Writing the Introduction Section

Overview

Writing a scientific article can be a daunting task, even for experienced writers. However, understanding the standard format of research articles can help. This format is known as IMRAD, for the following parts of a scientific article: the Introduction, Methods, Results, and Discussion. The other 2 main parts of an article are the title and the abstract. Breaking your paper into these parts and writing each separately can make writing the paper easier.

The Introduction is the first section of the body of a scientific article:

Introduction:	**Why did you do the study?** **What was your hypothesis or purpose?**
Methods:	What did you do?
Results:	What did you find?
Discussion:	What do your findings mean?

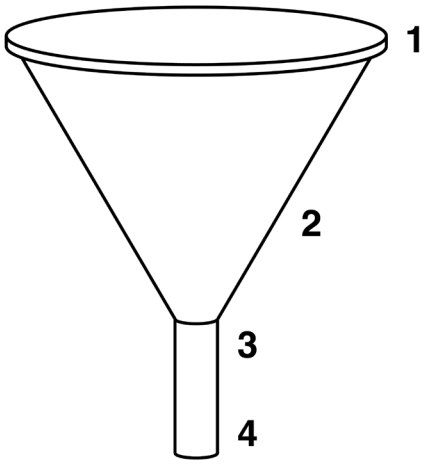
Topics to be covered in this chapter include

- Purpose and general structure of the Introduction
- Parts of the Introduction
- Verb tenses
- Tailoring the Introduction to your audience

Purpose and General Structure of the Introduction

The Introduction sets the stage for your article. After reading your Introduction, readers should understand what led to your study, what specific hypothesis you investigated, and what general experimental approach you used to investigate your hypothesis. The Introduction should also explain why your study is exciting and important.

Information in the Introduction should be organized like a funnel, narrowing "step by step from a starting point to a question," according to Mimi Zeiger, author of *Essentials of Writing Biomedical Research Papers* (McGraw Hill, Inc., 1991).



1 Known (background)

2 Unknown (gap in knowledge your study will fill)

3 Hypothesis or purpose statement

4 Strategy for testing the hypothesis

In other words, concepts in the Introduction should be presented in order from general to specific, from known to unknown—from established principles to the unanswered question that your research was designed to answer. As you plan your Introduction, you may find it useful to sketch out your ideas in a reverse funnel: first think of your hypothesis or purpose, and then retrace the reasoning and facts that led you to it.

In general, Introductions should be about 10% to 15% of the total length of the text of a manuscript, not counting the abstract, references, tables, and figure legends. If the Introduction is much more than 15% of the article, the Introduction may need to be shortened.

Parts of the Introduction

A good Introduction includes these elements:

- Background information
- Gap in knowledge
- Hypothesis or purpose statement
- Strategy for testing the hypothesis
- Conclusions (optional)

Following the guidelines below will help ensure that you have included all the necessary elements.

Background Information

Provide background information relevant to your article at a level of detail appropriate for your reader. State what led you to your hypothesis. Give only enough background information for readers to understand why you asked the research question you asked. Avoid topics that are not directly relevant to your study. Present background information in order from the most general to the most specific (funnel structure). Be sure to make clear why you performed the study and what you expected to learn from the research.

Deciding how much background information to provide in the Introduction is 1 of the most difficult issues writers face. The appropriate level of detail depends on the target audience, which in turn depends on the journal to which you plan to submit your manuscript. Provide enough information to make the reason for your study clear to readers with limited knowledge of your area of investigation, but avoid a detailed discussion of topics that more knowledgeable readers already understand. This topic is discussed in greater detail later in the chapter, in the section “Tailoring the Introduction to Your Audience.”

Gap in Knowledge

Write your background information so that it leads to a statement of the gap in knowledge your study tried to fill. Emphasize the importance of filling this gap in knowledge—for example, state how filling the gap could change medical practice or scientific thought.

