really mean “stamped on logo”? In my experience, not often.

Another is “paradigm shift”. I once heard an NIH grant review administrator go on at length on how high-scoring grants must represent paradigm shifts. She had no idea how much baggage the term carried.

“Paradigm shift” was introduced in 1969 by Thomas Kuhn in “Structure of Scientific Revolutions”, in which he argued that science is not cumulative. His view was that some revolutions were so profound that they falsified everything that went before (think of gravity before and after Einstein). To make this work,

he had to separate technology (which clearly is cumulative) from science, which seems to me a bit forced. The NIH administrator had no idea she was demanding that reviewers only support research that falsified large fields—what she dimly intended to support was really high impact science.

Compare the vision of a government clerk talking about “paradigm shifts” to David Foster Wallace’s description of guys in withdrawal with “eyes rolling like palsied cattle”. My recommendation is to avoid using “hallmark”, “paradigm shift”, and all similar tired metaphors and phrases. Because of blurry overuse, different people will interpret these differently, causing confusion. Just say what you mean simply and precisely, or find a new image (“palsied cattle”) that is particularly apt.

WRITING AND EDITING PARAGRAPHS

Start paragraphs with punchy topic sentences.

A topic sentence should introduce and summarize what follows in the paragraph. You can’t compress the whole paragraph into the first sentence, but you can indicate what is to follow and create interest. Think of the hook in the first paragraph of a newspaper article. Ideally, reading through the topic sentences alone overviews the whole piece.

Here is an example of a poor topic sentence:

“The bacterial microbes that inhabit the intestinal tract, together with their genes and the environment collectively known as the gut microbiome, is a densely populated and complex community dominated by obligate anaerobic organisms from both the *Firmicutes* and *Bacteroidetes* Phyla.”

Anonymous, *early paper draft*.

A reader groans—slogging through such lengthy and tortuous sentences for a whole paper will be an ordeal.

The next example, in contrast, is simple and to the point:

“The repressor of bacteriophage lambda is a protein containing two domains of approximately equal size.”

Mark Ptashne and coworkers²

After reading this sentence you expect another short sentence that expands on the function of lambda repressor and begins to develop the direction of the paper.

End paragraphs with sentences that collect what was important and set up what follows.

Consider the last sentence of the abstract of Howard Nash's classic bend-swap paper:

"In recent years the capacity of proteins to bend DNA by binding to specific sites has become a widely appreciated phenomenon. In many cases, the protein-DNA interaction is known to be functionally significant because destruction of the DNA site or the protein itself results in an altered phenotype. An important question to be answered in these cases is whether bending of DNA is important per se or is merely a consequence of the way a particular protein binds to DNA. Here we report direct evidence from the bacteriophage lambda integration system that a bend introduced by a protein is intrinsically important. We find that a binding site for a specific recombination protein known to bend DNA can be successfully replaced by two other modules that also bend DNA; related modules that fail to bend DNA are ineffective".

Goodman and Nash³

The final sentence both presents the main data and serves to wrap up the story. Nash had the guts to end his abstract describing a control, confident that the simple presentation of the idea and experiment made further comment unnecessary. How many less secure writers would have gone on to add "Thus we conclude that the data supports a hypothesis in which..."? Nash's last sentence leaves a reader eager to continue on to the main text.

One idea per paragraph

Help your readers by presenting a single idea in each paragraph. When editing, it is often possible to improve your prose by breaking a lengthy complicated paragraph into two or more shorter paragraphs with one idea each. It is fine to write paragraphs with only three sentences, or even two or one.

To avoid the underlining mentioned in the introduction, consider creating a short paragraph presenting each idea you wish to emphasize. That way the prominence of the topic sentence adds emphasis while allowing the prose to read more smoothly. To be fair, opinions do vary among good scientific writers on the virtues of underlining—more on this in the chapter on grants.

Avoid starting with lengthy generalizations.

Mark Ptashne tells a story of his experience writing a review article for editor Al Hershey (Nobel laureate). Hershey was a leader in the lambda field, and Mark the rising star. In Mark's words⁴:

"I wrote a 20 page paper for him and got it back with most lines crossed out and the occasional phrase circled and marked 'Good'. So I rewrote and rewrote and it came back with not a mark on the first page! Not a mark on the second! Then the third page: a line through the middle, a penciled-in 'START HERE', and then most lines thereafter crossed out."

Inexperienced writers often begin with lengthy generalizations, and only get to specifics part way in. It is usually best to get to the facts as early as possible. Be confident that the general points will be implicit in the specifics.

Cutting deadwood makes possible more cutting

When editing is going well, you sometimes find upon rereading that you can dispense with a lot more text. As the meaning becomes clearer, you don't need to keep reminding readers of stuff that is already fixed in their minds--you can just cut out the unneeded reminders.

FURTHER CONSIDERATIONS

Scientific writing and gender.

Women comprise half of the population but are under-represented in top positions in science. The Hopkins Report disclosed that from 1985 to 1997, the MIT faculty was comprised of less than 10% women. Despite the report, by 2011 the proportion had risen to only 19% women. The history of gender discrimination at MIT was the topic of the Pulitzer Prize winning book "The Exceptions", by Kate Zernike, which is an excellent example of clear expository writing.

In scientific writing, it is common to see the masculine "he" or "him" used when both women and men are intended. The sexist use of "he" for both genders is grating like fingernails on a blackboard--inaccurate writing that also highlights gender inequity. Of course, there are cases where gender-specific pronouns are correct and necessary, as in a medical case report on a female participant. However, "he" appears to be overused in the scientific literature. On June 27, 2015, I carried out a PubMed search using "he" as a keyword, and obtained 132,253 hits. A search on "she" yielded only 87,810 hits.

So what to do? There is no single answer. Substituting "he" with "he or she" is one solution, though wordy. "They" is often used today, and may be a simple solution in some cases.

Often it is possible to rephrase a sentence to avoid sexist language. Zinsser was eloquent on this point—he recognized that early versions of "On Writing Well" contained sexist sections, and in later editions he described a variety of remedies. "Where a certain occupation has both a masculine and feminine form,

look for a generic substitute. Actors and actresses can become performers”. “You guys” can become “you folks”.

In summary, gender bias is part of the history of science and is with us today. Learn to recognize sexist language and rephrase to avoid it.

Respectful person-first language

Language surrounding clinical research has been undergoing extensive re-examination. Many phrases used historically are now recognized as insufficiently respectful. For example “research subjects” is dehumanizing, blurring the line between humans and lab rats.

The preferred solution is “person-first” language. “People living with HIV” is preferred over “HIV-positives” because it emphasizes the humanity of the people involved. “Research subjects” can be replaced with “participant” or “volunteer”, emphasizing the agency of the people involved.

A guide to respectful person-first language once could be found on the NIH web site, but it was taken down following the Trump inauguration. The guide is now appended to the end of this PDF (“HIV Language Guide”). The guide is focused in part on HIV research, where many of these points have been energetically discussed, but the language guidance applies to biomedical research broadly.

Avoid over-condensing your writing.

It is possible for writing to be over-condensed. You do need to anticipate questions that a reader may have and write in a way that answers them. Give your readers what they need to follow your points, and do so in short simple sentences. It is fine to use an occasional sentence as a road map, telling the reader what follows and why. Be a generous guide, while keeping your prose spare and effective.

In math and chess, it is common to see phrases like “the rest of the proof is obvious” (which it often isn’t), or in chess “the win is now a matter of technique”. This is arrogant grandstanding designed to highlight the intelligence of the writer. It is also cowardly—if you wrote out how to win the chess game, you would be exposing yourself to the possibility that another player could find a hole in your analysis. Far better to briefly spell out the specifics.

In “In Defense of Food”, Michal Pollan condensed all the advice in his book into three short sentences: “Eat food. Not too much. Mostly plants.” To unpack a little, by “Eat food” he meant avoid rebuilt chemical confections from the food industry (Twinkies etc.). “Not too much” and “Mostly plants” are self-evident. All of an outstanding book condensed into three short sentences. Is this over-condensed?

The whole book is well worth reading, but I think the seven word summary is useful, and even brilliant.

Recognize and enjoy outstanding expository writing

Great expository writing is great art. Here is the entire introduction to Hershey's paper on the discovery of circularization of phage lambda DNA.

"Aggregation of DNA is often suspected but seldom studied. In phage lambda we found a DNA that can form characteristic and stable complexes. A first account of them is given here".

Al Hershey⁷

A perfectly appropriate introduction section in three short sentences.

Also from the lambda field, here is an outstanding short abstract from Mark Ptashne.

"The lambda phage repressor is both a positive and a negative regulator of gene transcription. We describe a mutant lambda phage repressor that has specifically lost its activator function. The mutant binds to the lambda phage operator sites and represses the lambda phage promoters P_R and P_L . However, it fails to stimulate transcription from the promoter P_{RM} . The mutation lies in that portion of repressor--namely, the amino-terminal domain--that has been shown to mediate stimulation of P_{RM} . We suggest that the mutation has altered that region of repressor which, in the wild-type, contacts RNA polymerase to activate transcription from P_{RM} ".

Guarente, Ptashne and coworkers⁸

Orwell's Rules

George Orwell ends "Politics and the English Language" with six rules for writing clearly, which are as pertinent today as in 1946. Orwell's rules make an appropriate finish here.

1. Never use a metaphor, simile, or other figure of speech which you are used to seeing in print.
2. Never use a long word where a short one will do.
3. If it is possible to cut a word out, always cut it out.
4. Never use the passive where you can use the active.

5. Never use a foreign phrase, a scientific word, or a jargon word if you can think of an everyday English equivalent.
6. Break any of these rules sooner than say anything outright barbarous.

3. Writing scientific papers

This section presents specific advice on writing a scientific paper. There are many ways to do so, and approaches vary among experienced authors. I recommend the recipe below for those just starting out.

Generating a draft

Begin by writing an outline. Use separate headings for Introduction, Materials and Methods, Results, Discussion, and Figure Legends. List the main points for each section under the appropriate heading. Discuss the outline with mentors and colleagues.

Writing the text requires a clear idea of the overall direction and the specific data to be included. What is the main story? Writing the outline focuses attention on your most important points.

The next step is to work up relatively final versions of the figures and figure legends. Show the figure prototypes to coauthors and coworkers. Edit based on common reactions from experienced commentators.

Next write the Materials and Methods. After completing the Figures and Materials and Methods, the experimental content of the paper should be fairly clear.

Then write the Results. The text proceeds with a sequential discussion of each Figure. End the section on each Figure with a brief statement of the conclusion, but leave detailed interpretation for the Discussion section.

Next write the Discussion. The first paragraph is typically a summary of the main findings of the paper. Additional paragraphs expand on the interpretation and relationship to previous work. Don't just repeat the Results section—instead focus on questions like “what can we do now that we have this new data” or “what gap in previous knowledge is now filled” or “what surprises did we encounter”.

Then go back and write the Introduction. Keep it relatively brief—just enough to get things started. Explain why this study addresses an important question.

At this point, show the draft to coworkers. Go through cycles of editing until the draft becomes easily readable and the main points plain and obvious.

Around this stage the references can be put in. I use Endnote. Make a separate database for each paper (big databases can lead to big problems).

Once the manuscript draft is in near-final form, circulate it to lab members and colleagues for comments. Then carry out another round of editing based on comments.

Finishing a paper is a lot of work. Everything needs to be consistent—it is amateurish to have “Fig.”, “Fig”, and “Figure” in the same paper. Reviewers notice. Italicize Linnean names according to standard conventions (check Wikipedia or PubMed on usage if uncertain). Search on in-text markers (I use XXX) to get out all marked comments. Make sure all spelling is correct. If using Microsoft Word, remove all the trash Microsoft adds to documents (comments, marked edits etc). Check each figure call out. Check that the references are consistent—for example, database screw-ups often result in duplicating references in the final list. Check that all figures are of high quality after uploading to the journal and downloading the final PDF.

It is important to check and adhere to the Author Instructions for the journal selected for submission. Check the order of elements and reference style of the journal to which the paper will be submitted--if the wrong journal format is used, the editors might think paper was already rejected by another journal. You need to adjust each of these items for each journal submission

Take responsibility for producing a clean submission-ready document.

Plagiarism

It is not rare for prose in one scientific paper to be similar or identical to prose in another. Sophisticated software for detecting plagiarism is available online (e. g. <http://plagiarism.bloomfieldmedia.com/wordpress/software/wcopyfind/>) and regularly run over the scientific literature. Findings are reported. If a researcher is found guilty plagiarism, severe punishment is likely.

Don't take chances. Never copy paste prose from others into your work. Check prose sections contributed to your papers by collaborators if you have any suspicions. Don't even copy paste from your own papers—rephrase sections despite the fact that they may be saying the same thing.

Writing about statistics

For your results to be convincing, it is important to carry out and document statistical analysis of your data. All measurements are a mixture of signal and noise. It is usually necessary to carry out replicates of experimental and control measurements, and assess the outcomes statistically by comparing variation

within each condition to variation between conditions. Construct your prose around how you reject the null hypothesis of no difference between groups.

There are various ways of presenting statistical analysis. I suggest a detailed presentation in the Results section of the main text. After all, you are trying to convince a reader of the soundness of your conclusions, and it is the statistics that do the job. There are cases where analysis may be better placed in the Figures, Methods, or Supplemental sections, but I favor the Results where possible.

As an example of good style, here is a sentence from a paper by Jeff Gordon and coworkers on immaturity in the microbiota of malnourished children⁹.

“Family membership explained 29% of the total variance in relative microbiota maturity measurements (log-likelihood ratio=102.1, $P < 0.0001$; linear mixed model).”

The paper set up an index to quantify maturity of the gut microbiota, then applied it to their samples. As they say, one of the most important determinants turned out to be family membership. They report on the effect size (29% of the variance), the log-likelihood ratio, the statistical significance as the P value, and the test used. Insertion of the parenthetical details does disrupt the text slightly, but it answers the question “why should I believe this”, which to me outweighs the downside of the interruption.

Unpacking the above a bit more—p values conflates sample size and effect size. It is possible to have highly significant differences that are tiny effects. This is part of the basis of Mark Twain’s grumbling about “lies, damn lies, and statistics.” Gordon documents the effect size by specifying the amount of the variance explained. There are many types of statistical tests, and often more than one can be applied to a particular data type. Thus it is important to specify the test used as well.

Note that writing the statistics out carefully allows economies in other areas. There is no need to say “Family membership significantly...”. The P value not only establishes that the result is significant, but quantifies how significant. With a clear explanation in the Results, the presentation of statistical approach in the Methods or Supplemental section can be truncated.

Responding to reviewers’ comments.

Research papers are typically submitted for peer review, then comments come back to the authors. The paper may be rejected outright or accepted subject to revision and re-review as specified in the reviewers’ comments. If the paper is rejected, you need to resubmit to another journal. Don’t despair! Many famous papers have been rejected as early submissions. An important component of

success in science is the ability to withstand rejection and keep moving forward. There is always another journal, and the quality of the editorial staff is famously uneven.

If the editors indicate interest in a resubmission, then the text is modified based on the reviewers' comments. Reviewers may ask for more experiments and data, more explanation of the results, or clarification of specific points. In responding, be careful to address to every comment. Remember that the paper will likely be reread by the first round reviewers, and that this is burdensome for them. Reviewing is a duty to the scientific community, but it takes time away from other activities. Write responses to every comment as a gesture of respect. Say clearly how you changed the paper in response to feedback. If you don't, your reviewers may well respond unfavorably.

Slogging through a response to reviewers' comments can itself be slow and annoying. You recruit support by keeping your responses clipped and short while doing a thorough job of addressing the reviewers' comments.

Add data

Responses to reviewers' comments are always strengthened by saying you added more data. Find something to add, and mention it in the first paragraph of the response letter. It doesn't need to be a major new finding. Additional data does need to be meaningful and is best packaged as a response to reviewers' comments, but this can take many forms. Create a favorable first impression.

4. Writing grant applications

There's a lot on the line when scientists write grants, often millions of dollars. Effective grant writing can have a huge effect on your career. If you write effective grants you are expanding and pushing frontiers. Struggle for funding and you are dragged into a grinding battle to survive.

The effect of good writing on grant success is hard to overstate.

Imagine a grant review committee. Reviewing grants is pretty much torture. The writing of the typical applicant is so outlandishly bad that making it through is like climbing Mt. Everest. The rare well-written grant, in contrast, can be an enjoyable opportunity to learn about advanced ideas in an unfamiliar area. Grant reviewers respond strongly to well written grants, often without fully realizing that they are doing so.

You can greatly improve your chances of success by writing strong prose. Below are a few tips.

Write simple prose

The recommendations for simplicity in earlier chapters apply with particular force to grant applications. Write in simple short sentences. Edit out every unnecessary word. Write simple short paragraphs with one idea per paragraph. Let the facts carry the story.

Write readable prose and you are way ahead of the competition.

Follow the instructions

Read the instructions carefully, and talk with grant administrators at the program to which you are applying. It is their job to work with you, so don't be shy about cold-calling them. Most are well-meaning and glad to help. Hopeless applications are no fun for them either.

Work hard to figure out what the funding agency is seeking to support. Explain in clear simple prose why your proposal is aligned with the agency's goals. Work with grant administrators to craft a proposal that matches what they want to fund.

Propose a hypothesis

Historically the scientific process has moved forward by hypothesis generation followed by rigorous testing of the implications. If tests fail to falsify predictions generated by the hypothesis, then the idea moves toward provisional acceptance. In later stages, if an idea can form the basis for new technology, it achieves considerable further support.

For grants, it is generally expected that you will propose a hypothesis and approaches to testing it. A strong grant will usually have a strong hypothesis, stated early on, along with specific experiments to test key predictions. Failure to state a clear hypothesis will usually result in a poor score.

There are exceptions. For example, there can be grant calls specifically targeted to developing a new technology, or creating a clinical cohort to gather comprehensive specimens to interrogate aspects of disease or health. Even here, it is often expected that a hypothesis will be grafted on—check with program staff at the granting agency for their thoughts.

All this can feel a bit off given contemporary research strategies. Today it is common for researchers to generate rich large data sets, and then use them to address many different hypotheses. Nevertheless, for the purpose of grant proposals, it is still usually best to articulate a hypothesis, even if it only captures a subset of the goals of the study.

Write to recruit support for your proposal.

Study sections are tough. Imagine a room full of mid-career scientists who have been going over poorly written prose for many hours. People are tired and grumpy. Maybe the same two panelists have been bumping heads all morning. Today NIH doesn't even provide coffee, making things even worse.

There are far more good grants than there is funding. This is well known to the study section members, adding to the gloom.

