

Considerations for Pain Management With OTC Analgesics

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Welcome

Please remember to silence or turn off mobile phones, tablets, and laptops for the duration of the presentation.





Speaker Notes:

Pain has a significant impact on all aspects of patients' lives. It can limit physical activity, impair mobility, disrupt sleep, and affect productivity at work. HCPs are in a position to help patients manage pain so that they can perform the activities associated with their everyday lives.

Today's Objectives

- 1** Discuss the impact of pain on patients
- 2** Educate on important considerations for HCPs in determining an appropriate choice of OTC analgesic to recommend to a patient
- 3** Provide insights to help ensure appropriate use of OTC analgesics

HCPs=healthcare providers; OTC=over-the-counter.

Speaker Notes:

This presentation will focus on not only the impact of pain on patients, but also considerations for HCPs when recommending an appropriate OTC analgesic for each patient. Patients take OTC analgesics for a variety of indications; therefore, it is important for HCPs to ensure appropriate use of these medications, including reviewing dosing recommendations with patients.

The Pain Management Approach Should Be Tailored to the Individual Patient

GOALS

- HCPs should let their patients know all of the factors that need to be considered when choosing an analgesic to help ensure the appropriate one is selected

Speaker Notes:

There is no “one size fits all” approach to pain management; rather, it should be tailored to each individual.

Among the factors that HCPs should consider when choosing an OTC analgesic are the patient’s goals, nature of the pain, presence of coexisting conditions, and use of concomitant medications. It is important for patients to understand all of the factors involved in making a safe and appropriate OTC analgesic choice.



Speaker Notes:

[Utilize this slide to describe the flow of today's presentation.]

In our presentation today, we will:

- Discuss the impact of pain on patients and the various conditions that can cause pain
- Consider how each pain management plan is specific to the individual patient:
 - Address how coexisting medical conditions influence OTC analgesic recommendations
 - Review potential drug interactions between common concomitant medications and OTC analgesic options
- Share how patient education can help ensure appropriate OTC analgesic use

Patient Case: Meet Sheila

- Is a 48-year-old woman
- Has 2 young children
- Works as an elementary school teacher
- **Complains of lower back pain**
 - Worsening over the past 6 weeks



Fictional case; for discussion only.

Speaker Notes:

As a framework for our discussion, we will review a patient case in the ambulatory care setting. This case will help us understand how considerations specific to the individual patient can help determine each patient's unique treatment plan.

Our patient, Sheila, has come to the office for her annual physical exam, and she has a complaint of lower back pain. We ask Sheila to describe her pain. Is it dull, sharp, intermittent, mild, or severe? Is there any activity that exacerbates the pain?

Sheila explains that the pain has been getting worse. Because she is a teacher, she spends a large part of the day standing, and she is worried that the pain will impact her ability to do her job.



Speaker Notes:

Patients can experience changes in their pain. Therefore, it is important for HCPs to talk to patients about the type(s) and severity of their pain and the impact on their lives. These factors may influence the approach to pain management.

Patients Can Experience Changes in Their Pain

Depression and **anxiety**
may affect pain sensitivity¹

92% of breakthrough pain with
an identifiable source is
attributed to **activities** such
as **sitting, standing,** or
driving²

1. Angst MS, et al. *Pain*. 2012;153(7):1397-1409. 2. Portenoy RK, et al. *J Pain*. 2006;7(8):583-591.

Speaker Notes:

Management of moderate to severe pain can be challenging due to interindividual differences in pain sensitivity; genetic and environmental factors can contribute to these differences. In a randomized, double-blind, placebo-controlled study, twins were administered precisely controlled opioid infusions and quantitative experimental pain tests under laboratory-type conditions.¹ Several covariates potentially linked to the large variability in pain sensitivity were assessed.¹ The study demonstrated that increasing anxiety scores were associated with a modest increase in cold pressor pain sensitivity.¹ The authors note that in other reports, depression has been linked to pain sensitivity and severity.¹