Hypothesis or Purpose Statement

After identifying the gap in knowledge, state your hypothesis or the purpose of your study. Closely tying your hypothesis to an important gap in knowledge will make readers want to read your article. Use the same words and phrases in the statement of the gap in knowledge and the statement of the hypothesis. Word the hypothesis so that readers will be able to assess whether the hypothesis was proven or disproven by the experiments you performed.

Stating the gap in knowledge and then the hypothesis and presenting only the background information directly related to the topic **builds momentum** for the article and **sets an appropriate level of expectation.** Be careful not to raise questions in your reader's mind that you will not answer in the article—limit the background information to what is directly related to the gap in knowledge and the research question.

Strategy for Testing the Hypothesis

After stating your hypothesis, describe how you tested it. State briefly and clearly what experimental methods you used. (For example, "We identified the sequences downstream from the TATA box in basal PolIII snRNA using BLAST searches.") If necessary, explain why you chose your experimental design.

Conclusions

In articles describing basic science studies, consider including a brief statement of your study's conclusions at the end of your Introduction. This practice is uncommon in articles describing clinical studies. Your decision about whether to include your study's conclusions will depend on your personal preference and the style of your target journal. (Look at articles previously published in the journal to see if the Introductions end with the study's conclusions.) A concluding statement should say enough to make readers want to read the article but should not reveal all of the important findings.

Verb Tenses

Pay attention to how verb tenses are used in the Introduction:

- Use the **present tense** to describe the **present state of knowledge** (the funnel, the conclusions of others):
  "X *is* a component of Y."
- Use the **past tense** to describe events that occurred in the past, including **specific findings in previous studies** (your own or others'):
  "Sausman et al. (2003) *found* that half of mice *died* when *treated* with Y that *contained* a high concentration of X."
  "We *found* that a quarter of mice *died* when *treated* with Y that *contained* a low concentration of X (Yung et al., 2003)."
- Use the **present perfect tense** to describe **something that began in the past and has continued to the present:**
  "Several researchers *have investigated* the effects of Y on the survival of mice."
- Also use the **present perfect tense** to describe **something that has not yet happened**:
  "It *has not yet been determined* whether X is responsible for the decrease in survival seen in mice treated with Y."
- Use the **present tense** to state the **verb in your hypothesis**:
  "We hypothesized that X *is* fatal to mice at high concentrations."
- Use the **past tense** to describe the **strategy in the present study**:
  "We *tested* the effects of several concentrations of X on the survival of nude mice."

For more information and examples, refer to "Quick Verb Tense Review" on pages 3-8 to 3-9.

Activity 1

Choosing the Correct Verb Tense for the Introduction

See page 3-10.

Examples of Good and Bad Introductions

At the end of this chapter are well-written and poorly written Introductions for a basic science study and for a clinical study. Why the examples are considered well written or poorly written is indicated on each one.

Tailoring the Introduction to Your Audience

As you write your article, tailor to the journal's audience your explanation of the background information and why filling the gap in knowledge is important. For example, suppose your hypothesis is "Mutations in the promoter of the *X* gene increase the probability of prostate cancer metastasis." In your Introduction, you will need to describe the evidence suggesting a link between mutations in the *X* gene promoter and prostate cancer metastasis. If your audience is mostly molecular biologists, then you may need to provide more details about prostate cancer metastasis but fewer details about the *X* gene. If your audience is mostly physicians, then you may need to provide more details about the *X* gene but fewer details about prostate cancer metastasis.

In this example, filling the gap is important because prostate cancer metastases can be fatal. If the hypothesis is correct, then *X* gene mutations could be used to identify men at risk for metastasis and the metastases could be detected and treated earlier and perhaps more successfully. Molecular biologists might not know that, so you probably need to explain this implication for a molecular-biologist audience. Physicians might need just a brief reminder. Also, the protein encoded by the *X* gene might be a target for interventions designed to prevent or treat prostate cancer metastasis. That fact might have to be explained in detail for a physician audience but not for molecular biologists.

Avoid stating very obvious information that all your readers will know. For example, do not start your Introduction by saying that cancer is a terrible disease.