There is no hope of getting your grant application funded unless it earns the support of an advocate on the review panel. Someone on the panel needs to read your grant and be genuinely excited about it, so that they step up and support your grant before the group. If something new and exciting comes along, it lightens the mood, relieves the depression, and recruits the support of all involved. To be funded, yours needs to be that grant.

So write with your advocate in mind. Most scientific projects are well conceived and have some clever technology involved. Write in a simple and clear way to describe the goals of the project and why they are important. Explain new technology in detail, so that anyone could understand it. Explain in an honest way why you are excited about it. Hit the main points as early as possible.

Remember that your advocate on the panel needs something relatively simple to relay to the study section, most of whom have not read the grant. Write out a simple factual pitch for why your idea is a major advance. Elsewhere, in the more technical sections, explain to specialists exactly what you are going to do and why they should believe your goals are achievable.

This may sound daunting, but the competition makes you look good. If you can describe an exciting project in simple effective prose, you have a strong chance of obtaining funding.

To underline or not to underline?

I try to avoid highlighting text in grants by underlining or bold lettering, but I'm in the minority. Underlining seems to me unnecessary if the prose is well written. Instead I use paragraph structure to highlight important sections. By writing short paragraphs, each with a single idea, you can use the topic sentence to highlight your point. So why disrupt your text with cheesy underlining?

However, good grant writers have argued this with me, and I think they have a point. Think of a tired grant reviewer trying to remember what they liked about a grant among the dozen they read. It may be easier to glance over the highlighted sentences to review the main points, then relay these points to the committee. Given the burden on grant reviewers, the argument goes, anything to make it easier is useful.

You can make your own decision.

Avoid inverted pyramids

When a funding agency supports a project, they want there to be a return on their investment. If a project might fail completely, then it is unlikely to be funded. As a result, the review process is quite conservative.

A common source of problems is the “inverted pyramid”, where a key experiment needs to work for the downstream investigation to be warranted. What if the key step doesn't work? The whole research program is finished, and the grant money wasted. If your proposal is judged to be an inverted pyramid, it will usually receive a poor score.

There are various solutions for this. The best is to work through the pivotal experiment in advance of funding, then explain in your proposal how your preliminary data makes possible the downstream steps. Another is to propose multiple routes to the same goal, so that you are not dependent on any one experiment working. Ideally, you can use your preliminary data to bolster the idea that the program is feasible.

Inverted pyramids are a common pitfall for new grant writers. After you write a proposal, get away from it for a bit, then reread to check for inverted pyramids. If necessary, rewrite or generate new data to strengthen the case.

Get way back and get way in—minimize the middle ground

It is common for inexperienced grant writers to write much of their application at a middle level of detail. Writers jump right into the problem, and explain mechanism in vague conceptual diagrams. Experimental details are presented in a general sense only. This can be dull and ineffective.

Far better is to get way back from the data and describe why yours is an important question, then get way in and be specific about the engineering involved, particularly for the most novel parts.

Some of the best lectures I've heard were by Matt Meselson in the 1980s, and the same aesthetic holds for scientific writing. He used relatively few slides. At the start, he walked forward from the podium, sat on the edge of the stage, and described at some length why he began the research projects he planned to present. He discussed his thinking leading up to the study, conversations with other scientists, and how he ultimately began experimentation on the topic. This was followed by a small number of slides describing key pieces of new data. In presenting each slide, he described the x and y axes, and went over the distribution of data in each graph in an unrushed fashion. This was followed by a sophisticated discussion of the relationship of data to ideas, models for causality, and a realistic assessment of the importance.

It is painfully common today to see scientists in lectures waving at ultra-complicated slides and summarizing the conclusions, usually in a rushed tone. This is then followed by another slide with many complicated graphs, and no orderly discussion of the blizzard of details.

Grants applications are often the equivalent. Over-compressed in both the conceptual and technical parts, boring and baffling at the same time.

Say in a careful way why you care about the problem, then describe the engineering in depth. Get way back, and get way in. Use short simple sentences that follow one another in an orderly fashion. With a little practice, your grant can be the one that brightens up a study section.

5. Writing preliminary exam proposals

Students in PhD programs will typically take a preliminary examination at the end of their second year. The exam can take many forms. At the University of Pennsylvania, in the Microbiology, Virology, and Parasitology program, preliminary exams take the form of a grant proposal describing planned thesis work. The proposal is refined in consultation with faculty and students, then defended in front of a faculty panel.

A well-written prelim proposal will be a good grant proposal, and the advice on grant writing applies to prelims as well. Present a thoughtful and testable hypothesis. Avoid inverted pyramids. Get way back, and get way in. Write clear and simple prose. There are, however, a few features that are more emphasized in Prelim proposals.

You are documenting your scholarship, so be careful to include all the main citations in your field. Be prepared to answer questions on background. Similarly, on the engineering side, explain in professional terms the engineering steps required, and be prepared to answer questions. Committee members will likely keep quizzing you until they reach the limits of your knowledge. Don't be afraid to say you don't know, but this sounds much better if you have described a bunch of important factual information before getting there. Typically the most important facts are written into the proposal up front.

Don't be boring. Students presenting in front of faculty often take a very conservative approach, in the hope that they will be less exposed to criticism. This can erode support, because over-conservative proposals are usually dull. Be clear on why your work will result in high impact papers. If it will not, find a better project.

The committee will want to see some doable sections to the prelim, so that they believe the student can complete the PhD, but it is also important to put in ambitious studies that might not work. Just be clear that you are aware that some of the proposed experiments are hard, and that you will re-prioritize if things don't go well. Many huge advances were only possible because a talented fanatic confronted a gigantic challenge. Think of Barbara McClintock discovering transposons, gene control, and epigenetics all at the same time. It is OK to say that you are taking on a daring challenge--just make sure your committee is also convinced that you can complete a doctoral degree.

6. Writing emails

Write simple emails.

Email is murder. I receive hundreds of emails a day. It's gotten to the point where I think of dealing with the onslaught as "killing" emails as I process each one.

When you write an email, think of the recipient who is dealing with this deluge. The goal of the email recipient, as they open your message, is to carry out what needs to be done as quickly and simply as possible, then get on the next damn email.

For this reason, professional email needs to be distilled and simplified. Indicate what the point is in the subject line. Aim to write the minimum number of words that achieves the job that needs to be done. Write in complete sentences to avoid confusion about who is doing what. Provide any needed context and background at the start, so that the business to be done is easily grasped on first reading. Jaunty jokes and blurry personal references can obstruct communication in professional email.

For example, consider this email announcing a seminar on limb transplantation:

"Given the number of times you said that you'd give an arm or a leg for something, compared to the number of limb transplants actually performed, I'd have to say, really? And yet, there is a chance to redeem yourself, or at least to calibrate your bargaining position. Today's speaker does limb transplants and more..."

It is just annoying to wade through someone's free association to get to the point. Even if you succeed you often are only 80% sure you understood the intended meaning. In the above email, you need to read through two needless sentences to get the point. He thinks he is being funny. I'm pissed off.

I suggest using the following framework for business emails. Begin by writing "Dear Dr. Smith (or whoever)". Often there are multiple people cc'ed, and it can be unclear for whom the email is intended. Then write a first sentence that overviews the purpose of the email and the business to be done--"I'm writing to explain the reason for delays in completing this year's budget". Once the email recipient understands the purpose of the email it is fine to go into the details, but be careful not to add more detail than is necessary to get the job done. End with a sentence summarizing action items "Thus I may need your support in obtaining the needed information from the Cancer Biology Department".

Write clear simple prose that gets the job done in the fewest possible words.

Be careful to distinguish between professional and personal email.

It is fine to write in a more personal tone in emails or texts between friends, where the primary goal is not completing some professional task. Just be careful with this distinction. Try to indicate at the start of an email whether the intent is personal or professional.

Email is not private.

Professional emails are not private. When writing an email, imagine a hostile lawyer waving the text at you in court. I've been close to multiple cases of people being fired for the content of their emails.

Keep a professional tone in email correspondence, using short clear sentences and appropriate content.

7. Notes on usage

Below are some troublesome words and phrases. The list comes from years of wrestling with definitions in papers, grant applications, and student theses. The list is intended to be read from start to finish, not consulted like a dictionary.

Basic. A word that is fine when describing pH, but which has no meaning when used synonymously with “fundamental”. Always delete in the second case.

Briefly. Also “In brief”. Never write this. Just be brief.

Certainly. Just invites skepticism. Always delete this.

Fundamentally. See “basically” and “certainly”. Always delete these useless words.

Gene. A widely used word for the unit of genetic function, which has a surprisingly vague meaning. Gene regulatory regions can extend for long regions along DNA, making the edges of genes hard to define. Genes can overlap. In flies, there are even effects on regulation by sequences on sister chromosomes (synapsis-dependent complementation, termed “transvection”). Where possible, favor more precise words, like “transcription unit”, indicating just the part that’s transcribed, or “locus”, meaning just a linear region of a chromosome.

Gender. Actually not a synonym for “sex”. “Gender” implies both biology and the cultural context that comes with it. Today some people would prefer to describe their gender as nonbinary. “Sex” is the strictly biological attribution based on morphology and function. “Gender” is the preferred usage when the focus is human culture, “sex” is preferred when the topic is animal phenotype.

If. “If” is often used incorrectly for “whether”. David Foster Wallace explains: “They are not synonyms—*if* is used to express a conditional, *whether* to introduce alternative possibilities...in this case there’s a wonderfully simple test you can use: If you can coherently insert an “[or not]” after either the conjunction or the clause it introduces, you need *whether*. Examples: “He didn’t know whether [or not] it would rain”; “She asked me straight out whether I was a fetishist [or not]”; “We told him to call if [or not, no] he needed a ride [or not? no]” (from “Twenty-Four Word Notes”, in “Both Flesh and Not”).

Impact. When used as a verb, as in “the intervention impacted health”, the word is a needless neologism. Favor “influence”.

Influence. A good verb that should be favored over “impact”.

In vitro. In vitro means “in glass”, as in a test tube or culture dish. This means different things to different people. In mechanistic biochemistry, “in vitro” usually means reactions in test tubes using purified components. In virology, “in vitro” may mean studies of viral replication in culture dishes. The phrase “in vitro” can be useful, but consider whether more specific phrases can be substituted (e. g. “reconstituted reactions”, “studies of HIV replication in SupT1 cells”, etc.).

In vivo. This means “in a living organism”, but usually a more specific phrase can be used. Consider instead writing “in *Drosophila*”, or “in teenage human participants”, taking the opportunity to remind your readers of the system tested using only a small number of additional syllables.

Life cycle. This is the process of replication from birth through reproduction and death. Generally a fine phrase, but when describing viruses favor “replication cycle”, in order to avoid picking a fight over the unanswerable question of whether or not viruses are alive.

Participant. Individuals undergoing testing in clinical trials are understandably sensitive about the way researchers refer to them. “Participant” is respectful and collegial. “Patient” often isn’t right, because participants may be healthy controls, or participants with a chronic disease may not currently be in treatment. “Subject” can sound dehumanizing, in the direction of “laboratory animal”. Favor “participant”.

Protein. Proteins are linear polymers of amino acids. Avoid blurry mixing of protein and DNA, as in “we mutated alanine 161 to valine”. Mutations happen in DNA. Favor either “we mutated DNA encoding alanine 161 to encode valine”, or “we substituted alanine for valine in the protein”.

Prove. Also proof. Acceptable to use in the specific sense of a mathematical proof. Not appropriate in biomedical science—data never proves a model or idea true or false, but only influences our assessment of the likelihood.

Replication cycle. All biological entities replicate, but whether viruses are alive or not is debatable. The word “life” is so loosely defined that it is not possible to test borderline cases--such as viruses--to determine whether they are alive or not. Nobel Laureate Harold Varmus wisely taught his trainees to favor “replication cycle” for viruses over “life cycle”.

Sex. See “gender”.

Significant. Use in scientific prose only in the sense of “p value <0.05”--that is, statistically significant. Still better, just cite the p value, leaving “significant” implicit.

Subject. See “participant”.

Utilize. On this one David Foster Wallace said it all: “A noxious puff-word. Since it does nothing that good old *use* doesn’t do, its extra letters and syllables don’t make a writer seem smarter; rather, using *utilize* makes you seem either like a pompous twit or like someone so insecure that she’ll use pointlessly big words in an attempt to look sophisticated. The same is true for the noun *utilization*, for *vehicle* as used for *car*, for *residence* as used for *house*, for *presently*, *at present*, *at this time*, and *at the present time* as used for *now*, and so on. What’s worth remembering about puff-words is something that good writing teachers spend a lot of time drumming into undergrads: “formal writing” does not mean gratuitously fancy writing; it means clean, clear, maximally considerate writing.” (from “Twenty-Four Word Notes”, in “Both Flesh and Not”).

Very. The quintessential weak intensifier. Always delete this.

Whether. See “if”.

8. Constructing figures

The same aesthetic applied to scientific prose above applies equally to figures. If you strip away everything unnecessary, you highlight what is important. This then provides the opportunity to add more content in the same space.

Edward Tufte wrote a series of outstanding books on this topic. I strongly recommend his first book “The Visual Display of Quantitative Information”. All his books beautifully present good and bad visual summaries of data. He teaches how to remove “chart junk” to focus attention on the intended point, allowing addition of more layers of information in the same graphic.

Below I go over a few examples, applying Tufte’s technique of pointing out strengths and weaknesses.

The first figure, from a paper of mine, attempts to summarize the results of reactions in vitro testing the properties of purified HIV integrase¹⁰. The figure is needlessly difficult and the legend is almost unreadable.

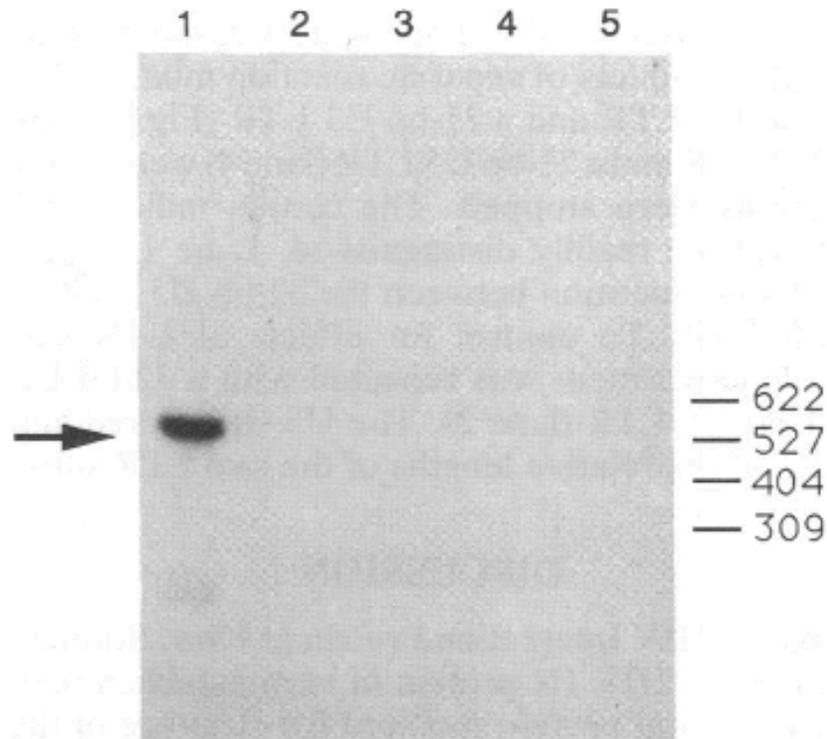


FIG. 4. Insertion of model LTR substrates into a circular DNA target. Standard strand transfer reactions, modified as described, were carried out in the presence of 5 ng of a 174-bp circular DNA. Lane 1, complete reaction mixture. The predominant product is marked with the arrow. Lane 2, 15 mM $MgCl_2$ substituted for 15 mM $MnCl_2$; lane 3, 15 mM EDTA substituted for 15 mM $MnCl_2$; lane 4, target DNA omitted; lane 5, control protein fraction from insect cells infected with a wild-type baculovirus substituted for the IN protein-containing fraction. The dashes beside the gel mark the mobility of size standards (pBR322 digested with *Msp* I) of the indicated length (given in bp). The labeled LTR substrate used in this experiment, LTR J, is identical to LTR A except for an addition of 11 bp to the right side as drawn in Fig. 1. The sequence of this addition was 5'-GGATCCTATCG-3' and its complement. The use of the 174-bp circular target, synthesized using the *loxP*-*cre* recombination system of phage P1, and this lengthened LTR substrate facilitated subsequent characterization of reaction products after denaturation (see text).

The original version does not tell a story by itself. One needs to read the wandering figure legend and maybe the rest of the paper to work out what's what.

Compare the revised version of the figure below.

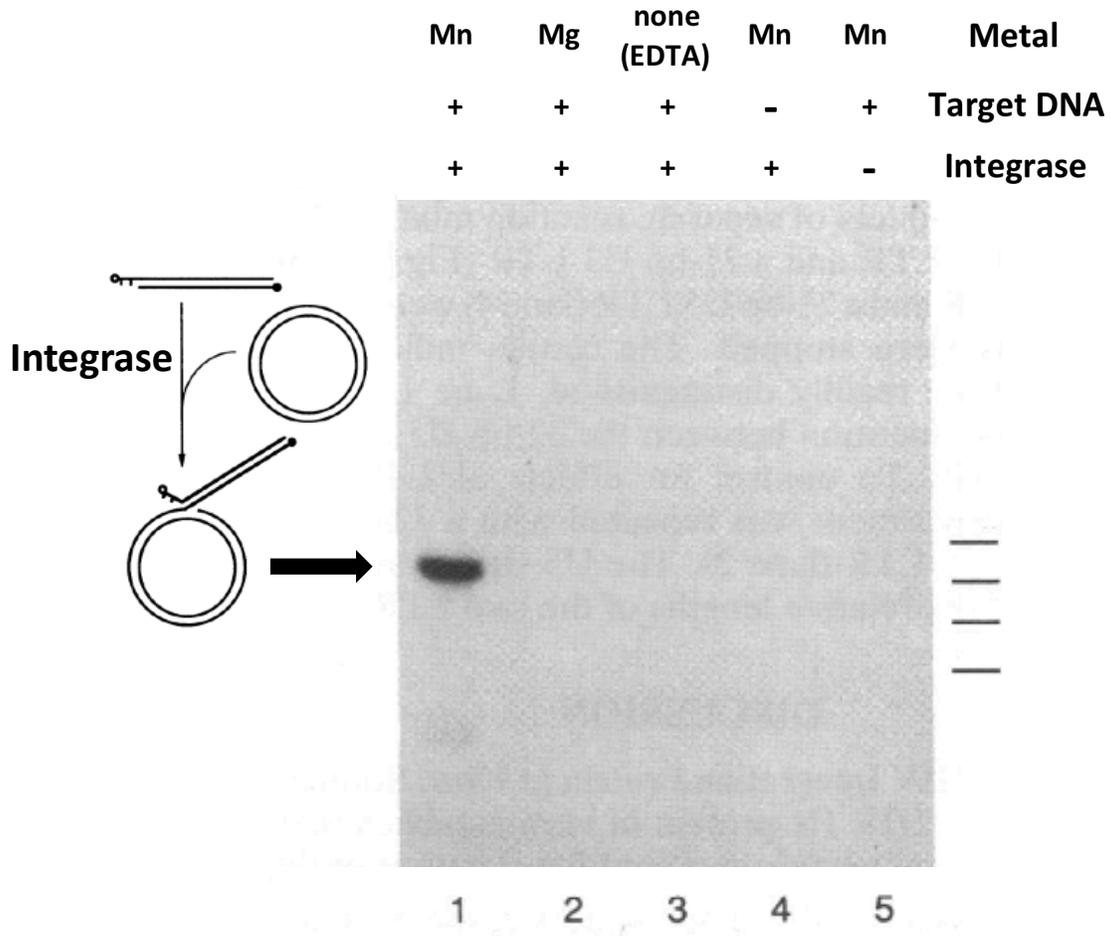


Figure legend. Requirements for HIV DNA integration in vitro. The reaction is diagrammed at the left. A linear DNA mimicking the viral DNA end (top left) becomes integrated into a small circular DNA in the presence of integrase. The viral end oligonucleotide was end labeled, and reaction products separated on a native electrophoresis gel and visualized by autoradiography. Reactions contained: lane 1, complete mixture; lane 2, Mg instead of Mn; lane 3, no added metal (containing only the chelator EDTA); lane 4, no target DNA; and lane 5, a blank protein fraction lacking integrase. Dashes to the right indicate size markers of 622, 527, 404, and 309 bp.