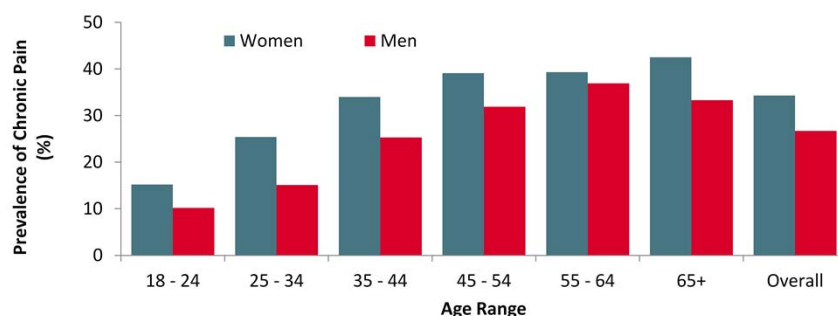
Certain activities can also cause patients to experience changes in their pain. Breakthrough, or episodic, pain is defined as pain that occurs in patients with otherwise controlled chronic pain.² A survey of a diverse population with chronic noncancer pain treated at 9 pain management programs in the United States between February and April 2004 revealed that 92% of patients with breakthrough pain had participated in activities such as sitting, standing, or driving.² By understanding how pain can change, HCPs can tailor treatment to each patient.

1. Angst MS, et al. *Pain*. 2012;153(7):1397-1409.

2. Portenoy RK, et al. *J Pain*. 2006;7(8):583-591.

Prevalence of Pain Increases With Age

- In an Internet survey of more than 27,000 adults¹:
 - 30.7% experienced pain >6 months in duration
 - About 50% reported experiencing pain daily
 - 32% classified their pain as severe (≥ 7 out of 10)



1. Johannes CB, et al. *J Pain*. 2010;11(11):1230-1239.

Speaker Notes:

Age is an important factor that may influence the onset of pain. A cross-sectional, Internet-based survey of more than 27,000 US adults was conducted to estimate the prevalence of self-reported chronic pain (defined as pain lasting ≥ 6 months).¹ Assessments included pain duration, frequency, and intensity.¹ Of the survey respondents, 30.7% revealed that they experienced chronic pain.¹

The overall prevalence of chronic pain increased with age; however, prevalence decreased among men in the oldest age category (65+).¹ Half of the respondents reported that they experienced primary chronic pain daily, while nearly a third (32%) classified the average intensity of their primary pain in the past 3 months as severe (≥ 7 out of 10).¹

1. Johannes CB, et al. *J Pain*. 2010;11(11):1230-1239.

What is the most common type of pain that you see in your practice?