Activity 2

Outlining Your Introduction

Keeping the funnel structure in mind, write either an informal outline or a list of phrases or statements for the Introduction to a paper on your current research. Some outlines will be discussed in class. If yours is not discussed in class, we will be happy to review it afterward and discuss it with you later. Please put your name on it before giving it to an instructor.

Quick Verb Tense Review

Present Tense

Use the **present tense** for

- The current state of knowledge
- *Your* hypothesis* and general conclusions

Present tense examples:

- Progressive modifications in gene expression *direct* the process of….
- We *conclude* that Nkx6.1 *functions* as….
- All four endocrine cell types *derive* from a common set of….
- Progressive modifications in gene expression *direct* the process of….
- We hypothesized* that Nkx6.1 *is* involved in β-cell formation.

*When your hypothesis statement begins with "We hypothesized that…," the verb *hypothesized* is in the past tense.

Past Tense

Use the **past tense** for

- Others' subjects or experiments
- *Your* procedures and findings

Past tense examples:

- We *found* that Nkx6.1 functions as….
- In a similar study, Sanders et al. *identified* the critical pathway….
- To investigate underlying molecular mechanisms, we *transfected* rodent hippocampal neurons with….
- We *used* a xenograft model of a human high-grade CHSA to address this hypothesis.

Present Perfect Tense

Use the **present perfect tense** for

- Something that began in the past and has continued to the present
- Something that has not yet happened
- Something that happened in the recent past

Present perfect tense examples:

- Although Nkx2.2 plays an essential role in β-cell development, no transcription factor *has been identified* thus far that selectively controls β-cell formation.
- Similar studies *have not yet been performed* in monkeys.
- Recent reports *have demonstrated* that ET-743 can interfere with….

Activity 1

Choosing the Correct Verb Tense for the Introduction

Circle the correct verb tense and explain why it is correct.

1. Our transfection experiments (a) _____ that BDNF (b) _____ a role….

(a) reveal / revealed / have revealed

(b) plays / played / has played

2. Human musculoskeletal sarcomas _____ a number of proangiogenic factors.

express / expressed / have expressed

3. Previous work in our laboratory (a) _____ that PRP-B (b) _____ the growth of tumors….

(a) establishes / established / has established

(b) can inhibit / could inhibit / could have inhibited

4. Together, these results strongly argue that ET743 _____ effective against CHSA.

is / was / has been

5. On the basis of this finding, we (a) _____ that $p14^{ARF}$ hypermethylation (b) _____ during the progression of ulcerative colitis mucosa to carcinoma.

(a) hypothesize / hypothesized / have hypothesized

(b) occurs / occurred / has occurred

6. This question _____ a subject of controversy since the early 1990s.

is / was / has been

7. Despite substantial progress in animal studies, BDNF's relevance in humans _____ directly.

is not examined / was not examined / has not been examined

8. To test these hypotheses, we _____ the effects of the BDNF Val66Met substitution in a cohort of normal controls….

examine / examined / have examined

Example of an Introduction Needing Improvement (Basic Science Study)

UC is a chronic disease characterized by inflammation of the mucosa and submucosa of the large intestine. UC and Crohn's disease are the 2 main types of inflammatory bowel disease. The incidence of UC is approximately the same in men and women. Increasing duration and severity of UC correlate directly with an increased propensity to develop CR carcinoma (1,2). For patients who have had UC for >20 years, the incidence of colorectal cancer is 10- to 20-fold greater than that of the general population, and the average age of onset is 20 years earlier (3). Sporadic CR carcinoma arises from adenomatous polyps. UC-associated CR carcinoma progresses from areas of dysplastic mucosa. The molecular events that facilitate the progression of adenoma to carcinoma in sporadic CR cancer have been well investigated (4). Identifying the events involved in progression of UC mucosa to dysplasia and carcinoma would allow us to identify patients with UC at increased risk for developing CR carcinoma.