The new version of the figure is much more self-explanatory, diagramming the reaction substrates and products, and specifying the contents of each of the five assays. We learn at a glance that you need integrase, Mn, and target DNA for the reaction to yield product. Improving the figure also allowed simplification of the figure legend.

In the new age of Big Data, it is common to see network diagrams like those in the examples below. These and other Big Data displays are often easy to make, but their value is variable.

In the first example below, a network diagram was generated summarizing co-occurrence among different types of viral genes on a collection of partial viral genome sequences from human gut¹¹. The value of the diagram is modest.

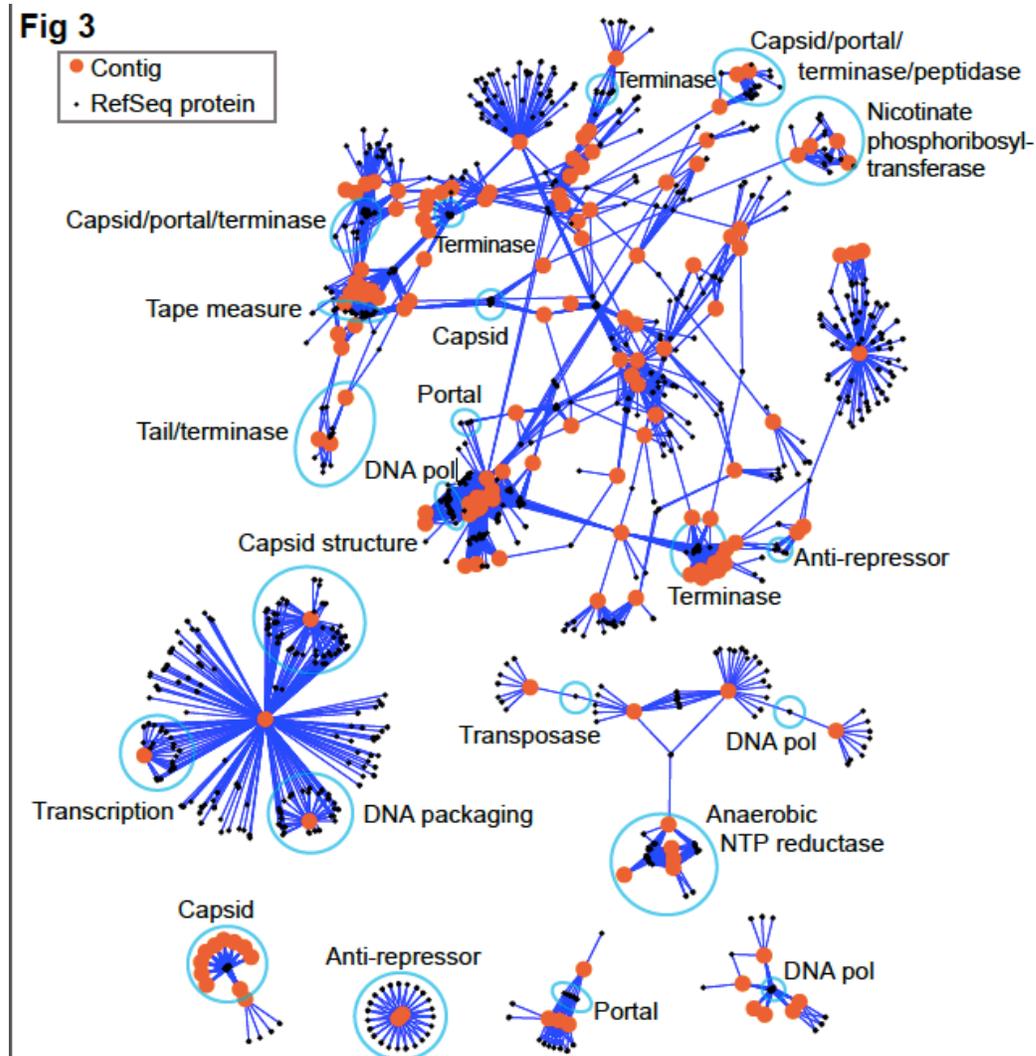


Figure legend. Network based annotation of viral contigs. Orange circles represent viral contigs no shorter than 3 kb. Black circles represent proteins in the RefSeq viral database. RefSeq proteins are connected to viral contigs when an ORF encoded by that contig resembles that protein at $E < 10^{-50}$ (blastp). Blue outlines indicate groups of RefSeq proteins and ORFs from contigs that share the function indicated by the adjacent label.

The image shows viral genes linked up by their co-occurrence in DNA sequence populations. The diagram is a fair presentation of the results, but there is not much further you can do with this--if the diagram had come out a lot differently, it wouldn't have made much difference. The picture is purely descriptive and does not support any larger conclusions or follow up. Many of the complicated visual presentations of Big Data today have this quality.

The second example (below) is much more useful. This figure was generated for a training grant application to support HIV research. The nodes indicate researchers participating in the training program. The lines indicate whether any pair of trainers shared a joint publication, and the thickness of the lines indicates the number of joint publications.

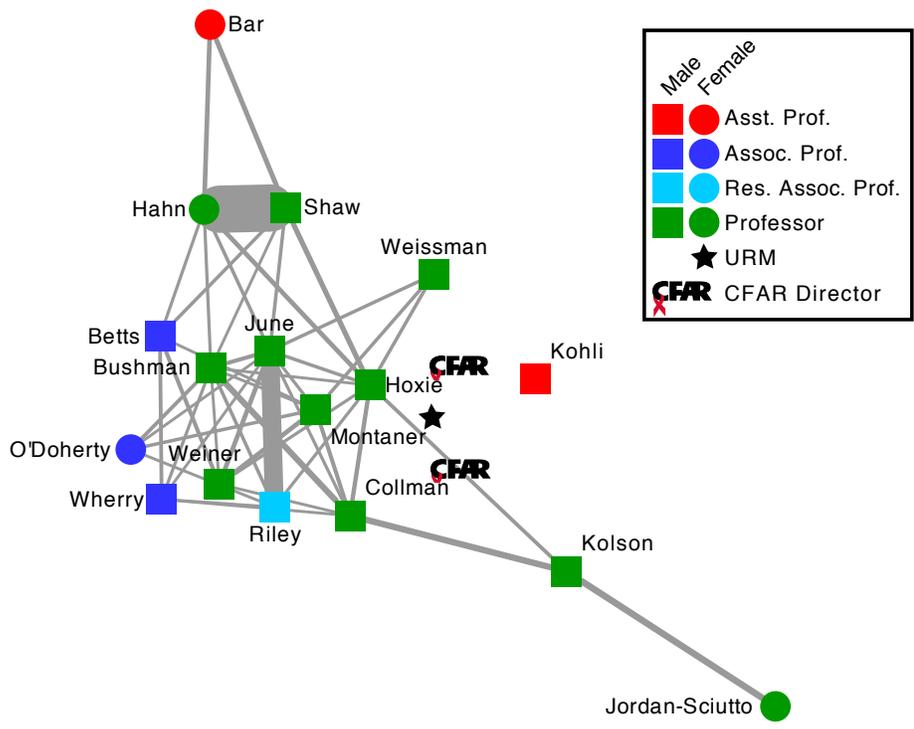


Figure 2. Network analysis of joint publications linking our trainers. The Figure summarizes joint publications as a cytoscape interaction network. The thickness of the gray lines indicates the number of joint publications linking each pair of trainers (e. g. the thin line linking Shaw and Bushman indicates a single publication, the thick line linking Hahn and Shaw indicates 151 publications). The colors show academic rank and the shapes indicate female or male trainers. CFAR directors are marked by the CFAR logo; the star indicates our URM trainer. Analysis and visualization were carried out using R.

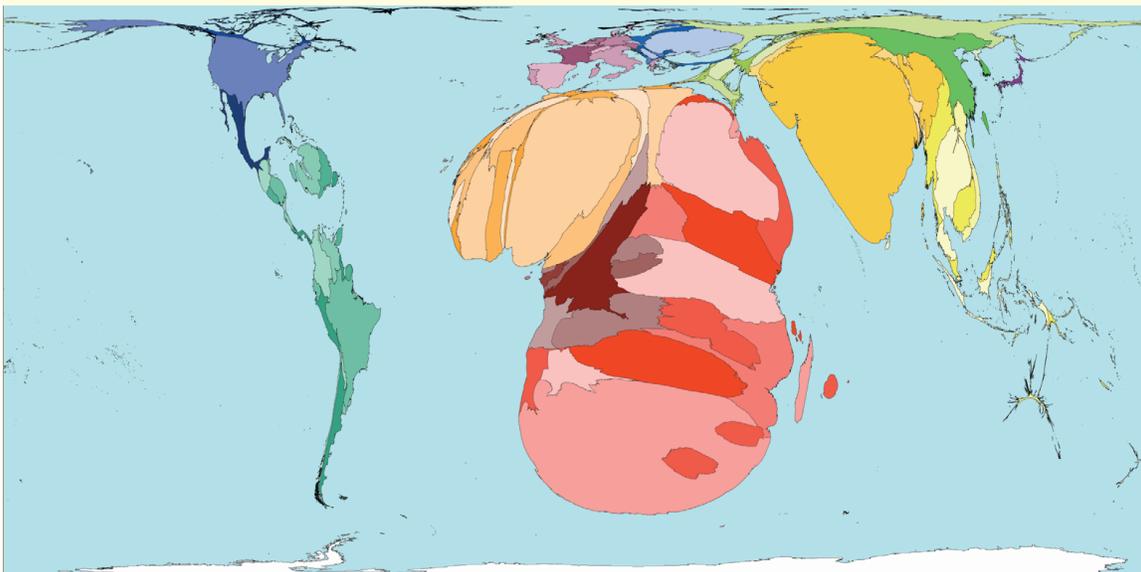
Image by Kyle Bittinger.

POPULAR SUPPORT, and NARCOTICS are each in capital letters and about the same point size, but one is a political institution, one is a sentiment, and the last is a class of physical objects. If your goal is to confuse your readers, nonparallel lists are a great choice.

Upon seeing this, General McChrystal, leader of US forces in Afghanistan, remarked that “when we understand that slide, we’ll have won the war”. A rebellion against such diagrams followed. General James Mattis commented “Powerpoint makes us stupid”, and some military leaders began banning powerpoint from their staff meetings.

Take advantage of the strengths of data visualization, but prune out the unnecessary. Focus on what you want your readers to get out of your diagram, and edit to highlight your point. In the war diagram above, there was no point to begin with, which the author tried to conceal with extreme complication.

Arresting images often relay your points effectively. A picture isn’t always worth a thousand words, but sometimes it is. The image below was made using “WorldMapper” software, where countries are resized in proportion to their burden of HIV infections.



It is clear at a glance that Africa and India are particularly hard hit. The impact is amplified by the fact that the figure shows a distorted version of a well-known image—we are drawn in by the contrast between the familiar and strange.

Enlarge the lettering

Almost every time a trainee prepares a figure, I end up asking them to make the lettering larger. Among computational biologists, there seems to be a religion based

on making the lettering as small as possible. Be careful about the type size in labeling each figure--make size consistent and don't use very large point sizes and very small point sizes in the same figure. Remember that figures are typically reduced in size upon publication, so the lettering needs to be abnormally large at the start to be readable after reduction.

DNA structure

Often the DNA helix is shown in scientific diagrams. It is common in the popular press and even advertising. Few people seem to realize that B-form DNA comes in two mirror images, which are right-handed and left-handed helices, and only one is found biologically.

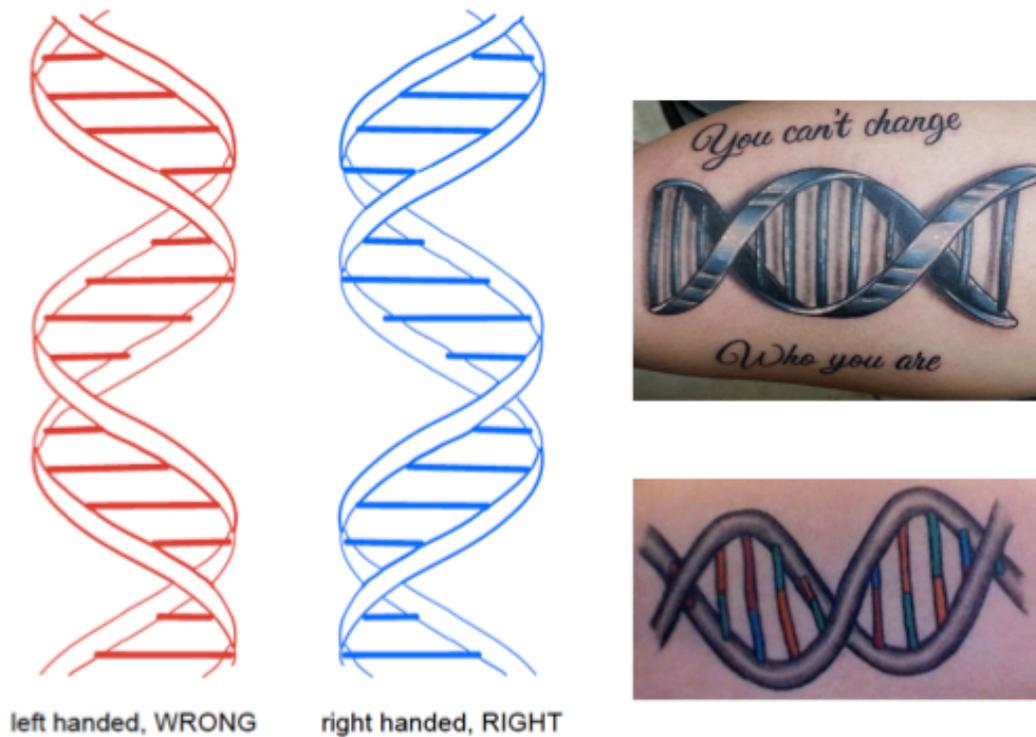


Figure legend: Comparison of lefthanded (wrong) and right handed (correct) B-DNA, and some examples of left handed B-DNA tattoos.

Biologically occurring B-DNA is right-handed only. In the 1980s there was a proposal for left handed B-DNA in *E. coli*¹², but it was later shown to be wrong¹³. Z-DNA is genuinely left handed, but Z-DNA is not a simple B-DNA-like helix and forms only under extreme conditions that are rare or absent inside cells.

In popular culture images are split about 50:50 right-handed versus left-handed B-DNA. Many people who think they are professional biologists make this mistake. I once saw the Chair of a Genetics Department show diagrams with left-handed B-DNA in a lecture, a needless credibility buster.

Learn to recognize right and left-handed helices. Get it right in your own work. Don't be like the woman I saw in the New Orleans airport, who had a left-handed B-DNA helix tattooed on her upper arm.

Color

It is possible to write precisely about color. Charles Darwin, on the voyage of the Beagle, brought along "Werner's Nomenclature of Colours", which had pictures of over 100 colors, and names for each tint. Darwin held up the book to natural objects, matched the object's color to the entry in the book, and used the name of the closest color in his writing.

Today, we have several digital scales, for example RGB, that allows us to be precise about color. Pantone color scales provide names. Once in a while, color is really important, for example in describing the look of an infected tissue, or the extent of bleaching in a coral. Use quantitative color scales to increase your precision.

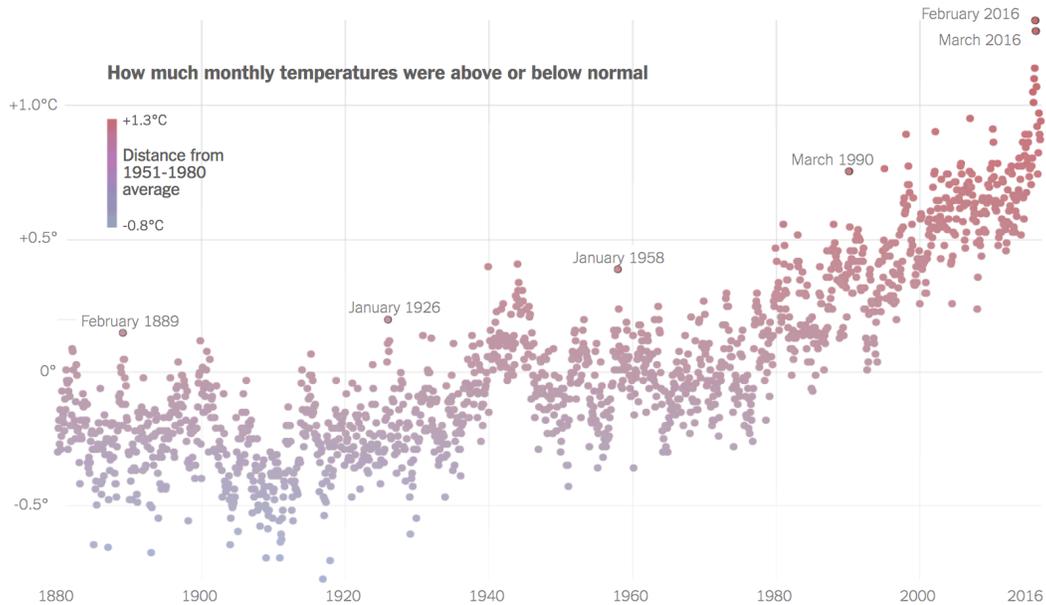
And avoid sexism in coloring your figures. Early in the days of transcriptional profiling, it was common to see heat maps transitioning from red to green. Unfortunately, 10% of the male population is red-green colorblind. The simplest solution is to use other colors in your diagrams. However, as an alternative, today there are online tools that allow you to upload an image and ask how it would appear to people with various forms of color blindness.