A

Back pain

B

Migraine or severe headaches

C

Neck pain

D

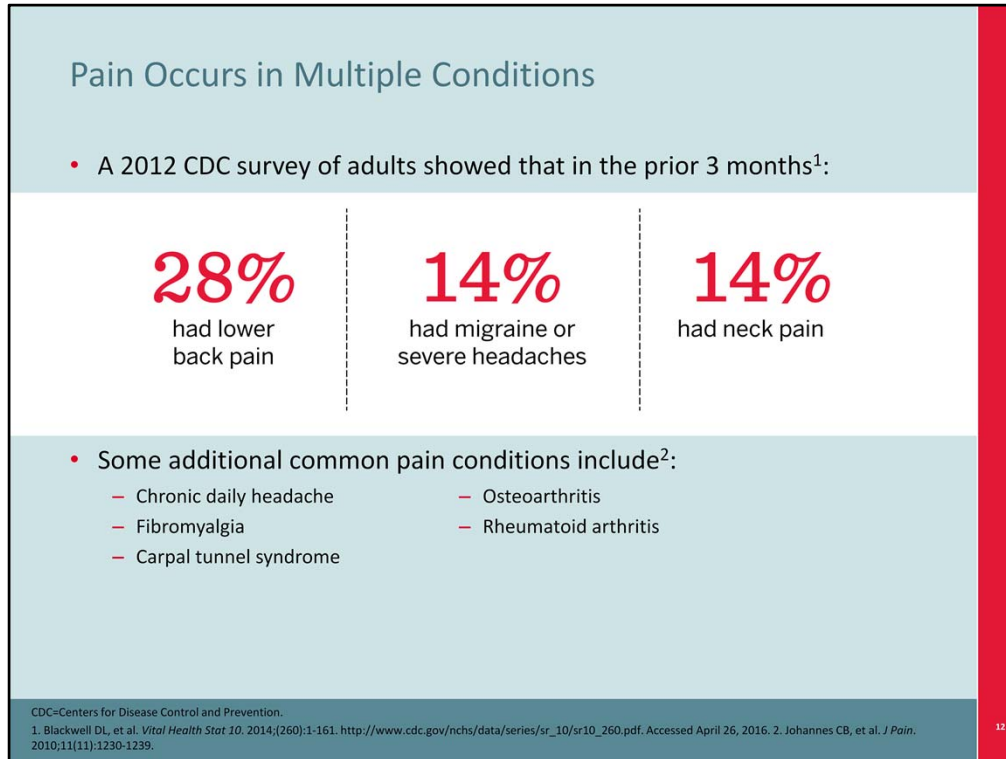
Joint pain

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Speaker Notes:

What is the most common type of pain that you see in your practice?

[Poll the audience and reveal the most common answer.]



Speaker Notes:

A CDC report summarizing data from the 2012 National Health Interview Survey provided national estimates for a broad range of health measures for the US civilian noninstitutionalized adult population.¹ In the 3 months prior to the survey, 28% of respondents had lower back pain, 14% had migraine or severe headaches, and 14% had neck pain.¹

In a cross-sectional, Internet-based survey, the majority of respondents with chronic pain reported at least one HCP-diagnosed pain condition as the cause of their chronic pain.² These pain conditions commonly included chronic daily headache, fibromyalgia, carpal tunnel syndrome, osteoarthritis, and rheumatoid arthritis.²

1. Blackwell DL, et al. *Vital Health Stat 10*. 2014;(260):1-161.

http://www.cdc.gov/nchs/data/series/sr_10/sr10_260.pdf. Accessed April 26, 2016.

2. Johannes CB, et al. *J Pain*. 2010;11(11):1230-1239.

The Impact of Pain on Sheila

- 
- 
- Pain has made it difficult for her to fall asleep at night
 - Pain has caused her to stop her regular workouts
 - She has a difficult time playing with her children
 - She is asking for a recommendation for an OTC analgesic

Speaker Notes:

As we return to our patient case, we will examine the impact of pain on Sheila's life. Her pain has made it difficult to fall asleep at night. In addition, because bending and other movements exacerbate her pain, she has stopped her regular workouts. She also has difficulty playing with her children.

The Impact of Pain on Sheila

?

What would you consider before making your recommendation?



Speaker Notes:

To appropriately manage pain in a patient like Sheila, it is important to consider a number of factors before making a treatment recommendation.



Speaker Notes:

It is important to consider how each pain management plan is specific to the individual patient:

- Address how coexisting medical conditions influence OTC analgesic recommendations
- Review potential drug interactions between common concomitant medications and OTC analgesic options

Consider Whether My Patient . . .

- ☐ Has cardiovascular disease?
- ☐ Has edema (due to congestive heart failure)?
- ☐ Has an increased risk of gastrointestinal bleeding?
- ☐ Has gastroesophageal reflux disease, dyspepsia, or peptic ulceration or a history of stomach problems?
- ☐ Has kidney disease?
- ☐ Has liver cirrhosis?
- ☐ Drinks 3 or more alcoholic beverages a day?
- ☐ Is 60 years of age or older?
- ☐ Takes prescription medications, such as NSAIDs, antihypertensive agents, diuretics, or anticoagulants?
- ☐ Takes OTC medications containing acetaminophen or NSAIDs, including cough and cold or allergy products, sleep aids, antipyretics, or analgesics?
- ☐ Takes aspirin for cardiovascular prophylaxis?