Inactivation of the p53 tumor suppressor gene is common in both sporadic and UC-associated CR carcinoma (4–6). Point mutation and loss of heterozygosity are the most commonly reported mechanisms resulting in p53 inactivation. Other genetic and epigenetic factors have been shown to modify p53 activity as well.

MDM-2 is inhibited by $p14^{ARF}$ (8). Homozygous deletion of the $p14^{ARF}$ locus has been reported in a variety of cancers (9–13), and gene knockout of $p14^{ARF}$ correlates with tumorigenesis (14). In addition to mutation, the $p14^{ARF}$ gene can be epigenetically inactivated through hypermethylation of its normally unmethylated CpG island. Esteller et al. (15) demonstrated that $p14^{ARF}$ hypermethylation occurs frequently in sporadic colorectal cancer. In the study reported here, we examined $p14^{ARF}$ hypermethylation in clinical samples ranging from nonneoplastic UC mucosa to CR carcinoma.

Adapted from the well-written introduction in Fumiaki Sato F et al. Hypermethylation of the $p14^{ARF}$ gene in ulcerative colitis–associated colorectal carcinogenesis. Cancer Res 62:1148–1151, 2002.

Example of a Well-Written Introduction (Basic Science Study)

Ulcerative colitis (UC) is a chronic disease characterized by inflammation of the mucosa and submucosa of the large intestine. Increasing duration and severity of UC correlate directly with an increased propensity to develop colorectal carcinoma (1,2). For patients who have had UC for >20 years, the incidence of colorectal cancer is 10- to 20-fold greater than that of the general population, and the average age of onset is 20 years earlier (3). Unlike sporadic colorectal carcinoma, which arises from adenomatous polyps, UC-associated colorectal carcinoma progresses from areas of dysplastic mucosa. Although the molecular events that facilitate the progression of adenoma to carcinoma in sporadic colorectal cancer have been well investigated (4), it is not known whether the same events underlie the progression of UC mucosa to dysplasia and carcinoma. Identifying the events involved in this progression would allow us to identify patients with UC at increased risk for developing colorectal carcinoma.

One such event, inactivation of the p53 tumor suppressor gene, is common in both sporadic and UC-associated colorectal carcinoma (4–6). Although point mutation and loss of heterozygosity are the most commonly reported mechanisms resulting in p53 inactivation, other genetic and epigenetic factors have been shown to modify p53 activity as well. Amplification of the MDM-2 gene (the protein product of which tags p53 for degradation) and expression of viral oncoproteins (which sequester p53) are 2 such examples (7).

MDM-2 is inhibited by $p14^{ARF}$ (8). Homozygous deletion of the $p14^{ARF}$ locus has been reported in a variety of cancers (9–13), and gene knockout of $p14^{ARF}$ correlates with tumorigenesis (14). In addition to mutation, the $p14^{ARF}$ gene can be epigenetically inactivated through hypermethylation of its normally unmethylated CpG island. Esteller et al. (15) demonstrated that $p14^{ARF}$ hypermethylation occurs frequently in sporadic colorectal cancer. We therefore hypothesized that $p14^{ARF}$ hypermethylation occurs during the progression of UC mucosa to carcinoma. To test this hypothesis, we determined the frequency and timing of $p14^{ARF}$ hypermethylation in clinical samples ranging from nonneoplastic UC mucosa to colorectal carcinoma.

Reprinted with permission from Fumiaki Sato F et al. Hypermethylation of the $p14^{ARF}$ gene in ulcerative colitis–associated colorectal carcinogenesis. Cancer Res 62:1148–1151, 2002.