<https://www.color-blindness.com/coblis-color-blindness-simulator/>
<https://pilestone.com/pages/color-blindness-simulator-1>

Thus if it is important to preserve certain reds and greens, it is possible to identify pairs that are still distinguishable to people with common forms of color blindness.

Emphasis

The attached diagram, from the January 19, 2017 New York Times, lays out the case for global warming in no uncertain terms.



The simple presentation of time on the x-axis and temperature differential on the y-axis makes the case, but in addition the diagram emphasizes the density of the data by showing each measurement individually. Increasing temperature is indicated twice for emphasis, both as the position on the y-axis and the color of the point.

Not much room for doubt looking at this.

Image manipulation

Today, given the vast tool set for digital image manipulation, it can be hard to be sure what is allowable. Young scientists commonly have excellent skills with computers, often extending to digital art. Photoshopping your lab-mate's head onto the body of a giraffe is standard fun. When managing data, often the first output from an experiment is an image in digital form. So what is fair manipulating the data?

For example, it seems benign to change the contrast on an image, so that a weaker signal is more evident. At the other extreme, making chimeric images, where data features important to the interpretation are added or removed, is clearly wrong. Other manipulations can fall in between. How to decide?

An excellent guide was published in the Journal of Cell Biology, titled "What's in a picture? The temptation of image manipulation" ¹⁴. This is a valuable read for

anyone training in the sciences. One message is that many manipulations are OK so long as you do the same thing to the entire image. Differential modification misrepresents the original. Another point is that it is critical to report fully any image manipulation carried out.

If images were generated in separate experiments, don't try to smooth over borders between figure panels—make it clear that different pieces are from different experiments.

Follow journal guidelines carefully. Going wild with image manipulation can result in fun art for the lab walls. Just keep it out of your papers.

9. Writing and thinking

Be your own toughest critic.

Garry Kasparov, probably the strongest chess player of all time, was famously hard on his own play. Kasparov:

“I've seen - both in myself and my competitors - how satisfaction can lead to a lack of vigilance, then to mistakes and missed opportunities.”

Kasparov annotated the games from his rise to fame in the 1986 book “The Test of Time”, where he pointed out flaw after flaw in his own play. It got to the point that other top players began weighing in to defend Kasparov’s play against his own attacks. Kasparov won the world chess champion in 1985 at the age of 22.

Like Kasparov, be your own toughest critic. When carrying out experiments, after a lot of hard work you sometimes get an exciting result. Many scientists see their hopes in the data, and not the reality. Easier to dream of glory than confront messy experimental flaws. You are far better off assuming that your result is the most embarrassing possible artifact, and getting to work trying to rule that out. If you fail to falsify your finding, move on to the second worst artifact, and test that. If, after a lot of hard work, you consistently fail to falsify your result, then maybe you are on to something.

Take the same attitude with your writing. Assume that what you just wrote is weak and look for ways to improve it.

The approach to experimentation described above lends itself to strong writing. Write carefully about the idea and the experiment supporting the idea. Then describe the control experiments that address alternative explanations. This moves the account forward in a natural way and earns the credibility of your readers.

Critique your own motives.

As a new assistant professor I once wrote a collaborative paper with the great chemist Leslie Orgel, who was an outstanding scientific writer. I wrote something like “We predicted that xxx would be the case, and so carried out the following experiments. The data in fact matched our prediction, supporting the idea that...”.

I can still hear Leslie saying “We predicted it, did we--now weren’t we clever...”

The pompous padding was removed from the next draft, shortening and improving the text.

Write to explain something important, not to express how great you are. Write to approach the truth. Readers get this. You advance your own cause much more with clarity and consideration of your readers than with any amount of self-serving chest pounding.

When smart people speak or write confusingly, they often are trying to get away with something.

This is one of the main points of “Politics and the English Language”. Orwell wrote the essay in 1946, having just lived through politics going horribly wrong in the Second World War. His essay spotlighted the deliberate misuses of language that went with it.

Obscurity in writing is often self-serving. Imagine someone saying “it’s not about the money”, then going off on some confusing tangent. It is, of course, about the money. Politics is rife with this kind of nonsense, which was pilloried by Orwell.

It is remarkably common to see scientists writing or speaking in a deliberately obscure way—implying “you can’t understand me, so I must be smart”. Such deliberate obfuscation is an epidemic among computational biologists. Once you take the skeptical Orwellian attitude, these tricks become quite transparent.

In your own writing or public presentations, respect your audience. Make an effort to learn their backgrounds. Start by briefly reviewing stuff they probably already know, to get everyone lined up at the same starting point. Then tell them what you are going to teach them. Follow up and explain your points in a simple step-by-step fashion in terms they can understand. Be realistic. It is extremely common for scientists to lapse into the jargon of their discipline and lose their audience due to laziness or arrogance. Explain the content in a simple and orderly way, be it in public speaking or writing. People notice and appreciate the effort.

Science and proof

It is common to find scientists, often MDs, writing about “proving” a model true. A search of the biomedical literature using PubMed on the keyword “prove” yielded more than 70,000 hits. The problem is that the relationship between idea and experiment is too complex for “prove” to be appropriate. A scientist forms an idea about how the world might work, then uses it to make a prediction for a non-obvious outcome in an experiment. If the experimental result is as predicted by the idea, then the idea is supported. A strong idea may further allow the development of new technology, providing further support.

None of this, however, means that an idea is proven true. It’s just increasingly likely. Never use “prove” or “proof” in scientific writing unless you are referring to the strict mathematical sense of proving theorems, which is fine.

Writing, thinking and public speaking.

Orwell, after blasting deliberately blurry language, pointed to even deeper issues. “If thought corrupts language, language can also corrupt thought”. Habitually vague writing not only reflects vague thinking, but makes the thinking all the more vague. Our thought processes are themselves often in words—think of your internal monolog--so that corrupted writing corrupts your core data processing.

The hard work of cleaning up your writing--stripping out every unneeded word, reorganizing for clarity, honing the key points--cleans up your thinking as well. And it doesn't stop there. Most scientists will regularly present their research in public lectures. I find that sentences I revised and improved in publications often come out when I describe the data in seminars. Feedback from lectures then refines the description. Questions asked by listeners are particularly valuable--in the next lecture, I commonly answer the best questions from the previous lecture during the seminar. The better-crafted wording is then available for the next paper in the series.

The refined words, and their implications, are in my mind as I stare out the window riding the train to work, chewing them over and searching for additional implications.

Good writing, clear public speaking, and effective thinking all reinforce each other. They are parts of the same whole. Refine them all together to boost your success as a scientist.

Last words

The main points again:

Write in short sentences.
Cut out every unnecessary word.
Start paragraphs with strong topic sentences.
One idea per paragraph.
Simplify wherever possible.
Let the facts carry the story.

The same holds for figures—cut out everything unnecessary to highlight the content.

Strip out the junk so the main points are inescapable.

David Foster Wallace once again:

“The truth is that most US academic prose is appalling—pompous, abstruse, claustral, inflated, euphuistic, pleonastic, solecistic, sesquipedalian, Heliogabaline, occluded, obscure, jargon-ridden, empty: resplendently dead.”

David Foster Wallace in “Authority and American usage” 1999.

Many scientists are horrible writers. You can write well.

10. Use of Artificial Intelligence programs such as ChatGPT

Our world changed in November, 2022, with the introduction ChatGPT, a free artificial intelligence algorithm that can write clearly (<https://chat.openai.com/chat>). Numerous additional AI tools have since become available. The repercussions are just starting to be felt. Below is an example of a prompt given to ChatGPT, and the output.

Prompt:

Write a five sentence paragraph on the importance of studying SARS-CoV-2 infection in deer.

ChatGPT output:

Studying SARS-CoV-2 infection in deer is important because it can provide insight into how the virus spreads and how it affects different species. It can also help scientists understand the role that wildlife plays in the overall transmission of the virus. Additionally, studying the infection in deer can help identify potential new treatments or vaccines that can be used to prevent the spread of the virus. Furthermore, it is important to study SARS-CoV-2 in deer because it can provide insight into the virus's evolution and how it may change over time. Understanding the virus in different species is key for preventing further outbreaks and controlling the spread of the disease.

Perhaps the text is a little dry and repetitive, but accurate and readable. The scientific literature contains much worse.

Furthermore, ChatGPT can edit effectively. Here is a paragraph from an early draft of a paper I coauthored:

Interest in the human microbiome is rapidly expanding due to increased capacity for DNA sequencing and analysis. The recognition that our microbes may be linked not only to acute infections such as *Clostridium difficile* but to chronic diseases such as heart disease, cancer, obesity, autoimmune disorders and multiple sclerosis is prompting substantial interest from both basic and clinical perspectives. Although we are all essentially identical at the level of our human genomes, our microbiomes are far more variable both in terms of which organisms are present, the relative abundance of shared organisms, and the genes they carry. Additionally, although our genome is static throughout life, each of our microbial communities changes profoundly from infancy through adulthood, when they continue to change through ongoing exposures to diet, drugs and environment. Understanding the microbiome may thus be critical for diagnostics and, eventually, interventions based on the microbiome itself.

Here are instructions given to ChatGPT (written by Dr. Joe Fraietta). The output follows below.

I want you to act as an AI writing tutor for academic research grants. I will provide you with text and your task is to use artificial intelligence tools, such as natural language processing, to re-write the text to be as clear and concise. In addition, the text should be easy to read and flow naturally. Furthermore, the text should use the active voice. You should also use your rhetorical knowledge and experience about effective writing techniques in order to improve the text without changing the underlying meaning of the text. You should consider at least 5 different versions and show me only the version that you think is the best one.

Output from ChatGPT:

The human microbiome refers to the diverse community of microorganisms that live in and on our bodies. Recent advances in DNA sequencing have revealed that the microbiome plays a role in a wide range of health conditions, including chronic diseases such as heart disease, cancer, obesity, autoimmune disorders, and multiple sclerosis. The composition and function of the microbiome vary greatly between individuals, and can change over time in response to factors such as diet, drugs, and environment. Understanding the microbiome is an area of active research, with potential applications in diagnostics and interventions based on manipulating the microbiome.

Perhaps the ChatGPT response was a little less detailed, but still shorter and more readable.

Where does this leave scientific writing? It is important to recognize that AIs are sometimes quite wrong, so relying on prose from ChatGPT or others risks embarrassing blunders. These are sufficiently common to have been nicknamed “hallucinations”. However, the prose is often fine.

It is tempting to forbid use of AIs in scientific writing, and some efforts have been made to create algorithms that will identify AI-generated prose. However, this just starts an arms race between AI detection and countermeasures that is in no one’s best interest.

So what is an appropriate use of ChatGPT and resources like it? As of January 2024 the community is still wrestling with this, and best practices are sure to evolve.

Current University of Pennsylvania policies can be found here:
<https://www.isc.upenn.edu/security/AI-guidance>

My initial recommendations are as follows:

-Don't use ChatGPT to generate first drafts. It is in your interest to learn to write clearly, so don't use AIs as a crutch. Whether use of AI constitutes plagiarism is still being determined—I think it probably does, but opinions vary. Large language models connect words that are frequently found together—you don't know how many words are strung together in an AI output that match a single source, so you don't know the extent of direct plagiarism. Don't take chances.

-It may be OK to use ChatGPT to help edit, but don't use the AI changes verbatim—treat them as suggestions.

-Always acknowledge use of ChatGPT at the end of any text it was used to generate or modify. Be specific regarding any prompts used, and which parts of the text were modified. This is now required by some journals.

-It is not permitted to edit descriptions of patient data with ChatGPT, even de-identified materials. Data entered into ChatGPT can be incorporated into program updates, and so used without permission.

-Allowable uses of ChatGPT will increasingly be specified by course directors, scientific journals, etc. Check up on pertinent regulations and follow them.

11. Suggested Reading

One of the most effective ways of improving your writing is to read examples of the best. Pay attention to how talented writers construct their prose and develop a written piece. Use the most effective of their methods in your own scientific writing.

Below are a few of my favorites.

Books and essays on expository writing:

William Zinsser. "On Writing Well." Harper and Row, New York, 1985.

A gem.

William Strunk Jr. and E. B. White. "The Elements of Style." Third Edition.

Macmillan Publishing Co., Inc. New York. 1979.

The early classic.

George Orwell. "Politics and the English Language."

Should be required reading for every citizen of the planet.

Examples of outstanding scientific writing:

Mark Ptashne. "A Genetic Switch." 3rd Edition. Cell and Blackwell Press.

On the growth of phage lambda.

Jonathon Weiner. "The Beak of the Finch". Random House.

Pulitzer Prize winning book on evolution of birds in the Galapagos.

Jonathon Weiner. "Time, Love, Memory". Random House.

On genes and behavior, focusing on the career of Seymour Benzer.

Ed Yong. "An Immense World". Random House.

How animal senses differ from ours, and the implications for their perceptions of the world.

Kate Zernike. "The Exceptions". Scribner.

Pulitzer Prize winning account of gender discrimination at MIT.

The classic research papers cited in the text above are also well worth reading.

Books on the visual display of quantitative information:

Edward Tufte. "The Visual Display of Quantitative Information".
Outstanding book on editing visual displays. Called "a visual Strunk and White" by the Boston Globe.

Edward Tufte. "Envisioning Information".
The successor to the above, also excellent.

Books and essays on scientific writing

Robert A. Day, Barbara Gastel. "How to Write and Publish a Scientific Paper",
7th Edition.
A detailed discussion of the elements of writing scientific papers.

Corelia Dean. "Am I Making Myself Clear?: A Scientist's Guide to Talking to the Public"

Maeve O'Connor. "Writing Successfully in Science"

Mimi Zeiger. "Essentials of Writing Biomedical Research Papers", Second Edition.
Excellent in many ways, but lengthy and published before the big data era.

"CBE (Council of Biological Editors) Style Manual, 8th Edition". Council of Biological Editors, Inc. Bethesda MD.

"The Chicago Manual of Style" 16th Edition Sixteenth Edition, by University of Chicago Press

12. Editing exercises

Below are three examples of scientific writing that can be improved. Try editing them yourself. Following each example is an edited version you can compare to your own efforts.

Example 1. A paragraph from a student thesis (125 words). “T/F” means “transmitted/founder” Hepatitis C virus genomes.

“In another study by Mitchell and colleagues, significant differences in the potency and nature of the innate responses to RNAs generated from T/F molecular clones were detected in cultured hepatocytes and immortalized cell lines. Additionally, these were found to correlate with respect to the genotypes of the T/F genomes with genotype 3 RNAs stimulating an enhanced pro-inflammatory profile as compared to that of genotype 1 and 4 T/F RNAs. The cell intrinsic response to genotype 3 RNAs included enhanced expression of RIG-1, STAT1, and TLR3. Intriguingly, these findings may provide a mechanistic explanation for the unique clinical characteristics of genotype 3 infections including a higher rate of spontaneous clearance, and a strong association with accelerated cirrhosis and hepatocellular carcinoma”.

Example 1, revised.

Here is a version edited for brevity (86 words).

“Mitchell and colleagues found differences in innate responses after transfection of T/F molecular clones of different HCV genotypes into cultured hepatocytes and immortalized cell lines. Transfection with genotype 3 clones, but not 1 and 4, resulted in a pro-inflammatory cellular response including enhanced expression of RIG-1, STAT1, and TLR3. In patients, genotype 3 HCV infections show a higher rate of spontaneous clearance, and a strong association with accelerated cirrhosis and hepatocellular carcinoma, potentially reflecting the proinflammatory properties seen in cell culture”.

After editing, the length is reduced to 86 words, for a savings of 39 words. Note how the use of “..., but not 1 and 4,…” allowed deleting a longer clause. Deleting the weak linkers “Additionally” and “Intriguingly” allowed the paragraph to read more smoothly. Rephrasing the sentences for simplicity allowed considerable further shortening with gain of clarity.

Example 2. An abstract from a published paper, a useful study of the gut microbiome and its possible roles in cardiovascular disease.

Intestinal microbiota composition modulates choline bioavailability from diet and accumulation of the proatherogenic metabolite trimethylamine-N-oxide.

Romano KA, Vivas EI, Amador-Noguez D, Rey FE

Choline is a water-soluble nutrient essential for human life. Gut microbial metabolism of choline results in the production of trimethylamine (TMA), which upon absorption by the host is converted in the liver to trimethylamine-N-oxide (TMAO). Recent studies revealed that TMAO exacerbates atherosclerosis in mice and positively correlates with the severity of this disease in humans. However, which microbes contribute to TMA production in the human gut, the extent to which host factors (e.g., genotype) and diet affect TMA production and colonization of these microbes, and the effects TMA-producing microbes have on the bioavailability of dietary choline remain largely unknown. We screened a collection of 79 sequenced human intestinal isolates encompassing the major phyla found in the human gut and identified nine strains capable of producing TMA from choline in vitro. Gnotobiotic mouse studies showed that TMAO accumulates in the serum of animals colonized with TMA-producing species, but not in the serum of animals colonized with intestinal isolates that do not generate TMA from choline in vitro. Remarkably, low levels of colonization by TMA-producing bacteria significantly reduced choline levels available to the host. This effect was more pronounced as the abundance of TMA-producing bacteria increased. Our findings provide a framework for designing strategies aimed at changing the representation or activity of TMA-producing bacteria in the human gut and suggest that the TMA-producing status of the gut microbiota should be considered when making recommendations about choline intake requirements for humans.

238 words

Example 2, revised. Here is a shortened version of this abstract.

“Choline is a water-soluble nutrient essential for human life. Gut microbial metabolism of choline results in the production of trimethylamine (TMA), which upon absorption by the host is converted in the liver to trimethylamine-N-oxide (TMAO). TMAO is reported to exacerbate atherosclerosis in mice and is positively correlated with the severity of atherosclerosis in humans. Which microbes contribute to TMA production in the human gut remains largely unknown. We screened a collection of 79 sequenced human intestinal bacterial strains from XXX phyla and identified nine strains capable of producing TMA from choline in vitro. Gnotobiotic mouse studies showed that TMAO accumulates in the serum of animals colonized with TMA-producing species, but not in the serum of animals colonized with strains incapable of generating TMA. Even low levels of colonization by TMA-producing bacteria significantly reduced choline levels available to the host—more efficient colonization reduced levels further. Our findings suggest approaches to controlling TMA production in human gut and optimizing recommendations for choline ingestion based individual microbiota composition.”