NSAIDs=nonsteroidal anti-inflammatory drugs.

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Speaker Notes:

When making an OTC analgesic recommendation, HCPs must consider a number of factors, including those listed here.

We will highlight some of these factors and discuss how they may impact a patient's treatment plan.

Patients With Pain May Have Coexisting Medical Conditions

- 49.8% (117 million) of US adults in 2012 had at least 1 of the 10 chronic medical conditions examined by the CDC¹:
 - Hypertension, coronary heart disease, stroke, diabetes, cancer, arthritis, hepatitis, weak or failing kidneys, current asthma, or chronic obstructive pulmonary disease

Based on the 2016 Heart Disease and Stroke Statistics Update²:

~80 million
adults have **hypertension**

6.2% of adults have
coronary heart disease

1 in 10 adults is
affected by
diabetes mellitus

>26 million
people suffer from
chronic kidney disease

1. Ward BW, et al. *Prev Chronic Dis*. 2014;11:130389. http://www.cdc.gov/pcd/issues/2014/13_0389.htm. Accessed May 2015. 2. Mozaffarian D, et al. *Circulation*. 2016;133(4):e38-e360.

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Speaker Notes:

HCPs must consider whether patients with pain have coexisting medical conditions, which may influence the treatment plan.

Data from the CDC's 2012 National Health Interview Survey were used to generate estimates of multiple (>2) chronic conditions among US adults.¹ Approximately half (117 million) of US adults had at least 1 of the 10 chronic conditions examined (ie, hypertension, coronary heart disease, stroke, diabetes, cancer, arthritis, hepatitis, weak or failing kidneys, current asthma, or chronic obstructive pulmonary disease).¹ Furthermore, 1 in 4 US adults had at least 2 chronic conditions.¹

According to a 2016 report from the American Heart Association, approximately 80 million (32.6%) US adults ≥20 years of age have hypertension; 1 in 10 US adults has diabetes mellitus, of which 90% to 95% of cases are type 2; 6.2% (estimated 15.5 million) of US adults ≥20 years of age have coronary heart disease; and more than 26 million (13%) people in the United States have chronic kidney disease.²

1. Ward BW, et al. *Prev Chronic Dis*. 2014;11:130389. http://www.cdc.gov/pcd/issues/2014/13_0389.htm. Accessed May 2015.

2. Mozaffarian D, et al. *Circulation*. 2016;133(4):e38-e360.

Consider Whether My Patient . . .

☐ Has cardiovascular disease?

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- ☐ Has kidney disease?
- ☐ Has liver cirrhosis?
- ☐ Drinks 3 or more alcoholic beverages a day?

☐ Is 60 years of age or older?