Example of an Introduction Needing Improvement (Clinical Study)

In 1983, Harris et al linked the presence of anticardiolipin antibodies with a syndrome of spontaneous thrombosis and fetal death.[1] Despite the many reports since then, the best treatment for the so-called antiphospholipid syndrome remains unknown. This is partly because the syndrome is complex. In fact, there are 2 syndromes, primary (no association with other diseases) and secondary (associated with lupus erythematosus or other rheumatic diseases). Up to one third of patients with lupus erythematosus have antiphospholipid antibodies.[2]

The name of the syndrome is problematic. Negatively charged phospholipids, such as cardiolipin, were originally considered the most important autoantigens in the syndrome. However, β_2-glycoprotein I, also known as apoliprotein H, has been shown to be more important.[3] β_2-Glycoprotein I binds cardiolipin and other anionic phospholipids and helps dispose of apoptotic cells. The former function likely induces a conformational change in β_2-glycoprotein I, resulting in exposure of an antigenic epitope. Some of the autoantibodies present in the syndrome also interfere with clotting—and in fact, a prolonged activated partial thromboplastin time is characteristic of lupus erythematosus. All these antibodies have been collectively known as phospholipid antibodies, although this is inaccurate. Diagnosis of the syndrome is also problematic, because the criteria used can apply to a wide range of other illnesses.

After a first episode of thrombosis, patients with antiphospholipid antibodies have a higher risk of recurrent thrombosis than do patients without antiphospholipid antibodies.[4] Retrospective studies suggest that patients with antiphospholipid antibodies have a high risk of recurrent thrombosis while receiving moderate-intensity warfarin therapy and that this risk is lower with a higher intensity of warfarin therapy.[5–7] However, these results must be interpreted with caution because the studies were retrospective case series, recurrent thrombosis was not confirmed by standardized methods, and the warfarin intensity at the time of the thrombotic events was uncertain. Furthermore, the patients in these studies attended special clinics where the staff had an interest in the management of complex problems in patients with antiphospholipid antibodies and the patients were therefore likely to be in a selected group at high risk for recurrent thrombosis.

We studied patients with arterial or venous thrombosis and a positive test for antiphospholipid antibodies on an least 2 occasions at least 3 months apart from 13 tertiary-care rheumatology and thromboembolism clinics in eastern Canada. Patients were randomly assigned to receive warfarin to a target international normalized ratio of 2.0 to 3.0 or of 3.1 to 4.0.

Adapted from the well-written Introduction in Crowther MA, Ginsberg JS, Julian J, et al. A comparison of two intensities of warfarin for the prevention of recurrent thrombosis in patients with the antiphospholipid antibody syndrome. N Engl J Med 349:1133–1138, 2003.

Example of a Well-Written Introduction (Clinical Study)

Antiphospholipid antibodies, which include anticardiolipin antibodies and lupus anticoagulant, are associated with both arterial and venous thrombosis.[1] After a first episode of thrombosis, patients with antiphospholipid antibodies have a higher risk of recurrent thrombosis than do patients without antiphospholipid antibodies.[1] Retrospective studies suggest that patients with antiphospholipid antibodies have a high risk of recurrent thrombosis while receiving moderate-intensity warfarin therapy [target international normalized ratio (INR), 2.0 to 3.0] and that this risk is lower with a higher intensity of warfarin therapy (target INR, above 3.0).[2–4] However, these results must be interpreted with caution because the studies were retrospective case series, recurrent thrombosis was not confirmed by standardized methods, and the INR at the time of the thrombotic events was uncertain. Furthermore, the patients in these studies attended special clinics where the staff had an interest in the management of complex problems in patients with antiphospholipid antibodies and the patients were therefore likely to be in a selected group at high risk for recurrent thrombosis.

To our knowledge, there have been no randomized trials of the efficacy and safety of high-intensity versus moderate-intensity warfarin therapy in patients with the antiphospholipid antibody syndrome. Because increasing the target INR from a range of 2.0 to 3.0 to a range of 3.1 to 4.0 is likely to be associated with a doubling of the risk of major hemorrhage, it is important to know whether the higher-intensity treatment is more effective.[5,6]

To test the hypothesis that high-intensity warfarin therapy is more effective than moderate-intensity warfarin therapy in patients with antiphospholipid antibodies and a previous episode of thrombosis, we undertook a randomized, double-blind trial to compare long-term warfarin therapy targeted to an INR of 2.0 to 3.0 with therapy targeted to an INR of 3.1 to 4.0.