166 words

In this case the original abstract wasn't too bad, and the research presented significant. Nevertheless, editing shortened the abstract by 72 words with gain of clarity. Phrases like “Recent studies revealed that” in the original can usually be shortened with thoughtful rephrasing. The sentence starting “However,...” was a 44 word run on, providing an opportunity for shortening with improved readability.

Example 3. Recently I wanted a challenging abstract as an editing exercise for a class. I thus searched PubMed on “basically”, and found some that were crying out for help. One is below.

Attention deficit hyperactivity disorder (ADHD) is a complex disorder, which can be seen as a disorder of life time, developing in preschool years and manifesting symptoms (full and/or partial) throughout the adulthood; therefore, it is not surprising that there are no simple solutions. The aim of this paper is to provide a short and concise review which can be used to inform affected children and adults; family members of affected children and adults, and other medical, paramedical, non-medical, and educational professionals about the disorder. This paper has also tried to look into the process of how ADHD develops; what are the associated problems; and how many other children and adults are affected by such problems all over the world basically to understand ADHD more precisely in order to develop a better medical and or non-medical multimodal intervention plan. If preschool teachers and clinicians are aware of what the research tells us about ADHD, the varying theories of its cause, and which areas need further research, the knowledge will assist them in supporting the families of children with ADHD. By including information in this review about the connection between biological behavior, it is hoped that preschool teachers and clinicians at all levels will feel more confident about explaining to parents of ADHD children, and older ADHD children themselves about the probable causes of ADHD.

223 words

Example 3, revised.

Attention deficit hyperactivity disorder (ADHD) is complex and lifelong. ADHD can develop in the preschool years and manifest symptoms (full or partial) throughout adulthood. There are no simple solutions. This paper provides a concise review of ADHD to inform medical and educational professionals, those with the disorder, and their family members. This paper also investigates how ADHD develops and associated problems, with the goal of improving interventions. Better information on ADHD will assist teachers and clinicians in supporting families with affected members.

83 words.

13. Sample submission and resubmission letters

Young scientists just starting out may never have seen the letters surrounding publication—their mentors usually handled it. Below are attached two letters from the publication process as models for correspondence of your own.

Cover letters are needed for initial submission of papers for publication. Once these were mailed along with paper manuscripts. Today they are uploaded into web sites, but the letters have not changed much. Reviews then come back with a cover letter from the Editor and several anonymous reviews. Once the paper is modified to address the reviewers' comments, it is resubmitted along with detailed responses.

Two letters from publications of ours are below. The first letter is a submission letter, the second a rebuttal letter.

For rebuttal letters, it seems that editors today want a letter with each reviewer comment repeated, then your response afterwards. There was a time when condensing reviewer comments and answering them collectively was allowable and in my opinion more readable and efficient, but journals have mostly gone in a different direction. Thus unfortunately I recommend the structure in the letter below. The letter involves a paper in a journal, mBio, in which the reviews are not confidential.



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Frederic Bushman,
Professor

March 14, 2013

Dear Madam or Sir,

Attached please find a draft paper, "Fungi of the murine gut: episodic variation and proliferation during antibiotic treatment", by Dollive et al., that we would like to submit for publication in PLoS One. Many clinical papers have suggested that fungi may grow out when patients are treated with antibiotics to suppress bacterial growth, but analysis in humans can be complicated by the complexities of the underlying condition and use of therapies in addition to antibiotics. To assess the effects of antibiotics on fungi in isolation, we treated mice with a cocktail of antibiotics, then used metagenomic methods to monitor fungal and bacterial growth.

We found that fungi indeed grew out prominently in the mouse gut, and that cessation of treatment allowed the community to return to a state that was similar but not identical to the starting state. Notably, *Candida* persisted at a higher level at the last time point tested. These data suggest that treatment with antibiotics can result in the outgrowth of a medically relevant fungus, and that antibiotic effects can persist for long periods after cessation of treatment. These data are also important because antibiotic cocktails are often used to deplete bacteria in immunological studies in mice, but the fact that they promote fungal growth may need to be considered as well.

In addition, we found to our surprise that fungal populations were highly variable even in control mice, and that variations were specific to each cage of mice studied, disclosing a new and likely important variable in microbiome research.

Reviewers qualified to comment on our paper include:

(Attach here names, addresses and email addresses for five reviewers. Aim for a good mix of geographic location, academic ranks, and genders.)

None of this work is submitted elsewhere for publication. All authors have viewed and approved the manuscript. Thank you very much for considering this submission.

Best regards,

A handwritten signature in black ink, appearing to read 'Frederic Bushman', with a long horizontal stroke extending to the right.

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Frederic Bushman,
Professor and Chair

November 22, 2017

Response to reviews of "Allometry and ecology of the bilaterian gut microbiome"

Dear Madam or Sir,

Attached are our responses to reviews from Dr. XXX and Dr. XXX of our paper "Allometry and ecology of the bilaterian gut microbiome" by Sherrill-Mix et al. We are grateful to the reviewers for their helpful comments. We have revised the manuscript extensively in response, and feel it is considerably improved as a result. Specific responses are as follows. In each case we copied the reviewers' points into the letter, then added our responses below.

Comments from Dr. XXX

We are gratified that Dr. XXX felt that "Overall the paper is very well done and an interesting read."

- 1) The authors note in the introduction that previous studies were mixed in whether species-area relationships exist for the gut microbiota, with ref 4 not showing a relationship and ref 5 reporting a relationship, which was again recovered here. It would be a nice addition to the discussion for the authors to reflect on why these inconsistencies between different studies may have occurred.

In the revised draft we have added more discussion on the possible origins of the discrepancy.

- 2) The samples from the larger animals were from feces and from smaller animals (insects) were generally from dissected intestines. How might these different methods affect the degree to which the entire intestinal microbiota is observed and thus species-area relationships? E.g. might we recover bacteria from more available niches in whole intestines versus feces? It would be good to add some discussion of this. Maybe this is why slope is not as large as may be expected?

We now mention this point in the Discussion as suggested.

- 3) At the bottom of page 7/top of page 8 the average sequence reads per specimen is described and the range in the number of OTUs across samples (e.g. 21 in box elder). Are these OTU estimates calculated on rarefied data and if so what level was the data rarefied at?

We mostly used data without rarefaction in order to maximize the amount of sequence information available. In cases where the amount of sequence analyzed could have affected the outcome, as in the species-area analysis, we did use rarefied data. We have expanded on this in the revised draft to improve clarity.

- 4) On the bottom of page 8 it is explained that “12 percent of the sequences remained unassigned using the greengenes classifier”. Does this mean that the classifier could not even characterize these as some type of bacteria? Also, what is the “greengenes classifier”? I think that greengenes is just a database. E.g. QIIME will use the RDP-classifier to assign sequences taxonomically using the greengenes database. It would be good if these results regarding unclassified reads were included in Figure 1.

We have clarified the description of the use of the Greengenes database, and added new analysis on the reads that could not be assigned using Greengenes (new Figure Axxx).

- 5) On the bottom of page 9 and Figure 1D, the proportion of OTUs unique to each species is reported and it is concluded that this did not correlate with phylogenetic placement of the host. How does it relate to how densely the different parts of the host tree is sampled? For instance the low amount of unique diversity in any given monkey species may be more related to that part of the host phylogeny being sampled pretty deeply.

We have removed the Proportion of unique OTUs from Figure 1 and supplementary figures in favor of using PD as suggested in 6 below, which we agree is better.

- 6) In addition to the # of unique OTUs per species, it might be interesting to look at the amount of unique branch length in the 16S rRNA phylogeny per species. This concept was described by Dan Faith as “G” for “Gain in phylogenetic diversity” in the same paper that he introduced the PD (Phylogenetic Diversity) concept (it is implemented in QIIME). G might be more interesting than number of unique OTUs because it also would give more information on whether those OTUs are on deep branching phylogenetic lineages.

We have added PD to Figure 1, and we explore deep branching lineages in more detail as described below.

- 7) For the unclassified sequences, it might be interesting to look at where they fall in the 16S rRNA phylogenetic tree to get a sense of whether there are any deep unclassified lineages that are widespread across animals. (e.g. do many of the unclassified 16S rRNA all cluster together?). David Relman’s group recently described novel deep branching lineages from the dolphin’s mouth. Might be a good paper to reference in terms of an example of a host-associated community revealing much novel diversity.

We have carried out an analysis of deep branching lineages, and added a figure on this to the supplemental information. We also now reference the Relman dolphin study.

- 8) On Page 14 it is described that “Almost all gut samples had a long tail of rare species with many OTUs..” The authors discuss how this tail of rare species is not likely an artifact driven by Chimeras since Chimeras were rare. In terms of artifacts that boost our measurement of the “rare biosphere” I actually worry more about sequencing error than Chimeras. There are a couple of new tools out there that work quite well for denoising. One is dada2, which I have used a lot and it really seems to clean things up nicely. The Knight lab also recently released a similar tool called “deblur”, which I have used less but I hear works better on really large datasets like this one than dada2. It would be interesting to see what happens to this long tail if one of these denoising tools was applied.

We have used deblur to denoise our data set and compared results. We still found the long tails of rare species in rank-abundance curves. This is now mentioned in the revised draft.

- 9) On Page 14, it is determined that a fit based on a Power Series or Poisson lognormal curve provides the closest match to the data. Does this tell us anything more about the ecological drivers of community structure beyond that it is not neutral?

We have been very interested in this point. In the revised draft we have added results for another version of the neutral model which incorporates vertical acquisition of microbes, but this too does not fit our observations. It would be exciting to devise generative models that produce the data we observe, but available models mostly don't make unique predictions. We now mention this and cite a thorough study.

10) On the top of page 21, the version of QIIME used should be noted.

The version of QIIME is now specified.

11) On line 6 of page 21 it is described that bacterial cell growth information was determined from Bergey's manual. Is this growth rate? Where is this information used? For both this and the oxygen information, what was done for species/OTUs that were not defined at the species level and/or not found in these textbooks?

Here, we use "aerobic" or "anaerobic" to indicate the designations from published literature, which capture information on whether bacteria can grow in aerobic or anaerobic environments. We have adjusted the text to clarify this point. In the methods section, we now describe our approach for assignment of OTUs that are not defined at the species level or not found in our references. We added an additional table in supplemental information (new Table A4) to provide details on the aerobic or anaerobic status of each taxon, and how the status was determined.

12) In the tree on Figure 1, it would be helpful if the class and order names that are used in Figure 2 were labeled on the tree. This might be too much info/messy, but it would help someone understand how these are related to each other when looking at Figure 2.

We wrestled with this, but could not find a way to make Figure 1 readable with added labeling. In the revised text we have directed readers to Figure A1, which has full information on phylogeny.

13) There are many supplemental figures that apply all of the analyses in Figure 1 to publicly available datasets. This is interesting/useful except that there is very, very little discussion of this plethora of results in the text. A little more interpretation on the degree to which these analysis of public data provide unique results and or results that are consistent across studies would benefit the paper.

We have added more discussion of the supplemental data to the main text as suggested.

- 14) Figure A2, The legend should have more info on what “dissection” “extraction: “NegControl” and “posControl” are showing exactly.

We have explained the nature of these controls in the figure legend as requested.

15) Typos

- a. Middle of Page 8, Bacteroides is misspelled as “Bacteriodes”

Corrected.

- b. Page 13 – line 5 “carried our a species-area analysis of over 1100”... -insert the word “of”

Corrected.

Comments from Dr. XXX

We are gratified that Dr. XXX felt “This will no doubt be of interest to many readers of mBio.”

As suggested, we have added more on toothed versus filter-feeding whales, thus bringing in more discussion of the supplementary material.

p.5: We added “rRNA” as suggested.

p. 5: We added “other processes” as suggested.

p.9: Reworded as suggested.

p.9: Reworded to make consistent.

p.11: The misspelling is corrected.

p.12: We have reworded to clarify the distinction between filter-feeding and toothed (carnivorous) whales.

p.14: The spelling mistake has been corrected.

p.16: We reworded to reduce redundancy as suggested.

p.16: We clarified that the indicated sentence is new information.

p.19: The question about the DNA purification protocol has been addressed in the revised text.

We again thank the reviewers for their thoughtful comments on our study, and hope the paper is now suitable for publication in mBio.

Sincerely,

A handwritten signature in black ink, appearing to read "Rick Bushman". The signature is fluid and cursive, with a long horizontal stroke extending to the right.

Rick Bushman

Acknowledgements

Thanks to Arwa Abbas, Thomas D. Bushman, Sara Cherry, Eric Clarke, Andrew Marques, Yvonne Patterson and Scott Sherrill-Mix for helpful comments on this manuscript.

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HIV Language Guide

NIAID

National Institute of Allergy and Infectious Diseases



U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health
National Institute of Allergy and Infectious Diseases

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Background

This update of the HIV Language Guide was led by the Workforce Operations, Communications, and Reporting Branch (WOCR) in the Division of AIDS (DAIDS) in the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH).

The first iteration of the NIAID HIV Language Guide (hereafter referred to as “Language Guide”) was created in February 2020 by the NIAID Office of Communications & Government Relations (OCGR) News & Science Writing Branch (NSWB) with input from DAIDS WOCR. Input and review were solicited from representatives of NIH, other public health organizations, and community-based groups to help ensure scientific accuracy, community buy-in, and cultural relevance. The Language Guide was intended to be a living document, subject to change as language standards in various fields may evolve.

For this 2024 edition, the Language Guide was circulated for feedback from all the community groups associated with NIAID-funded research networks and programs, including network and site-level community working groups and community advisory boards (CABs) of the [AIDS Clinical Trials Group](#), [HIV Prevention Trials Network](#), [HIV Vaccine Trials Network](#), [International Maternal Pediatric Adolescent AIDS Clinical Trials Network](#), [the Martin Delaney Collaboratories](#), and the [Centers for AIDS Research](#) (CFAR). It also was shared with the [Legacy Project](#) and other working groups supported by the [Office of HIV/AIDS Network Coordination](#) (HANC), including the Women’s HIV Research Collaborative, the Latinx Caucus, Community Partners, the American Indian and Alaska Native Working Group, the New Investigators Working Group, the Communications Working Group, and the Minority-Serving Institution Working Group. Feedback and suggestions were incorporated as appropriate.

Guidance documents and learning modules compiled by the DAIDS Cross-Network Transgender and Gender Diverse Working Group and the [2019-2023 Trans-NIH Strategic Plan for Women’s Health Research](#), compiled by the Office of Research on Women’s Health (ORWH), also informed language standards in the section “Sex, Gender & Sexuality.”

Language guidance for the “Substance Use” chapter was initially informed by a 2017 Office of National Drug Control Policy [memorandum](#) entitled “Changing Federal Terminology Regarding Substance Use and Substance Use Disorders,” as well as by [training resources](#) compiled by the Substance Abuse and Mental Health Services Administration and its partners. This section was carefully reviewed and updated by the National Institute on Drug Abuse (NIDA) Communications Branch to align with NIDA’s [resources on non-stigmatizing language](#).

To ensure accuracy and consistency, the Language Guide was then reviewed by representatives from across NIH, including the Office of AIDS Research, the Sexual and Gender Minority Research Office, ORWH, the Tribal Health Research Office, as well as NIDA, National Institute of Mental Health, National Institute on Aging, National Institute of Alcohol Abuse and Alcoholism, National Institute on Minority Health and Health Disparities, and the *Eunice Kennedy Shriver* National Institute of

Child Health and Human Development. A review also was provided by the Tuberculosis Trials Consortium Community Research Advisory Group. The final review was provided by NIAID's OCGR and NIAID, DAIDS, and HANC leadership.

Contacts

If you are an NIH employee, the NIAID Office of Communications & Government Relations is available to assist with your communications needs and can consult on the appropriate use of language. Contact them at NIAIDNews@niaid.nih.gov.

About This Guide

This guide includes language suggestions for communicating about HIV and related topics. While it was originally designed to help NIAID staff communicate with empowering rather than stigmatizing language, especially as it relates to HIV, it was quickly recognized that it has value beyond NIAID.

This guide aims to help scientists, administrators, and researchers use fair, accurate, and respectful language and aid funded research networks, sites, centers, investigators, and stakeholders as they draft protocols and develop communications and outreach materials.

The Language Guide describes current thinking and best practices and procedures. NIAID strongly encourages use of person-first, non-stigmatizing language in all communications, including, but not limited to grant applications, contracts, publications, presentations, abstracts, and press materials. Prior to meetings and conferences, and when requests for reports, applications, and other communications are made, NIAID will emphasize its expectation that person-first language be used, and that stigmatizing language not be used (the most used stigmatizing terms will be highlighted and a link to the Language Guide made available). NIAID will actively work to advocate for the use of accurate and appropriate language throughout NIAID as well across the National Institutes of Health and the Department of Health and Human Services.

This document will be periodically reviewed and updated as needed to ensure that it remains current.

Note: The language guidance described in this guide applies primarily to English speakers in the United States. Language varies in different contexts, and translation can also change the connotation of certain phrases. While great care was taken to incorporate perspectives from many different communities, language varies over time and place and is constantly evolving. Similarly, while NIAID will continually review this document for accuracy and relevance, language guidance is subject to change.

Below are a few examples of the impact that language can have:

“Change the language to end HIV stigma. Hope I have communicated clearly.”

—Ugandan advocate Dric Adoni tweets about stigmatizing language around HIV from a popular youth HIV awareness event, the Y Plus Beauty Pageant.

“OMG! The current [#ACTGannualmeeting] plenary presenter stopped herself mid-sentence from almost saying ‘HIV-infected’ participants & changed it to ‘participants with HIV.’”

—American educator and autism and HIV advocate Morénike Giwa Onaiwu complimented person-first language used by a presenter at ACTG annual meeting.

“There are not ‘difficult to reach people’ only services which are not well designed, #language is part of creating #stigma #NHIVNA #HIV”

—UK-based HIV advocate Silvia Petretti makes the point that “difficult to reach people” puts the onus of obtaining HIV services on individuals facing adversity rather than on public health efforts.

Introduction

“We condemn attempts to label us as ‘victims,’ a term which implies defeat, and we are only occasionally ‘patients,’ a term which implies passivity, helplessness, and dependence upon the care of others.

We are ‘People With AIDS.’”