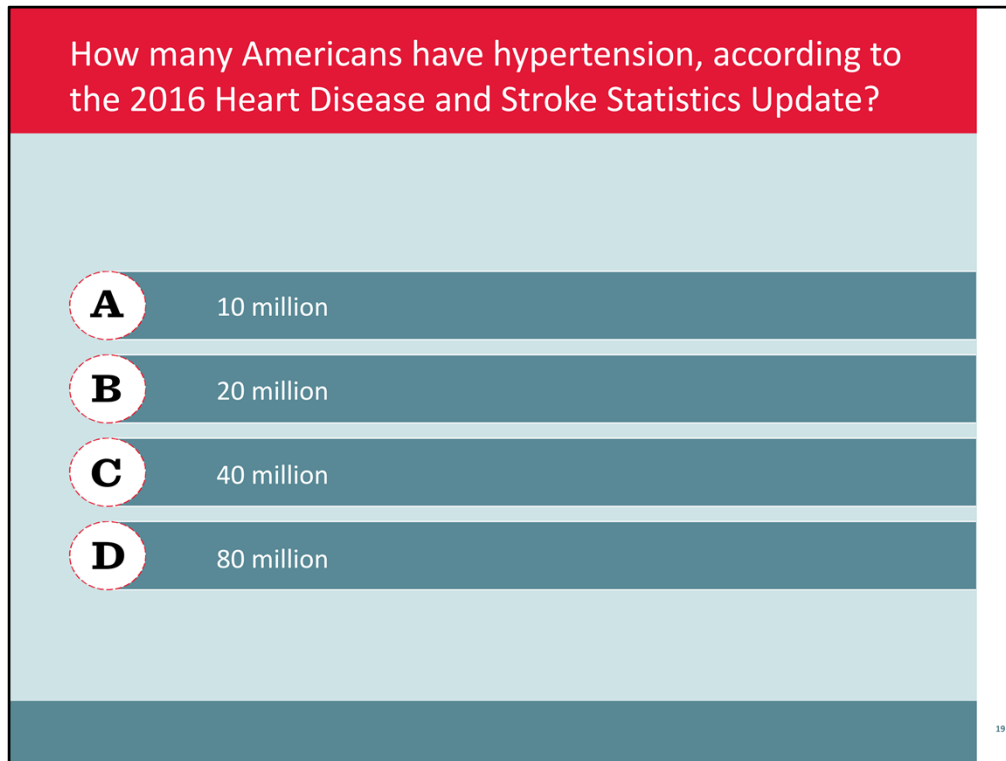
- ☐ Takes prescription medications, such as NSAIDs, antihypertensive agents, diuretics, or anticoagulants?
- ☐ Takes OTC medications containing acetaminophen or NSAIDs, including cough and cold or allergy products, sleep aids, antipyretics, or analgesics?
- ☐ Takes aspirin for cardiovascular prophylaxis?

NSAIDs=nonsteroidal anti-inflammatory drugs.

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Speaker Notes:

It is important to consider cardiovascular disease when making an OTC analgesic recommendation. We will review some of the challenges associated with pain management in this patient population.



Speaker Notes:

How many Americans have hypertension, according to the 2016 Heart Disease and Stroke Statistics Update?

[Poll the audience and reveal the most common answer.]

How many Americans have hypertension, according to the 2016 Heart Disease and Stroke Statistics Update?

A

10 million

B

20 million

C

40 million

D

80 million

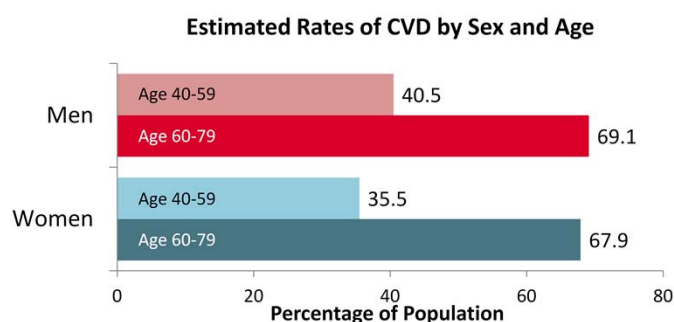
20

Speaker Notes:

The correct answer is 80 million.

Prevalence of Cardiovascular Disease¹

- 85.6 million US adults are estimated to have ≥ 1 type of CVD
 - Represents >1 in 3 adults
- 43.9% of Americans are projected to have some form of CVD by 2030



CVD=cardiovascular disease.
1. Mozaffarian D, et al. *Circulation*. 2016;133(4):e38-e360.