Adapted from Crowther MA, Ginsberg JS, Julian J, et al. A comparison of 2 intensities of warfarin for the prevention of recurrent thrombosis in patients with the antiphospholipid antibody syndrome. N Engl J Med 349:1133–1138, 2003.

Example of an Introduction Needing Improvement (Basic Science Study)

UC **[Abbreviation should be defined]** is a chronic disease characterized by inflammation of the mucosa and submucosa of the large intestine. UC and Crohn's disease are the 2 main types of inflammatory bowel disease. The incidence of UC is approximately the same in men and women. **[Preceding 2 sentences provide unnecessary background information]** Increasing duration and severity of UC correlate directly with an increased propensity to develop CR **[What does "CR" mean?]** carcinoma (1,2). For patients who have had UC for >20 years, the incidence of colorectal cancer is 10- to 20-fold greater than that of the general population, and the average age of onset is 20 years earlier (3). Sporadic CR carcinoma arises from adenomatous polyps. UC-associated CR carcinoma progresses from areas of dysplastic mucosa. **[Transition words could be added to preceding sentences to help show how they are connected]** The molecular events that facilitate the progression of adenoma to carcinoma in sporadic CR cancer have been well investigated (4). Identifying the events involved in progression of UC mucosa to dysplasia and carcinoma would allow us to identify patients with UC at increased risk for developing CR carcinoma. **[Gap is implied (there must not be much information available about molecular events in progression of UC to colorectal carcinoma) but not explicitly stated]**

Inactivation of the p53 tumor suppressor gene is common in both sporadic and UC-associated CR carcinoma (4–6). Point mutation and loss of heterozygosity are the most commonly reported mechanisms resulting in p53 inactivation. Other genetic and epigenetic factors have been shown to modify p53 activity as well. **[What is the connection between the preceding paragraph and the first paragraph of the Introduction?]**

MDM-2 is inhibited by $p14^{ARF}$ (8). Homozygous deletion of the $p14^{ARF}$ locus has been reported in a variety of cancers (9–13), and gene knockout of $p14^{ARF}$ correlates with tumorigenesis (14). **[What is the relationship between MDM-2 and UC?]** In addition to mutation, the $p14^{ARF}$ gene can be epigenetically inactivated through hypermethylation of its normally unmethylated CpG island. Esteller et al. (15) demonstrated that $p14^{ARF}$ hypermethylation occurs frequently in sporadic colorectal cancer. In the study reported here, we examined $p14^{ARF}$ hypermethylation in clinical samples ranging from nonneoplastic UC mucosa to CR carcinoma. **[Why did they do this? What was their hypothesis?]**

Adapted from the well-written introduction in Fumiaki Sato F et al. Hypermethylation of the $p14^{ARF}$ gene in ulcerative colitis–associated colorectal carcinogenesis. Cancer Res 62:1148–1151, 2002.

Example of a Well-Written Introduction (Basic Science Study)

Ulcerative colitis (UC) is a chronic disease characterized by inflammation of the mucosa and submucosa of the large intestine. Increasing duration and severity of UC correlate directly with an increased propensity to develop colorectal carcinoma (1,2). For patients who have had UC for >20 years, the incidence of colorectal cancer is 10- to 20-fold greater than that of the general population, and the average age of onset is 20 years earlier (3). Unlike sporadic colorectal carcinoma, which arises from adenomatous polyps, UC-associated colorectal carcinoma progresses from areas of dysplastic mucosa. **[Background information related to the study]** Although the molecular events that facilitate the progression of adenoma to carcinoma in sporadic colorectal cancer have been well investigated (4), it is not known whether the same events underlie the progression of UC mucosa to dysplasia and carcinoma. **[Gap in knowledge]** Identifying the events involved in this progression would allow us to identify patients with UC at increased risk for developing colorectal carcinoma. **[Importance of filling the gap]**

One such event, inactivation of the p53 tumor suppressor gene, is common in both sporadic and UC-associated colorectal carcinoma (4–6). Although point mutation and loss of heterozygosity are the most commonly reported mechanisms resulting in p53 inactivation, other genetic and epigenetic factors have been shown to modify p53 activity as well. Amplification of the MDM-2 gene (the protein product of which tags p53 for degradation) and expression of viral oncoproteins (which sequester p53) are 2 such examples (7).