— The Denver Principles (1983)

Since a group of people living with AIDSⁱ wrote the self-empowerment manifesto known as *The Denver Principles* in 1983, language has been a central theme in efforts to dismantle the stigma around HIV. Many HIV advocacy groups and media outlets embrace slogans such as “language matters” and promote primers on using empowering language, as do other advocacy and health organizations.

Conversations about language choice frequently come up during conferences and listening sessions.

While everyone agrees that language matters, not everyone always agrees on the appropriate or acceptable terminology.

Language norms vary geographically, culturally, and over time. It is best to embrace the reality that language is constantly evolving, and it is up to us to evolve with it from a place of respect and humility.

When scientists and administrators write or speak about HIV, the words they choose have the power to perpetuate ignorance, bias, and stigma. Conversely, they have the power to represent people and ideas respectfully and accurately.

Empowering language remains an important focus for the HIV workforce because language has the potential to perpetuate stigma, and as studies continue to show, stigma helps perpetuate the HIV epidemic.ⁱⁱ

While many factors that contribute to health-related and societal stigmas are entrenched and systemic, NIAID staff and other groups that work with NIAID, such as grantees, contractors, and collaborators, have the immediate power and opportunity to improve language and lead by example.

Quick Tips

Use the Platinum Rule

- **“Treat others as they wish to be treated.”**

Many learn as children that the best way to respect others is to follow the Golden Rule: “Treat others as you wish to be treated.” Many advocates in the HIV community promote the Platinum Rule: “Treat others as they wish to be treated.”

Use Person-First Language

■ **Generally, most people prefer person-first language that emphasizes humanity, highlights autonomy, and promotes the idea that most people’s disabilities are just one facet of their life and identity.**

This is particularly true for people with an acquired, chronic illness (i.e., “person with diabetes” instead of “diabetic”).

Know Your Audience

- **When possible, proactively seek input from the community you are discussing or describing.**

Remain receptive to feedback from those who are most affected by stigmatizing language and prioritize expertise from their lived experiences.

While some may find this to be a challenge, investing in respectful communication can strengthen the relationship between researchers and the public they are trying to reach.

Rephrase or Reframe

■ **Finding the most appropriate language may mean rephrasing or reframing a message instead of just replacing terms.**

Recognize that there may not be a universal “right” answer for how to discuss a certain topic.

Consider the Context

- **Choosing appropriate language always depends on the context in which the language appears.**

While the principles in this guide may be applied broadly to scientific talks, notices of funding opportunities (NOFOs), requests for proposals (RFPs), media interviews, developing study protocols, and public calls for clinical research participation, including outreach materials, other contexts may call for specific language that does not fit neatly into the following guidelines.

Choose the Right Image

- **Be mindful of how an image you use may affect diverse audiences.**

Written and spoken words are only two facets of communication. Images and body language also convey messages, tone, and—unfortunately—stigma.

Images can contribute to racial bias and stigma,ⁱⁱⁱ and advocates for people who use substances caution against using images of alcohol, syringes, or pills in relation to substance use, as these may be triggering for someone in recovery.

- **In the context of HIV, most advocates prefer images that highlight people living vibrantly with HIV to those that may show graphic depictions of symptoms of HIV.**

Consider how images related to pregnancy and perinatal transmission of HIV are used, considering pregnant people as individuals rather than just vessels for a baby.^{iv} For example, images showing the pregnant person's whole body are more humanizing than those cropped to show only the abdomen.^v

- **Images need to be representative of the demographics of a given region or country in terms of race, sex, age, and other characteristics.**

For example, in the United States, more than half of people living with HIV are over 50 years of age, and images should reflect this context.

Stigmatizing Terms and Alternatives

Key Terms To Avoid

Some of the more commonly used yet most critical terms to avoid are highlighted below; additional stigmatizing terminology and suggested alternatives, along with the rationale, are provided in the main text of the guide.

Stigmatizing Terms To Avoid	Use These Alternatives
HIV-infected, HIV-infection*, HIV-positive [people, individuals, populations]	People living with HIV, people with HIV (<i>*see page 8 for comments on use of “HIV-infection”</i>)
Subject	Participant, volunteer
Sterilizing cure	HIV elimination, HIV eradication, HIV clearance
AIDS (when referring to the virus, HIV)	HIV, HIV and AIDS when referring to both
Mother-to-child transmission	Perinatal transmission
Verticals	Lifetime survivors
At-risk or high-risk person/population	Person/population with greater likelihood of ..., high incidence population, affected community
Target population	Key population/engage or prioritize a population
Hard-to-reach population	Under-resourced, underserved by [specific resource/service], population(s) experiencing discrimination/racism/transphobia

HIV-Specific Terminology

Stigmatizing Terms To Avoid	Use These Alternatives	Here’s Why
<p>AIDS (when referring to the virus, HIV)</p> <p><i>Related terms to avoid:</i> <i>Died of AIDS</i></p>	<ul style="list-style-type: none"> ✓ HIV ✓ HIV and AIDS (when referring to both) ✓ Died from complications related to HIV ✓ Died of an AIDS-related illness 	<p>AIDS itself is not a condition; it is a range of conditions, or a syndrome, that occurs when a person’s immune system is weakened by HIV. There is stigma associated with AIDS, so HIV is preferred and most often more accurate. The other terms listed avoid the incorrect assumption that AIDS is uniformly fatal and clarify that opportunistic infections are the acute cause of death.</p>

HIV-Specific Terminology (continued)

Stigmatizing Terms To Avoid	Use These Alternatives	Here's Why
<p>HIV infection/HIV-infected</p> <p><i>Related terms to avoid: HIV-infected people, HIV positives, HIV carriers, people infected with HIV, HIV-uninfected people</i></p>	<ul style="list-style-type: none"> ✓ HIV ✓ People/person living with HIV ✓ People/person with HIV ✓ HIV status ✓ HIV diagnoses ✓ HIV acquisition ✓ HIV transmission 	<p>“Infection” carries the stigma of being contagious, a threat, or unclear. HIV advocates frequently highlight the damaging consequences of this word choice. In specific situations, the term “HIV infection” is necessary to describe the biological process. In most cases, however, “HIV” alone accomplishes the necessary communication.</p> <p>Person-first language emphasizes humanity. “Living with” is an affirmation of life many advocates prefer. “Poz” is also sometimes used by community members themselves.</p>
<p>HIV cases</p>	<ul style="list-style-type: none"> ✓ People/person living with HIV ✓ People/person with HIV ✓ People/person newly diagnosed with HIV ✓ People/person who recently acquired HIV 	<p>People should not be described as a “case,” as this term deemphasizes humanity and implies burden.</p> <p>Person-first language should be used when referring to people who are newly diagnosed with HIV. When referring to general incidence, however, it is acceptable to refer to the data using terms such as “cases,” “diagnoses,” and the term “incidence” itself, which is the most objective term.</p>
<p>Sterilizing cure</p> <p><i>Related terms to avoid: HIV elimination, natural cure, functional cure, remission*</i></p>	<ul style="list-style-type: none"> ✓ Clearance of HIV^{vi} ✓ Clearance cure ✓ HIV clearance ✓ HIV eradication ✓ Viral control off therapy^{vii} ✓ ART-free virologic control ✓ Post-intervention control ✓ Virologic suppression off therapy ✓ Investigational control 	<p>“Elimination” implies that people living with HIV must disappear to achieve an end to the epidemic. The other terms are considered offensive, inappropriate, or inaccurate. “Sterilizing” should not be used as it has a negative connotation given historic sterilization campaigns and may discourage participation in research.</p> <p>* “Remission” should not be used when referring to virologic control off therapy. Virologic control is defined as undetectable virus off therapy (outside of a clinical setting) using a standard clinical assay. Non-standard assays can detect the presence of replication-competent virus. Remission is appropriate when referring to an individual who was thought to have all replication-competent virus removed when samples were analyzed using non-clinical assays, however rebound eventually occurred.</p>

HIV-Specific Terminology (continued)

Stigmatizing Terms To Avoid	Use These Alternatives	Here's Why
<p>Unlikely or impossible to transmit HIV (with regard to PrEP use)</p> <p><i>Related terms to avoid: effectively impossible to transmit HIV, people who have an undetectable viral load have little risk of transmission, almost no risk greatly reduces risk, close to zero risk</i></p>	<ul style="list-style-type: none"> ✓ Undetectable equals Untransmittable (U=U) ✓ People with undetectable viral load cannot/do not/will not transmit HIV sexually 	<p>Describe the principle of treatment as prevention, or “Undetectable equals Untransmittable,” clearly and consistently. It is inaccurate to use qualifiers that suggest U=U is only somewhat effective. Unnecessary qualifiers perpetuate the overestimation of the likelihood of HIV transmission.</p>

Research Terminology

Stigmatizing Terms To Avoid	Use These Alternatives	Here's Why
<p>Subject</p> <p><i>Related terms to avoid: research subject, patient, client</i></p>	<ul style="list-style-type: none"> ✓ Participant ✓ Research or study participant ✓ Volunteer 	<p>“Subject” is dehumanizing and denotes a hierarchical system where a group of people are subject to the will of another (such as the researcher). The term does not recognize the autonomy of the individual. Not all participants are patients, particularly in research involving people who are generally in good health. “Client” and “consumer” do not typically apply to the research setting.</p>
<p>Experiment/ Experimental</p>	<ul style="list-style-type: none"> ✓ Clinical trial ✓ Study ✓ Novel ✓ Investigational* 	<p>“Experiment” tends to evoke the image of lab mice rather than people who are participating in research.</p> <p>*“Investigational” is a broadly used regulatory term that may be necessary to use in certain contexts; however, some people report “investigational” has a similar connotation to “experimental,” preferring “novel” be used when possible.</p>
<p>Target (a population)</p>	<ul style="list-style-type: none"> ✓ Engage (a population) ✓ Prioritize ✓ Priority population/group ✓ Key population/group 	<p>The preferred terms emphasize community-oriented, participatory approaches to ending an epidemic instead of paternalistic, top-down approaches.</p>

Research Terminology (continued)

Stigmatizing Terms To Avoid	Use These Alternatives	Here's Why
<p>Hard-to-reach (populations/ individuals)</p>	<ul style="list-style-type: none"> ✓ People who are underserved by [specific service/ resource] ✓ Underrepresented ✓ Population(s) experiencing discrimination/racism/transphobia ✓ People/person who are medically underserved or lack access to health care services ✓ People/populations with low incidence 	<p>“Hard to reach” places the blame on the individuals and communities in question. The preferred terms put the onus on the health sector rather than communities. Naming the specific systems and structures causing the lack of engagement (e.g., racism, transphobia) is better than being vague about why a population is not being reached.</p>

Research Terminology (continued)

Stigmatizing Terms To Avoid	Use These Alternatives	Here's Why
<p>At-risk or high-risk (people/population/group)</p> <p><i>Related terms to avoid: increased risk, vulnerable, marginalized</i></p>	<ul style="list-style-type: none"> ✓ Affected community/population ✓ High-incidence population ✓ People/populations with high incidence ✓ Communities overrepresented in the HIV epidemic ✓ Disproportionately affected ✓ People/person most in need of... ✓ People/person with greater likelihood of... ✓ People/person exposed to HIV ✓ People/person in communities with high HIV incidence ✓ People/person with certain risk factors ✓ People/person who could benefit from HIV prevention or treatment options <p>If possible, reference the specific causal factors.</p> <ul style="list-style-type: none"> ✓ Groups that have been [economically/socially] marginalized ✓ Groups at higher risk of [outcome] ✓ Groups experiencing disadvantage ✓ Groups experiencing a disproportionate impact [of HIV] ✓ Population of focus ✓ Under-resourced communities 	<p>People and communities are not inherently “risky” and “high-risk.” Terms such as “vulnerable,” “marginalized,” and “high-risk” are stigmatizing and convey judgment. The preferred terms acknowledge societal challenges and accurately reflect disease dynamics.</p>

Research Terminology (continued)

Stigmatizing Terms To Avoid	Use These Alternatives	Here's Why
Treatment default	<ul style="list-style-type: none"> ✓ Treatment non-completion ✓ Interruption in treatment 	<p>“Default” is a negative term that implies judgment about the person who did not complete treatment.</p>
<p>Compliance <i>Related terms to avoid: adherence/adherent*</i></p>	<ul style="list-style-type: none"> ✓ Continuity of treatment ✓ Continuity of care ✓ Taken as prescribed 	<p>“Compliance” implies passive behavior/ following instructions or orders. *While “adherence/adherent” is preferred to “compliance,” using “continuity of treatment” or “continuity of care” acknowledges that sometimes treatment is interrupted due to circumstances beyond a person’s control.</p> <p>This language shift is intended to focus on the circumstances (whether treatment is occurring for any reason) vs. the presumption that access to and taking of medicine is entirely at the will of the individual. Continuation of medication is not limited to treatment and should be revisited when discussing taking medications for PrEP use as well. “Taken as prescribed” provides a clear alternative that suggests that medication is taken whether needed daily or monthly.</p>

Sex, Gender, and Sexuality

Definition of Terms

Gender

Cisgender Person

A person whose gender identity is aligned with their sex assigned at birth, sometimes abbreviated as “cis.”

Gender

A composite of socially constructed roles, behaviors, activities, and/or attributes that a given society considers appropriate, often based on sex assigned at birth. The gender binary of “man” and “woman” has been imposed, perpetuated, and reinforced through colonialism, but many nonbinary genders have existed throughout human civilization and still exist today despite the widespread imposition of the gender binary.

Gender Expression

How one chooses to convey one’s gender identity through behavior, clothing, and other external characteristics.

Gender Fluid

Person whose gender identity shifts between different genders (or no gender).

Gender Identity

An individual's sense of being a man, boy, woman, girl, nonbinary, gender fluid, intersex, genderqueer, gender nonbinary, Two-Spirit (used by some indigenous peoples), etc.; culturally dependent and not necessarily visible to others.

Gender Nonbinary

A person who does not identify within the confines of a binary gender construct. “Nonbinary” is an umbrella term that refers to people who do not identify within a single category of man or woman. Other terms include genderqueer, gender nonconforming, and Two-Spirit.

Gender Nonconforming

A person whose gender expression is not consistent with the societal or cultural norms expected of that gender.

Genderqueer

A person who does not necessarily identify solely as a man or woman or subscribe to conventional gender distinctions.

Misgender

To refer to someone, especially a transgender person, using a word, pronoun, or address that does not correctly reflect their gender identity.

Transgender or Trans

An umbrella term that includes many different gender identities and that typically is used by people whose gender identity differs from the sex they were assigned at birth.

Two-Spirit

An umbrella term used by some indigenous people around the world to describe sexual and gender minority people in their communities, including individuals otherwise known as transgender, bisexual, gay, lesbian, and/or queer. The term was created by and for indigenous peoples, and it was not created to be used as an identity marker for non-indigenous people. Because the term “Two-Spirit” can have different meanings, it may be important to ask follow-up questions to understand what it means to a person who uses the term to describe themselves.

Identity and Specificity

In certain contexts, it may be appropriate to use language that explicitly references sexual behaviors instead of referencing sexual orientations and gender identities. For example, a study may evaluate the ability of an experimental modality to prevent HIV transmission during anal intercourse between people assigned male at birth who identify as men. While many participants enrolled in this study may identify as gay or bisexual, there may be others who do not identify this way but nonetheless have anal intercourse with other cisgender men. In other words, medical specificity to describe behavior should be accounted for outside of individuals' identity around sexual

orientation. In this case, an accurate description of the enrolled participants is “cisgender men who have sex with men.”

All science takes place in a cultural context, which must be considered when we prepare written materials for the public.

Pronouns

Because gender identity is an internal characteristic that should not be assumed, a person’s pronouns should not be assumed either. In addition to the binary English pronouns “she/her” and “he/him,” some people may use nonbinary pronouns, including the pronouns “they/them” used as singular terms, among others. When using the singular “they,” still conjugate the verb as a plural, as in, “they are gender nonbinary.” Nonbinary pronouns should be incorporated into study protocols and other study documents when gender identity is not a specific element describing the study population; the binary pronouns “he or she” should not be used by default.

It is always appropriate to ask someone what pronouns they use.

It is best to first model the behavior by stating your own pronouns before asking for someone else’s, which helps convey understanding and lets someone know that it is a safe space to disclose one’s pronouns. For example, “I’m Charlie, and I use he/him pronouns. How would you like me to address you?” It can be extremely offensive and harmful to misgender someone by using incorrect pronouns. When writing about a hypothetical person, like an anonymous participant in a study enrolling people of all genders, use the singular “they” or “their” rather than “he or she” or “his or hers” to be inclusive.

Relationships

Avoid language that assumes the nature of a given relationship.

Use the terminology described by the individual participant when possible, or simply use the neutral term “sexual partner(s).”

For example, be mindful that not all sexual partners are romantically involved, which may be implied by terms like “couples.” Similarly, do not assume that sexual partners are monogamous or that there is only one way to define monogamy.

Sex and Sexuality

Intersex

Term used for a variety of conditions that do not seem to fit the typical definitions of female or male, also known as variations in sex characteristics. Additionally, it can be used to refer to people who are born with genitals, reproductive organs, or chromosomal patterns that do not fit standard definitions of male or female or develop these differences in puberty. There are also genetic tests that can identify intersex conditions pre-birth^{viii}. In other contexts, it may be appropriate to highlight sexual orientation. Using this language can honor the contributions of these communities or connect with people on an identity level. For example, one might say, “The advocacy group aims to increase PrEP use among gay, bisexual, and other men who have sex with men of color.”

Sex

Typically categorized as male, female, or intersex based on chromosomes and genetics, hormones, and anatomy. Intersex and nonbinary sex assigned at birth exists in some places (e.g., currently, 17 U.S. states allow X on original birth certificates).^{ix}

Sex Assigned at Birth

Historically determined when a health care provider inspects a newborn baby’s genitalia and/or through genetic testing and anatomy scans during pregnancy. The infant’s sex is traditionally assigned as male or female on their birth certificate, although intersex and nonbinary sex assigned at birth exists in some places (e.g., currently, 17 U.S. states allow X on original birth certificates).^x

Sexual Orientation

Asexual

An umbrella term describing people on a spectrum of sexuality, including people who experience no sexual feelings or desires, to people who only experience sexual attraction under certain conditions (such as emotional attraction as a prerequisite for sexual attraction).

Bisexual

Having the potential to be emotionally, romantically, and/or sexually attracted to people of the same and different gender—not necessarily at the same time, in the same way, or to the same degree.

Gay

Having the potential to be emotionally, romantically, and/or sexually attracted to people of the same gender.

Lesbian

Refers to someone who identifies as a woman who has a romantic and/or sexual orientation toward other people who identify as women. Some nonbinary people also identify with this term.