Speaker Notes:

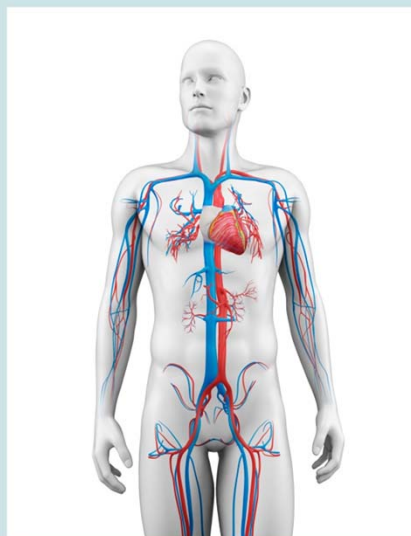
According to the American Heart Association, cardiovascular disease has been increasing over time in both men and women. An estimated 85.6 million (>1 in 3) US adults have ≥ 1 type of cardiovascular disease, including high blood pressure, coronary heart disease, myocardial infarction, angina pectoris, heart failure, and stroke.¹ By 2030, 43.9% of Americans are projected to have some form of cardiovascular disease.¹

The figure on the slide illustrates the prevalence of cardiovascular disease—including coronary heart disease, heart failure, stroke, and hypertension—in adults ≥ 20 years of age by sex and age (National Health and Nutrition Examination Survey 2009-2012).¹

1. Mozaffarian D, et al. *Circulation*. 2016;133(4):e38-e360.

NSAIDs and Cardiovascular Health

- For patients with cardiovascular risks:
 - The use of NSAIDs may increase the risk of cardiovascular complications, such as hypertension, MI, and stroke^{1,2}
 - Concomitant use of NSAIDs with antihypertensive agents may increase the risk of acute kidney injury³
 - NSAID use has been linked to an increase in systolic blood pressure⁴



MI=myocardial infarction.

1. Bavry AA, et al. *Am J Med*. 2011;124(7):614-620. 2. Antman EM, et al. *Circulation*. 2007;115(12):1634-1642. 3. Lapi F, et al. *BMJ*. 2013;346:e8525. 4. Aljadhey H, et al. *BMC Cardiovasc Disord*. 2012;12:93.

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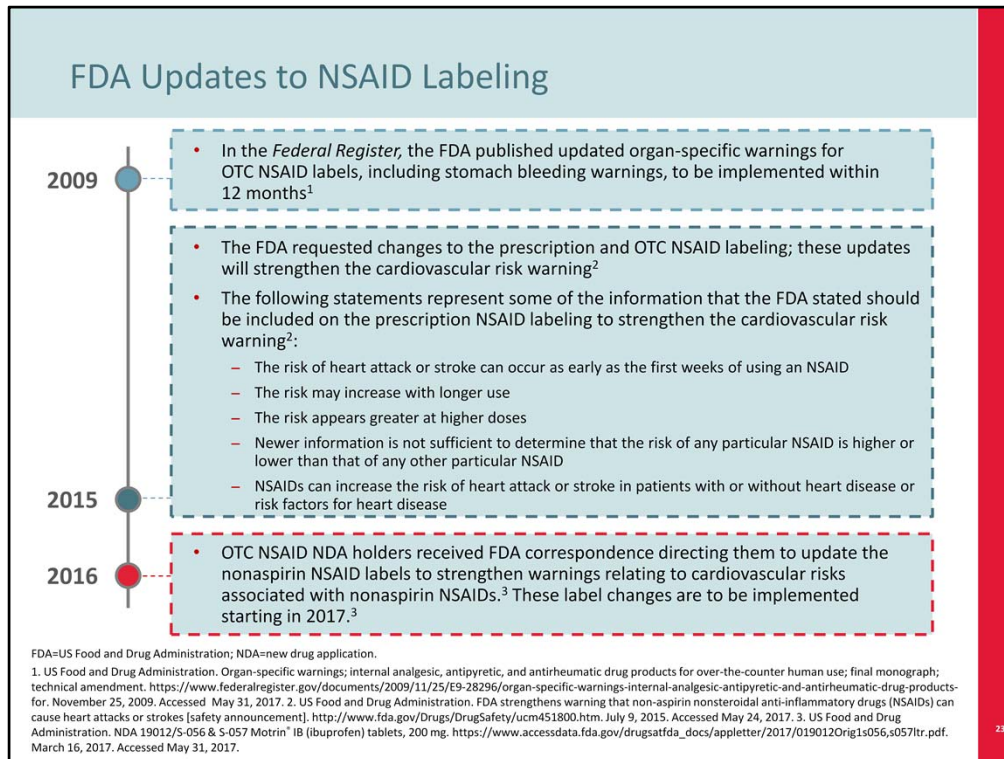
Speaker Notes:

HCPs may recommend NSAIDs for chronic or acute pain, but there are cardiovascular risks associated with their use.^{1,2}

A post hoc analysis of the International Verapamil SR/Trandolapril Study (INVEST), which enrolled patients with hypertension and coronary artery disease, aimed to explore the association among chronic NSAID use, blood pressure, and adverse outcomes.¹ Chronic self-reported NSAID use over a mean of 2.7 years was associated with a 47% increase in the first occurrence of death, nonfatal myocardial infarction, or nonfatal stroke during long-term follow-up.¹

Concurrent use of NSAIDs with antihypertensive drugs may also be associated with an increased risk of acute kidney injury, especially in patients receiving a triple-therapy combination.³ Chronic use of NSAIDs may disrupt control of blood pressure in hypertensive patients and lead to deleterious cardiovascular effects.⁴ Compared with acetaminophen, incident use of NSAIDs is associated with a small increase in systolic blood pressure in hypertensive patients.⁴

1. Bavry AA, et al. *Am J Med*. 2011;124(7):614-620.
2. Antman EM, et al. *Circulation*. 2007;115(12):1634-1642.
3. Lapi F, et al. *BMJ*. 2013;346:e8525.
4. Aljadhey H, et al. *BMC Cardiovasc Disord*. 2012;12:93.



Speaker Notes:

In reviewing the safety profiles of products such as NSAIDs, the FDA has continued to update its labeling requirements. In 2009, the FDA published updated organ-specific warnings for OTC NSAID labels, including stomach bleeding warnings, which were to be implemented within 12 months.¹

In 2015, the FDA requested changes to the prescription and OTC NSAID labeling to strengthen the warning regarding the risk of heart attack or stroke. Based on a comprehensive review of new safety information, the FDA requested updates to the drug labels of all prescription NSAIDs.² The label revisions reflect the sub-bulleted information on the slide.² The FDA stated that it would also request updates to the OTC nonaspirin NSAID labels.²

In 2016, OTC NSAID NDA holders received FDA correspondence directing them to update the nonaspirin NSAID labels to strengthen warnings relating to cardiovascular risks associated with nonaspirin NSAIDs.³ These label changes are to be implemented starting in 2017.³

1. US Food and Drug Administration. Organ-specific warnings; internal analgesic, antipyretic, and antirheumatic drug products for over-the-counter human use; final monograph; technical amendment.

<https://www.federalregister.gov/documents/2009/11/25/E9-28296/organ-specific-warnings-internal-analgesic-antipyretic-and-antirheumatic-drug-products-for>. November 25, 2009. Accessed May 31, 2017.

2. US Food and Drug Administration. FDA strengthens warning that non-aspirin nonsteroidal anti-inflammatory drugs (NSAIDs) can cause heart attacks or strokes [safety announcement].

<http://www.fda.gov/Drugs/DrugSafety/ucm451800.htm>. July 9, 2015. Accessed May 24, 2017.

3. US Food and Drug Administration. NDA 19012/S-056 & S-057 Motrin® IB (ibuprofen) tablets, 200 mg.

https://www.accessdata.fda.gov/drugsatfda_docs/applletter/2017/019012Orig1s056,s057ltr.pdf. March 16, 2017. Accessed May 31, 2017.