MDM-2 is inhibited by $p14^{ARF}$ (8). Homozygous deletion of the $p14^{ARF}$ locus has been reported in a variety of cancers (9–13), and gene knockout of $p14^{ARF}$ correlates with tumorigenesis (14). In addition to mutation, the $p14^{ARF}$ gene can be epigenetically inactivated through hypermethylation of its normally unmethylated CpG island. Esteller et al. (15) demonstrated that $p14^{ARF}$ hypermethylation occurs frequently in sporadic colorectal cancer. **[More background information related to the study]** We therefore hypothesized that $p14^{ARF}$ hypermethylation occurs during the progression of UC mucosa to carcinoma. **[Hypothesis]** To test this hypothesis, we determined the frequency and timing of $p14^{ARF}$ hypermethylation in clinical samples ranging from nonneoplastic UC mucosa to colorectal carcinoma. **[Strategy for testing the hypothesis]**

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Example of an Introduction Needing Improvement (Clinical Study)

In 1983, Harris et al linked the presence of anticardiolipin antibodies with a syndrome of spontaneous thrombosis and fetal death.[1] Despite the many reports since then, the best treatment for the so-called antiphospholipid syndrome remains unknown. **[Is this the gap in knowledge the study will fill? Not enough background information has been given yet for the reader to tell.]** This is partly because the syndrome is complex. In fact, there are 2 syndromes, primary (no association with other diseases) and secondary (associated with lupus erythematosus or other rheumatic diseases). Up to one third of patients with lupus erythematosus have antiphospholipid antibodies.[2] **[Background information is too general. So far, the reader can guess only that the study will involve the antiphospholipid syndrome somehow.]**

The name of the syndrome is problematic. **[Is this the gap in knowledge? Surely not. This information is inappropriate for the Introduction. Also, how does this paragraph relate to the preceding paragraph? No transition is provided.]** Negatively charged phospholipids, such as cardiolipin, were originally considered the most important autoantigens in the syndrome. However, β_2-glycoprotein I, also known as apoliprotein H, has been shown to be more important.[3] β_2-Glycoprotein I binds cardiolipin and other anionic phospholipids and helps dispose of apoptotic cells. The former function likely induces a conformational change in β_2-glycoprotein I, resulting in exposure of an antigenic epitope. Some of the autoantibodies present in the syndrome also interfere with clotting—and in fact, a prolonged activated partial thromboplastin time is characteristic of lupus erythematosus. All these antibodies have been collectively known as phospholipid antibodies, although this is inaccurate. **[The background information is still too general.]** Diagnosis of the syndrome is also problematic, because the criteria used can apply to a wide range of other illnesses. **[Is this the gap in knowledge? No, this is not the gap, either.]**

After a first episode of thrombosis, patients with antiphospholipid antibodies have a higher risk of recurrent thrombosis than do patients without antiphospholipid antibodies.[4] **[How does this paragraph relate to the preceding one? No transition is provided.]** Retrospective studies suggest that patients with antiphospholipid antibodies have a high risk of recurrent thrombosis while receiving moderate-intensity warfarin therapy and that this risk is lower with a higher intensity of warfarin therapy.[5–7] However, these results must be interpreted with caution because the studies were retrospective case series, recurrent thrombosis was not confirmed by standardized methods, and the warfarin intensity at the time of the thrombotic events was uncertain. Furthermore, the patients in these studies attended special clinics where the staff had an interest in the management of complex problems in patients with antiphospholipid antibodies and the patients were therefore likely to be in a selected group at high risk for recurrent thrombosis. **[The background information is still very general, and there is still no indication of what the true gap in knowledge is.]**