Pansexual

Not limited in sexual attraction with regard to sex, gender identity, or gender expression.

Queer

People who identify as queer may think of their sexual orientation and/or gender identity as characterized by nonbinary constructs of sexual orientation, gender, and/or sex. (The term is considered more fluid and inclusive than traditional categories for sexual orientation and gender identity, and some even use the term to describe their political beliefs. Once considered a pejorative term, queer has been reclaimed by some LGBTQIA+ people who self-identify as queer; however, it is not a universally accepted term.)

Stigmatizing Terms and Alternatives

Stigmatizing Terms To Avoid	Use These Alternatives	Here's Why
Sexual preference	✓ Sexual orientation	“Preference” suggests that non-heterosexuality is a choice, a concept often used to discriminate against LGBTQIA+ communities. “Preference” also suggests a single selection from two or more choices, excluding bisexual people and pansexual people, among others.
Men who have sex with men (MSM)	✓ Gay, bisexual, and other men who have sex with men (GBMSM)*	Many gay men do not like to be referred to solely as men who have sex with men. Spelling out MSM—gay, bisexual, and other men who have sex with men—is more respectful. *It is acceptable to use “MSM” for brevity or in a table/chart, preferably with the explanation that this covers gay, bisexual, and other men who have sex with men at first instance. It is also important to use this term inclusively for transgender men unless otherwise specified. When referring exclusively to cisgender men, always specify “cisgender” and vice versa.
Unprotected sex <i>Related terms to avoid: unsafe sex, protected sex, safe sex</i>	✓ Condomless sex ✓ Sex without the use of condoms or other prevention tools	The preferred terms are more specific, accurate, and remove judgment. Condomless sex may still involve prevention efforts because there are other ways to prevent HIV (e.g., TasP, PrEP).
Promiscuous	✓ Has multiple sexual partners	Avoid “promiscuity” and its derivatives as it is an unnecessary value judgment.
Female condom Male condom	✓ Condom ✓ Internal condom ✓ External condom	“Condom” should be used more generically, but when there is a specific reason, internal or external condom can be used. Some transgender men and nonbinary people may use internal condoms, and people of all genders can use internal condoms for anal sex. People of all genders may cut condoms to create dental dams.

Stigmatizing Terms and Alternatives (continued)

Stigmatizing Terms To Avoid	Use These Alternatives	Here's Why
<p>Sex at birth <i>Related terms to avoid:</i> <i>biological sex, born male/female, natal sex</i></p>	<ul style="list-style-type: none"> ✓ Sex assigned at birth ✓ Assigned female/male at birth (AFAB/AMAB) 	<p>The preferred terms factually recognize that sex—and, by extension, gender—is assigned. They affirm gender as a social construct that may differ from one's assignment at birth.</p>
<p>Female to male (FTM) <i>Related terms to avoid:</i> <i>used to be a woman, born a woman</i></p>	<ul style="list-style-type: none"> ✓ Transgender man ✓ Trans masculine ✓ Trans man 	<p>FTM refers to a person who identifies as a man but was assigned female at birth; it is not a respectful way of acknowledging or referring to someone's gender. "Trans" is an adjective that helps describe someone's gender identity, and it should be treated like other adjectives.</p>
<p>Male to female (MTF) <i>Related terms to avoid:</i> <i>used to be a man, born a man, male-to-female (MTF)</i></p>	<ul style="list-style-type: none"> ✓ Transgender woman ✓ Trans feminine 	<p>MTF refers to a person who identifies as a woman but was assigned male at birth; it is not a respectful way of acknowledging or referring to someone's gender.</p>
<p>Transgendered <i>Related terms to avoid:</i> <i>Transgenders, a transgender, transgenering</i></p>	<ul style="list-style-type: none"> ✓ Transgender person 	<p>"Transgendered" is a dated term that suggests a point in time in the past when a person "became" transgender, which diverges from the lived experiences of most transgender people. Similarly, "transgenders" is dated and does not emphasize humanity.</p>
<p>Sex change <i>Related terms to avoid:</i> <i>Pre-operative/post-operative, gender re-assignment surgery</i></p>	<ul style="list-style-type: none"> ✓ Gender affirmation ✓ Gender confirmation ✓ Transition ✓ Transitioning 	<p>"Gender affirmation" and "transition" define the interpersonal, interactive process whereby a person receives social recognition and support for their gender identity and expression. This process can but does not necessarily involve medical intervention, which can include hormone therapy and one or more surgeries to affirm one's gender. Gender-affirming hormone therapy (GAHT) is preferable to feminizing hormone therapy or masculinizing hormone therapy. "Pre-/post-operative" may still be used in medical literature but should not be applied to a specific person without their consent.</p>

Stigmatizing Terms and Alternatives (continued)

Stigmatizing Terms To Avoid	Use These Alternatives	Here's Why
Hermaphrodite	<ul style="list-style-type: none"> ✓ Variations in sex characteristics ✓ Intersex identity ✓ Person who is intersex 	<p>“Variations in sex characteristics” and “intersex identity” are preferred. “Variations in sex characteristics” is an inclusive umbrella term that refers to congenital atypical variations in the development of chromosomal, gonadal, or anatomical sex. Many, but not all, people with variations in sex characteristics identify as intersex. It is always best to ask how one identifies. Hermaphrodite is considered offensive because of its mythical origin and historically derogatory use.</p>
Man/men	<ul style="list-style-type: none"> ✓ Cisgender man/men (CGM) ✓ Transgender man ✓ Person assigned male sex at birth 	<p>In protocols, when the term “man” is used, people often intend it to refer to 1) cisgender men and/or 2) anyone who was assigned male sex at birth, regardless of current gender identity. It is important to be specific to ensure accuracy, as the term “man” is vague and does not encapsulate the distinctive features of either of these 2 groups. If used, it should be defined first.</p> <p>We recommend not using “men and women” unless people who are nonbinary and gender fluid are explicitly excluded, as that also reinforces the binary. Instead, it is best to use “people,” “people of all genders,” “all people,” or “men, women, and gender nonbinary people.” This last suggestion is the most inclusive option as it explicitly names the inclusion of gender nonbinary people.</p>
Woman/women	<ul style="list-style-type: none"> ✓ Cisgender woman/women ✓ Transgender woman ✓ Assigned female at birth 	<p>The same is true for the use of “women.”</p>

Pregnancy and Family

- Do not assume a given family dynamic or relationship between parent and child.

Be mindful that children are raised by biological parents, as well as by adoptive parents and other caregivers. Often, language around pregnancy, childrearing, and family can reinforce gender-stereotyped roles. Avoid language that implies childcare or ensuring a child’s health is the sole responsibility of women or mothers. Similarly, avoid language that portrays pregnant or breast/chestfeeding people as mere vessels supporting a child.

Pregnancy is not limited by gender, and language around pregnancy and birth should reflect this fact. In research protocols that do not contain gender-based eligibility criteria, language such as “pregnant women” and “mother” may incorrectly imply that participants who do not identify as women or mothers are not eligible, so gender-neutral language should be used. In studies that do contain gender-based eligibility criteria, it may be appropriate and even affirming to refer to “women” and “mothers;” however, studies with gender-based exclusion criteria must provide explicit justification for excluding potential participants based on their gender identity.

Stigmatizing Terms and Alternatives

Stigmatizing Terms To Avoid	Use These Alternatives	Here’s Why
Mother-to-child transmission (MTCT)	<ul style="list-style-type: none"> ✓ Perinatal transmission ✓ Vertical transmission 	The preferred terms do not place blame on pregnant people. They also focus objectively on the mode of transmission rather than the subjective, assumed identities of the people involved.
Verticals	<ul style="list-style-type: none"> ✓ Lifetime survivors 	People who acquire HIV in utero or during breastfeeding often refer to themselves as “lifetime survivors.” Another community-generated term is “dandelions,” which is based on the poem “Dandelion” by Mary Bowman.
Infants at risk (in utero, during labor, or through breastfeeding)	<ul style="list-style-type: none"> ✓ Infants exposed to HIV (in utero, during labor, or through breastfeeding/ chestfeeding/ nursing/lactation) ✓ Fetus exposed to HIV in utero 	“Infants exposed to HIV” will work on its own in some circumstances, but sometimes clarification may be needed to refer to the specific exposure. Before delivery, it may be more appropriate to refer to the “fetus.”

Stigmatizing Terms and Alternatives (continued)

Stigmatizing Terms To Avoid	Use These Alternatives	Here's Why
<p>Mother (referring to the person who gave birth) <i>Related terms to avoid: pregnant woman, maternal, mother-infant pair</i></p>	<ul style="list-style-type: none"> ✓ Birth parent ✓ Gestational parent* ✓ Pregnant people or individuals ✓ Pregnant participant ✓ Postpartum participant ✓ Parent-infant pair ✓ Participant-infant pair/parent-participant pair ✓ Parental 	<p>Not all pregnant people identify as mothers. “Mother” or “maternal” may imply the pregnant person is a woman or identifies as female. This terminology can exclude trans men and nonbinary people. It is appropriate to use the term “mother” when you are sure that the person identifies this way.</p> <p>*“Gestational parent” refers to a person involved in the birth and care of a child, whereas “gestational carrier” may be a more fitting term for a person who carries a fetus to term and then either has little or no long-term involvement in the care of the child.</p>
<p>Women (or girls) of childbearing potential <i>Related terms to avoid: women (or girls) of reproductive potential</i></p>	<ul style="list-style-type: none"> ✓ People/person of childbearing potential ✓ Individual of childbearing potential ✓ People/person able to become pregnant ✓ People/person with reproductive potential ✓ Parental 	<p>The preferred language is more inclusive and encompasses people who may become pregnant but do not identify as women.</p> <p>People of all genders and sexes may have reproductive potential.</p>
<p>Breastfeeding <i>Related terms to avoid: Breast milk</i></p>	<ul style="list-style-type: none"> ✓ Breast/chestfeeding ✓ Nursing or lactating ✓ Breast/chest milk ✓ Human milk 	<p>Some individuals, including in some cases trans men or gender nonbinary individuals, may not refer to this part of their body as “breasts,” and the term “chest” is used instead. As with many terms, people have different preferences for specific terms such as “chestfeeding,” “nursing,” or “lactating” as alternatives. When speaking to individuals about HIV and infant feeding, it is always best to determine and use their preferred terminology.</p>
<p>Birth control</p>	<ul style="list-style-type: none"> ✓ Contraception 	<p>“Birth control” is very female-centric and typically is only used in reference to products used by “women.” This does not appropriately include people with transgender or nonbinary identities. Contraception can be used in reference to people of any sex assigned at birth or gender identity.</p>

Substance Use

Definition of Terms

Substance Use Disorder, Addiction, and Dependence

“Substance use disorder,” “addiction,” and “dependence” are related but frequently confused terms.

Substance use disorders are chronic, treatable medical conditions from which people can recover. They are defined in part by continued substance use despite negative outcomes. Substance use disorders may be diagnosed as mild, moderate, or severe based on whether a person meets defined diagnostic criteria.

Addiction is not a formal diagnosis, and the term is used in many ways. Some people use the term to describe some substance use disorders, especially more serious presentations but the correct terminology should be used.

Dependence describes a condition in which withdrawal symptoms are experienced if substance or medication use is abruptly ceased or significantly reduced. Dependence can occur with the chronic use of many substances, including many medications, even if taken as prescribed. While dependence can be one of the symptoms used to diagnose a substance use disorder, dependence should not be confused as synonymous with substance use disorder or addiction.

Drug Misuse and Alcohol Misuse

While the term “drug abuse” has been shown to perpetuate stigma, there is disagreement about the utility of “drug misuse.” Many people find the term helpful when discussing nonmedical use of substances that also have medical uses, such as prescription opioids. While an instance of nonmedical use of a medication like a prescription opioid is misuse, it does not necessarily mean the person has an opioid use disorder. “Misuse” can also be used to describe adult consumption of legal substances like alcohol (or, in some states, cannabis) in ways that may negatively impact health and safety.^{xi}

“Misuse” and “substance use disorder” should not be used interchangeably, as not all people who misuse substances experience substance use disorder or require treatment to stop using substances. For example, a single occasion of binge drinking is considered alcohol misuse but may not amount to an alcohol use disorder diagnosis in a given individual.

Because “misuse” can also suggest fault on the part of people with substance use disorders, the neutral term “use” is generally preferred for most substances, except alcohol, when it will not create confusion.

Illicitly manufactured substances used outside of medical settings (such as heroin or illicitly manufactured fentanyl, cocaine, or methamphetamine) can be described in terms of “use” (NIH, 2023). The term “use” can also be used to describe the illegal consumption of legal substances by underaged youth.^{xiii}

“Alcohol misuse” should be used instead of “alcohol abuse” when referring broadly to drinking in a manner, situation, amount, or frequency that could cause harm to the person who is engaging in drinking and/or to those around them.

For individuals younger than the minimum legal drinking age of 21, or for pregnant individuals, any alcohol use constitutes alcohol misuse. Alcohol misuse can be acute (e.g., binge drinking on a weekend night) or chronic (e.g., drinking associated with alcohol use disorder).^{xiii}

Stigmatizing Terms and Alternatives

Stigmatizing Terms To Avoid	Use These Alternatives	Here’s Why
<p>Clean syringes/dirty syringes</p> <p><i>Related terms to avoid: contaminated syringes</i></p>	<ul style="list-style-type: none"> ✓ New or unused/used syringes ✓ Sterile syringes 	<p>“Clean” and “dirty/contaminated” evoke value judgments and specific visual assumptions that may not be accurate. The preferred terms are clearer and more accurate when discussing syringes and related injection equipment. “Needles” may also be used when engaging a community that is more likely to use that terminology.</p>
<p>Injection drug user (IDU)</p> <p><i>Related terms to avoid: drug user/abuser, drug addict, drug-addicted</i></p>	<ul style="list-style-type: none"> ✓ People/person who injects drugs (PWID) ✓ People/person who uses drugs 	<p>Person-first language emphasizes humanity. If an acronym is needed for “people who inject drugs”, PWID can be used but to the extent possible, it is better not to refer to people, especially individual people, using an acronym.</p>
<p>Alcoholic</p> <p><i>Related terms to avoid: abuser or drunk</i></p>	<ul style="list-style-type: none"> ✓ People/person with alcohol use disorder ✓ People/person who misuses alcohol or who engages in alcohol misuse 	<p>Person-first language emphasizes humanity.</p>
<p>Drug abuse</p> <p><i>Related terms to avoid: drug dependence, drug habit</i></p>	<ul style="list-style-type: none"> ✓ Substance use disorder 	<p>“Substance use disorder” is a medical term used to describe a chronic, treatable condition from which a person can recover. Substance use disorders are defined in part by continued substance use despite negative outcomes.</p> <p>“Dependence” is not synonymous with substance use disorder or addiction; see “Substance Use Disorder, Addiction, and Dependence” in the substance use section, definition of terms.</p>

Stigmatizing Terms and Alternatives (continued)

Stigmatizing Terms To Avoid	Use These Alternatives	Here's Why
<p>Alcoholism <i>Related terms to avoid: alcohol abuse, alcohol dependence</i></p>	<ul style="list-style-type: none"> ✓ Alcohol use disorder 	<p>“Alcohol use disorder (AUD)” is characterized by an impaired ability to stop or control alcohol use despite adverse social, occupational, or health consequences. It is a spectrum disorder and can be mild, moderate, or severe. AUD can cause lasting changes in the brain that make patients vulnerable to relapse. Most people with AUD can benefit from treatment with behavioral therapies, medications, or both.</p> <p>In the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), AUD replaces the older categories of alcohol abuse and alcohol dependence with the single disorder, AUD.</p>
<p>Clean/dirty</p>	<ul style="list-style-type: none"> ✓ Currently using or not currently using substances ✓ Negative (for a toxicology screen) ✓ Positive (for a toxicology screen) 	<p>Labeling the use of drugs as “dirty” and the absence of drug use as “clean” invites a value judgment that stigmatizes people who use drugs and does not accurately reflect the complexities of substance use disorder and recovery.</p>
<p>Born addicted <i>Related terms to avoid: addicted infant</i></p>	<ul style="list-style-type: none"> ✓ Born in withdrawal ✓ Born dependent on [drug] ✓ Infant with neonatal abstinence syndrome 	<p>Infants cannot be born with addiction because they cannot meet the behavioral diagnostic criteria for substance use disorders. Rather, they may be born manifesting a withdrawal syndrome.</p>
<p>Opioid replacement <i>Related terms to avoid: methadone maintenance, drug substitution, medication-assisted treatment (MAT)</i></p>	<ul style="list-style-type: none"> ✓ Medication for opioid use disorder (MOUD) ✓ Pharmacotherapy ✓ Opioid agonist therapy (for buprenorphine and methadone specifically) 	<p>“Replacement” and “substitution” imply “substituting” one drug or one addiction for another, fueling a stigmatizing misconception that prevents people from accessing treatment. MOUD aligns with the way other psychiatric medications are understood (e.g., antidepressants, antipsychotics) as critical tools that are central to a patient’s treatment plan.</p> <p>MAT should not be used when referring to or inclusive of medications used to treat alcohol use disorder or opioid use disorder because “assisted” implies medications are secondary to other forms of treatment, which is no longer considered to be the case.</p>

Stigmatizing Terms and Alternatives (continued)

Stigmatizing Terms To Avoid	Use These Alternatives	Here's Why
Rehab/detox center	✓ Treatment center	“Rehab” and “detox center” carry cultural stigmas and misconceptions.
Recovering addict/ alcoholic <i>Related terms to avoid: former addict/alcoholic, reformed addict/ alcoholic</i>	✓ People/person in recovery ✓ People/person in remission	These person-first terms honor the belief that recovery is an ongoing and variable process. Some individuals with lived experience of substance use disorders may use a term like “addict” or “alcoholic” as part of their recovery program. These terms should only be used for personal stories, not general health information, and only with the person’s consent.
Relapse <i>Related terms to avoid: slip, slip-up, fall off the wagon</i>	✓ Return to use ✓ Recurrence	Suggested language removes the implication that a return to use is a moral failing and avoids negative associations.

Racial and Ethnic Identities

Collecting data on race and ethnicity reveals a great deal about health disparities and provides information needed for population health.^{xiv}

Generally, NIH uses racial and ethnic standards and definitions aligning with the Revisions to the Standards for the Classification of Federal Data on Race and Ethnicity.^{xv}

It should be noted that in 2022, a federal interagency working group was formed within the U.S. Office of Management and Budget (OMB) to review and develop recommendations for revising OMB’s Standards for Maintaining, Collecting, and Presenting Federal Data on Race and Ethnicity (SPD 15) with the goal of improving the quality and usefulness of federal race and ethnicity data.^{xvi}

Racial groups:^{xvii}

- American Indian or Alaska Native
- Asian
- Black or African American (Black is a term that can be applied to people anywhere in the world, including the United States, while African American refers specifically to American persons of African descent)
- Native Hawaiian or Other Pacific Islander
- White

The OMB guidance suggests that people of more than one race have the ability to select more than one racial group rather than have a “multiracial” category.

Ethnic groups (per OMB):

- Hispanic or Latino
- Not Hispanic or Latino

While these are the OMB-defined categories for ethnicity data collection purposes, we recognize that many individuals do not feel “seen” with those terms. Latino or Latina are broad terms that have been used for people of origin or descent from Cuba, Mexico, Puerto Rico, and some countries in Central America, South America, and the Caribbean, but again, individuals may prefer to specify their country of origin.

We recommend the use of Latina/o/e/x to be inclusive of individuals of all genders rather than Latino. When writing about known groups of individuals, more specific identifiers should be used. For example, when speaking about only cisgender women, Latina might be most appropriate. When discussing groups inclusive of transgender and gender diverse individuals, Latine or Latinx would be more appropriate.

Although Latinx is not recognized by OMB or NIH overall, it has been proposed as a gender-neutral, all-inclusive term. Its use may be considered on an audience-specific basis, particularly when addressing LGBTQIA+ communities in the United States, although some in those communities may prefer Latine.

Latine was created by LGBTQIA+ Spanish speakers and uses the letter “e” to illustrate gender inclusivity within existing Spanish pronunciation. In a Spanish-speaking context, Latine flows more naturally than Latinx in terms of grammar and pronunciation. When Latine is used as an adjective in Spanish, the noun that it describes can also be modified to reflect a similar gender-neutral variant (as in *niñes Latines*, meaning Latine children). The substitution of -e endings for the gendered -o and -a is already present in Spanish in nouns such as *estudiante* (student) and adjectives such as *interesante* (interesting).

Not everyone with Latin American heritage uses Latine or Latinx; many continue to use Latino as a gender-neutral default. Use specific language (e.g., Guatemalan American, if appropriate) and ask for personal identity preferences whenever possible.

- Latina/e/o/x can also be used to acknowledge the various communities, or one or more of these can be selected depending on the context:
 - Latino (individual man, group of men, or group of people including men and women)
 - Latina (individual woman or group of women)
 - Latine (gender-neutral term encompassing all genders)
 - Latinx (gender-neutral term encompassing all genders)

In keeping with the NIH Style Guide, the following should be noted:

- Avoid using “race/ethnicity” because the slash implies that these are interchangeable terms. Instead, use “race and ethnicity” or “race or ethnicity,” as appropriate.
 - Include context when writing about race and other demographic language. Populations should be described specifically whenever possible, and we should not default to using

“minorities” or “racial and ethnic groups” when we are really talking about specific populations. If the language cannot be made more specific (e.g., Black Americans, Asian Americans), then writing “racial and ethnic minority groups” is preferred over “minorities” alone; there are also sexual and gender minorities, etc.

Below are some additional considerations that also go beyond OMB racial and ethnic categories:

BIPOC refers to Black, Indigenous, and other People of Color. Many prefer this term to “racial minorities” and to “people of color.” It is considered inclusive of all communities of color while prioritizing Black and Indigenous peoples, who face particularly urgent social and structural disparities. Always use specific racial terms (e.g., Black or Indigenous) on their own instead of BIPOC if applicable; BIPOC should not be used when referring to an individual or an issue that affects a specific group of people.

American Indians and Alaska Natives are the only federally recognized political minority in the United States. Tribes hold a unique government-to-government relationship with the United States. When referring to a specific person or group of people, the best practice is to use a specific tribal identity whenever possible. American Indian or Alaska Native should only be used to describe persons with different tribal affiliations or when the tribal affiliations are not known or not known to be the same.

When referring to the diverse group of people with indigenous ancestry in the United States as a whole, the term American Indian is generally used. However, some communities may prefer Indigenous American or Native American, so it is best to ask how communities describe themselves.^{xviii} Never use pejorative terms, which include Eskimo instead of Alaska Native.

Indigenous is a broader term that includes people indigenous to any place in the world.

The term “Indian Country” describes reservations, lands held within tribal jurisdictions, and areas with American Indian populations. The term is used with positive sentiment within Native communities and by Native-focused organizations such as the National Congress of American Indians (NCAI) and news organizations such as *Indian Country Today*. In law, the term Indian country (lower case “c”) is found in several areas of the United States Code and is also an official legal term referenced in many Supreme Court opinions, collectively articulating the meaning as it pertains to federal law relating to American Indian land and people.^{xix}

People With Disabilities

People with disabilities are not a monolith, and this diverse community holds different views about whether person-first (person with disabilities) or identity-first (disabled person) language is appropriate in most contexts. Generally, most people prefer person-first language that emphasizes humanity, highlights autonomy, and promotes the idea that most people’s disabilities are just one facet of their life and identity. This is particularly true for people with an acquired, chronic illness (i.e., person with diabetes instead of diabetic).

However, some disabled people explain that their disability is an intrinsic part of their identity and should not be appended after “person.” For example, many autistic people prefer identity-first language because they view autism as a way of thinking and living rather than a disorder. This is sometimes called the “social model” of disability, as opposed to the “medical model.” This concept is also related to disability pride movements. For example, because deafness is associated with a unique education system, language, and subculture, most people in this population prefer to be called “Deaf.”

Stigmatizing Terms and Alternatives

Stigmatizing Terms To Avoid	Use These Alternatives	Here’s Why
Obese people <i>Related terms to avoid: the obese, overweight people</i>	<ul style="list-style-type: none"> ✓ People/person with [BMI or other metabolic score] of [X] ✓ People/person who are overweight or obese 	Use specific, neutral, person-first language when describing weight and fat distribution. Being overweight is a medical condition defined by body mass index. “Obesity” should be referred to as a disease, not a condition.
Handicapped <i>Related terms to avoid: handi-capable, differently-abled, the disabled</i>	<ul style="list-style-type: none"> ✓ People/person with disabilities ✓ Disabled people/person (preference varies) 	Community preference for person-first or identity-first (“disabled people”) varies, but most agree that euphemistic language further otherizes people with disabilities.
Able-bodied <i>Related terms to avoid: normal, healthy, in contrast to people with disabilities</i>	<ul style="list-style-type: none"> ✓ Able ✓ Non-disabled ✓ Does not have a disability ✓ Enabled 	“Able” to refer to all people without disabilities is preferable to “able-bodied” to be inclusive of cognitive disabilities and other disabilities not considered primarily physical. “Enabled” acknowledges the role of systems that privilege certain ability levels above others.
Corrective device/ technology <i>Related terms to avoid: wheelchair-bound, confined to a wheelchair</i>	<ul style="list-style-type: none"> ✓ Assistive device/ technology ✓ Accommodation ✓ Wheelchair user ✓ Person who uses a wheelchair 	Assistive technologies and services should be portrayed as helping and accommodating a person rather than making them “correct” or emphasizing limitations.

Other Terms and Topics

Stigmatizing Terms and Alternatives

Stigmatizing Terms To Avoid	Use These Alternatives	Here's Why
Prostitute <i>Related terms to avoid: prostitution, commercial sex work</i>	<ul style="list-style-type: none"> ✓ Sex worker/sex work ✓ Person/people who exchange(s) sex ✓ Transactional sex ✓ Person/people who engage(s) in transactional sex ✓ Sale of sexual services 	<p>“Sex work” implies ownership over a person’s own career choice, while “prostitution” and its derivatives carry engrained cultural stigmas. “Commercial sex work” is redundant and otherizes. There are nuances in discussing sex work that should not be overlooked: Some sex workers choose the work they do, while others are forced into it because they have no other options. Others are trafficked and survivors of rape. Minors cannot consent and should not be referred to as sex workers. (See below.)</p>
Sexual slavery <i>Related terms to avoid: forced prostitution, child prostitution</i>	<ul style="list-style-type: none"> ✓ Sex trafficking ✓ Sex trafficking of minors 	<p>In the context of forced or coerced transactional sex involving minors, the preferred term emphasizes the role of exploiters because children cannot consent to sex work.</p>
Rape victim	<ul style="list-style-type: none"> ✓ Survivor of sexual assault 	<p>“Survivor” is more empowering than “victim,” which evokes defeat and helplessness. When referring to a specific person, always use a term they approve.</p>
Domestic violence	<ul style="list-style-type: none"> ✓ Intimate partner violence ✓ Gender-based violence 	<p>The preferred terms are more specific to two separate ideas: violence between intimate partners and violence specifically based on gendered power imbalances. They also each include relevant violence outside of a shared home.</p>
Abuse victim	<ul style="list-style-type: none"> ✓ People/person who have experienced violence ✓ Survivor of violence 	<p>Use more empowering or neutral terms than “victim,” which evokes defeat and helplessness. When referring to a specific person, always use a term they approve.</p>

Stigmatizing Terms and Alternatives (continued)

Stigmatizing Terms To Avoid	Use These Alternatives	Here's Why
<p>Tuberculosis (TB) contact</p> <p><i>Related term to avoid: household contact</i></p>	<ul style="list-style-type: none"> ✓ Contact person^{xx} ✓ Close contacts ✓ Proximity-acquired TB ✓ Person recently exposed to TB 	<p>It is best to use person-centered language when describing someone who was exposed to <i>M. tuberculosis</i>.</p> <p>Significant TB exposure can occur both within and outside the household. Therefore, the term “household contact” is confusing and should no longer be used. “Contacts” is more accurate for those with significant TB exposure.</p>
<p>TB suspect</p>	<ul style="list-style-type: none"> ✓ People/person to be evaluated for TB ✓ People/person with presumed TB 	<p>“Suspect” evokes suspicion and personal fault.</p> <p>It is important to differentiate between TB disease and infection.</p>
<p>TB control</p>	<ul style="list-style-type: none"> ✓ TB prevention and care ✓ Prevention of TB transmission ✓ TB response 	<p>“Control” evokes paternalism. Also, there has been a shift from approaches that seek to “control” TB to one that focuses on “ending” the TB epidemic.</p>
<p>TB or hepatitis co-infected people/participants</p>	<ul style="list-style-type: none"> ✓ People/persons with concomitant hepatitis or concomitant TB 	<p>“Co-infect” and its derivatives carry the same stigma as “infect.”</p>
<p>TB cases</p>	<ul style="list-style-type: none"> ✓ People/person with tuberculosis/TB ✓ People/person with TB infection 	<p>Person-first language emphasizes humanity.</p>
<p>Monkeypox/monkey pox</p>	<ul style="list-style-type: none"> ✓ Mpox 	<p>The name of the disease was officially changed due to concerns that the original name could be construed as discriminatory and racist. Monkeypox still refers to the name of the virus, but efforts should be made to just say the virus that causes mpox rather than use monkeypox. Mpox is not capitalized unless it begins a sentence.</p>

Stigmatizing Terms and Alternatives (continued)

Stigmatizing Terms To Avoid	Use These Alternatives	Here's Why
<p>Babies, school-age children, teenagers</p>	<ul style="list-style-type: none"> ✓ Infants ✓ Children ✓ Adolescents 	<p>Try to avoid vague terms without first defining them. Age categories defined by the American Medical Association are provided below:</p> <ul style="list-style-type: none"> • Neonates or newborns (birth to 1 month) • Infants (1 month to 1 year) • Children (1 year through 12 years) • Adolescents (13 years through 17 years) • Adults (18 years or older) • Older adults (65 and older)
<p>The aged</p> <p><i>Related terms to avoid: (the) elderly, seniors/ senior citizens, old adults, geriatric (except in medicine)</i></p>	<ul style="list-style-type: none"> ✓ People over [age X] ✓ Elders (culturally dependent) 	<p>When possible, use a specific age or age range. “Adults” affirms agency and personhood, as does person-first language. Stigmatizing terms such as “elderly” can evoke frailty. In indigenous communities and LGBTQIA+ communities, the term “elders” may be preferred and culturally appropriate.</p>
<p>Caretaker</p>	<ul style="list-style-type: none"> ✓ Caregiver ✓ Care partner ✓ Care team 	<p>“Caretaker” typically refers to a person taking care of something, such as a house. A “caregiver” provides care to someone who needs help, such as a person who is ill or an aging parent. The term “care partner” is sometimes used to show that caregiving is a two-way street involving both the caregiver and the person needing care. However, a partnership may not be possible if a loved one needs significant help or cannot care for themselves. A “care team” refers to all the people who are providing care to a person.^{xxi}</p>
<p>Felon</p> <p><i>Related terms to avoid: convict, offender, inmate, prisoner, the incarcerated</i></p>	<ul style="list-style-type: none"> ✓ People/person who are incarcerated ✓ People/person in prison 	<p>Person-first language emphasizes humanity.</p>
<p>Mentally ill person</p> <p><i>Related terms to avoid: insane person, the mentally ill, [specific person] is bipolar, mental illness</i></p>	<ul style="list-style-type: none"> ✓ People/person with [specific mental disorder], e.g., person with bipolar disorder ✓ Mental health condition 	<p>Person-first language emphasizes humanity and dispels the misconception that mental disorders are untreatable. Also, “insanity” is a legal—not medical—definition (and it is highly stigmatizing).</p>

Stigmatizing Terms and Alternatives (continued)

Stigmatizing Terms To Avoid	Use These Alternatives	Here's Why
Committed suicide	<ul style="list-style-type: none"> ✓ Died by suicide ✓ Attempted suicide 	<p>“Committed” evokes associations with the legal or moral issues of “committing” a crime or sin, whereas “suicide” is often the consequence of an unaddressed illness.</p> <p>“Suicide attempts” should not be described as successful, unsuccessful, or failed. Instead, use “survived a suicide attempt,” just as one might describe an individual who has survived cancer or a heart attack.</p>

Acknowledgments

We extend our sincere gratitude to our diverse group of community reviewers, including people living with and without HIV, those from various regions across the United States and around the globe, and those with a range of racial, ethnic, and gender identities as well as sexual orientations. A variety of source materials was consulted in the writing of this Language Guide including the Centers for Disease Control and Prevention’s (CDC) [Ways To Stop HIV Stigma and Discrimination](#) and “Why Language Matters: Facing HIV Stigma in Our Own Words” by [Vickie Lynn](#), Ph.D., M.S.W., M.P.H., materials from [The Well Project](#), the University of California San Francisco HIVE Online #LanguageMatters campaign, the [NIH Style Guide’s Person-first and Destigmatizing Language](#), and other preferred language resources within and external to the NIH.

Websites

[A Guide to Talking About HIV \(CDC\)](#)

[Changing Federal Terminology Regarding Substance Use and Substance Use Disorders](#)

[FHI 360 Changing Language, Changing Minds: Using Restorative Language to Promote Solidarity and Equity RESTORATIVE LANGUAGE GUIDE, March 2022](#)

[Language for HIV Cure \(AVAC\)](#)

[NIH Style Guide’s Person-first and Destigmatizing Language](#)

[Oxfam Inclusive Language Guide \(openrepository.com\)](#)

[Preferred Terms for Select Population Groups and Communities \(CDC\)](#)

[Reporting and Indigenous Terminology, Preferred Native American Journalists Association](#)

[The Culturally Competent Gender-Related Communications \(C3\) Resource, NIH Sexual and Gender Minority Research Office](#)

[Trans-NIH Strategic Plan for Women’s Health Research - 2019-2023](#)

[The Power of Perceptions and Understanding: Changing How We Deliver Treatment and Recovery Services](#)

[Ways To Stop HIV Stigma and Discrimination \(CDC\)](#)

[Words Matter Language Guide \(Stop TB Partnership\)](#)

[Words Matter – Terms to Use and Avoid When Talking About Addiction \(NIDA\)](#)

[When It Comes to Reducing Alcohol-Related Stigma, Words Matter, NIAAA](#)

[Why Language Matters: Facing HIV Stigma in Our Own Words](#)

Endnotes

- ⁱ While AIDS is not as widely used now due to the associated stigma, some people may use the term when referring to the early years of the epidemic when HIV was not yet identified or understood, and when the word itself conjures the social and cultural impact the disease had at the time and for years to come.
- ⁱⁱ <https://www.stigmaindex.org/>
- ⁱⁱⁱ <https://theconversation.com/people-of-colour-theres-a-bias-in-how-pictures-are-used-to-depict-disease-in-global-health-publications-196056>
- ^{iv} <https://blogs.scientificamerican.com/voices/the-headless-legless-pregnancy-bump/>
- ^v Eunice Kennedy Shriver National Institute of Child Health and Human Development, Office of Communications
- ^{vi} AVAC Language for HIV Cure (AVAC), <https://avac.org/resource/language-for-hiv-cure/>
- ^{vii} Ibid
- ^{viii} Grimstad, F., Kremen, J., Streed, C. G. Jr., & Dalke, K. B. (2021). The health care of adults with differences in sex development or intersex traits is changing: Time to prepare clinicians and health systems. *LGBT Health*, 8(7), 439–443. <https://doi.org/10.1089/lgbt.2021.0018>
- ^{ix} Sex and Gender, Office of Research on Women’s Health, NIH. <https://orwh.od.nih.gov/sex-gender> and National Academies of Sciences, Engineering, and Medicine. (2022). Measuring sex, gender identity, and sexual orientation. [White paper]. The National Academies Press. <https://doi.org/10.17226/26424>
- ^x Ibid
- ^{xi} National Institute on Drug Abuse (NIDA) Communications Branch
- ^{xii} Ibid
- ^{xiii} When It Comes to Reducing Alcohol-Related Stigma, Words Matter, NIAAA, <https://www.niaaa.nih.gov/alcohols-effects-health/reducing-alcohol-related-stigma#:~:text=Use%20person%2Dfirst%20language%20to,person%20with%20alcohol%20use%20disorder>
- ^{xiv} <https://jamanetwork.com/journals/jama/fullarticle/2783090>
- ^{xv} https://obamawhitehouse.archives.gov/omb/fedreg_1997standards
- ^{xvi} <https://spd15revision.gov/>
- ^{xvii} Racial and Ethnic Categories and Definitions for NIH Diversity Programs and for Other Reporting Purposes, <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-089.html>
- ^{xviii} Native Knowledge 360°
- ^{xix} <https://www.ncai.org/news/ncai-response-to-usage-of-the-term-indian-country>
- ^{xx} <https://www.ncai.org/news/ncai-response-to-usage-of-the-term-indian-country>
- ^{xxi} Caregiver’s Handbook, NIA, <https://order.nia.nih.gov/publication/caregivers-handbook>.



National Institute of
Allergy and
Infectious Diseases

NIH Publication No. 24-AI-7480
April 2024