We studied patients with arterial or venous thrombosis and a positive test for antiphospholipid antibodies on an least 2 occasions at least 3 months apart from 13 tertiary-care rheumatology and thromboembolism clinics in eastern Canada. Patients were randomly assigned to receive warfarin to a target international normalized ratio of 2.0 to 3.0 or of 3.1 to 4.0. **[There is a very detailed—too detailed—description of the strategy used, but no hypothesis or purpose has been given. The reader can tell that the study is comparing 2 intensities of warfarin therapy, but reason for the comparison is not clearly stated.]**

Adapted from the well-written Introduction in Crowther MA, Ginsberg JS, Julian J, et al. A comparison of two intensities of warfarin for the prevention of recurrent thrombosis in patients with the antiphospholipid antibody syndrome. N Engl J Med 349:1133–1138, 2003.

Example of a Well-Written Introduction (Clinical Study)

Antiphospholipid antibodies, which include anticardiolipin antibodies and lupus anticoagulant, are associated with both arterial and venous thrombosis.[1] After a first episode of thrombosis, patients with antiphospholipid antibodies have a higher risk of recurrent thrombosis than do patients without antiphospholipid antibodies.[1] Retrospective studies suggest that patients with antiphospholipid antibodies have a high risk of recurrent thrombosis while receiving moderate-intensity warfarin therapy [target international normalized ratio (INR), 2.0 to 3.0] and that this risk is lower with a higher intensity of warfarin therapy (target INR, above 3.0).[2–4] However, these results must be interpreted with caution because the studies were retrospective case series, recurrent thrombosis was not confirmed by standardized methods, and the INR at the time of the thrombotic events was uncertain. Furthermore, the patients in these studies attended special clinics where the staff had an interest in the management of complex problems in patients with antiphospholipid antibodies and the patients were therefore likely to be in a selected group at high risk for recurrent thrombosis. **[Background information related to the study]**

To our knowledge, there have been no randomized trials of the efficacy and safety of high-intensity versus moderate-intensity warfarin therapy in patients with the antiphospholipid antibody syndrome. **[Gap in knowledge]** Because increasing the target INR from a range of 2.0 to 3.0 to a range of 3.1 to 4.0 is likely to be associated with a doubling of the risk of major hemorrhage, it is important to know whether the higher-intensity treatment is more effective.[5,6] **[Importance of filling the gap]**

To test the hypothesis that high-intensity warfarin therapy is more effective than moderate-intensity warfarin therapy in patients with antiphospholipid antibodies and a previous episode of thrombosis **[Hypothesis]**, we undertook a randomized, double-blind trial to compare long-term warfarin therapy targeted to an INR of 2.0 to 3.0 with therapy targeted to an INR of 3.1 to 4.0. **[Strategy for testing the hypothesis]**

Adapted from Crowther MA, Ginsberg JS, Julian J, et al. A comparison of 2 intensities of warfarin for the prevention of recurrent thrombosis in patients with the antiphospholipid antibody syndrome. N Engl J Med 349:1133–1138, 2003.

Introduction Section Worksheet

Reminders:

- Include only enough background to make the reason for the study clear.
- Organize the information like a funnel, from general to specific.
- Use transitions between sentences and paragraphs to make the information flow logically.
- Use the same words and phrases in the gap and hypothesis or purpose statement.

Background

Known (general to specific)

Unknown: gap, how study will fill gap, and why filling gap is important

Until now, it has not been possible to identify...

However, we do not know what effect this treatment will have on...

There has been some disagreement, however, in the findings with this model...

So far, only qualitative findings have been obtained...

Because of the rarity of this cancer, it has been difficult to determine survival rates with statistical certainty...

Hypothesis

The purpose of our study was to determine...

We hypothesized that...

Our hypothesis was that...

Strategy

We tested our hypothesis by examining...

To do this, we used... and analyzed... in an in situ model...

Conclusion (optional)

Overall, our findings that… confirm…

In this study, we found that…