Based on the pertinent OTC Drug Facts label, which of the following may block the cardioprotective effects of low-dose aspirin?

A

Ibuprofen

B

Acetaminophen

C

Naproxen

D

Opioids

Speaker Notes:

Based on the pertinent OTC Drug Facts label, which of the following may block the cardioprotective effects of low-dose aspirin?

[Poll the audience and reveal the most common answer.]

Based on the pertinent OTC Drug Facts label, which of the following may block the cardioprotective effects of low-dose aspirin?

A

Ibuprofen

B

Acetaminophen

C

Naproxen

D

Opioids

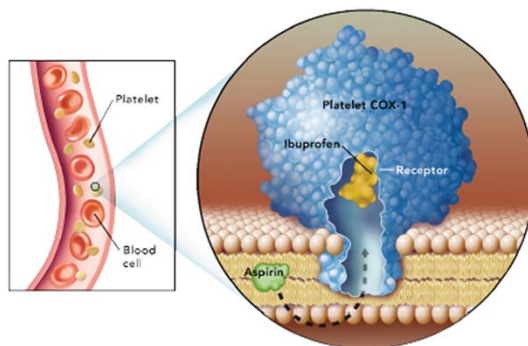
25

Speaker Notes:

The correct answer is ibuprofen.

Ibuprofen May Interfere With Aspirin Heart Therapy^{1,2}

- Ibuprofen may compete with aspirin to occupy platelet COX-1 receptors, which may compromise the cardioprotective benefit of aspirin



COX-1=cyclooxygenase type 1.

1. Catella-Lawson F, et al. *N Engl J Med*. 2001;345(25):1809-1817. 2. MacDonald TM, et al. *Lancet*. 2003;361(9357):573-574.

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Speaker Notes:

Aspirin has repeatedly been shown to be protective against cardiovascular disease. However, it has been proposed that treatment with ibuprofen in patients with increased cardiovascular risks may limit the cardioprotective effects of aspirin, potentially increasing the risk of all-cause and cardiovascular mortality.¹ Aspirin irreversibly inhibits platelet COX-1 receptors. However, as shown in the figure on the slide, concurrent treatment with ibuprofen antagonizes this irreversible platelet inhibition, impairing platelet aggregation by aspirin.²

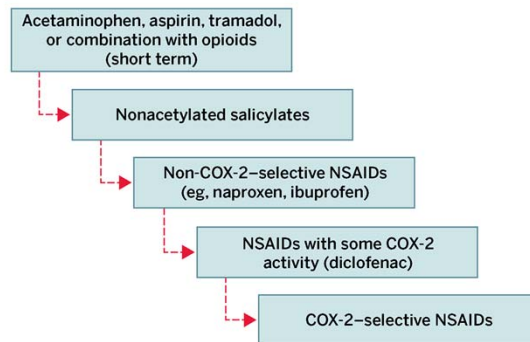
It is important for HCPs to consider other medications that patients are taking, particularly patients with increased cardiovascular risks, to decrease the potential for competitive interactions, such as between aspirin and ibuprofen.

1. MacDonald TM, et al. *Lancet*. 2003;361(9357):573-574.

2. Catella-Lawson F, et al. *N Engl J Med*. 2001;345(25):1809-1817.

The American Heart Association Recommends a Stepwise Approach to Pain Management¹

- In patients with CVD when nonpharmacologic treatment has failed



COX-2=cyclooxygenase type 2.
1. Antman EM, et al. *Circulation*. 2007;115(12):1634-1642.

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Speaker Notes:

The American Heart Association recommends a stepwise approach to pain management for patients with known cardiovascular disease or a risk of ischemic heart disease in whom nonpharmacologic treatment has failed.¹ This approach focuses on use of agents with the lowest reported risk of cardiovascular events and then progresses toward use of other agents, with consideration of the benefits and risks at each step.¹

1. Antman EM, et al. *Circulation*. 2007;115(12):1634-1642.

Consider Whether My Patient . . .

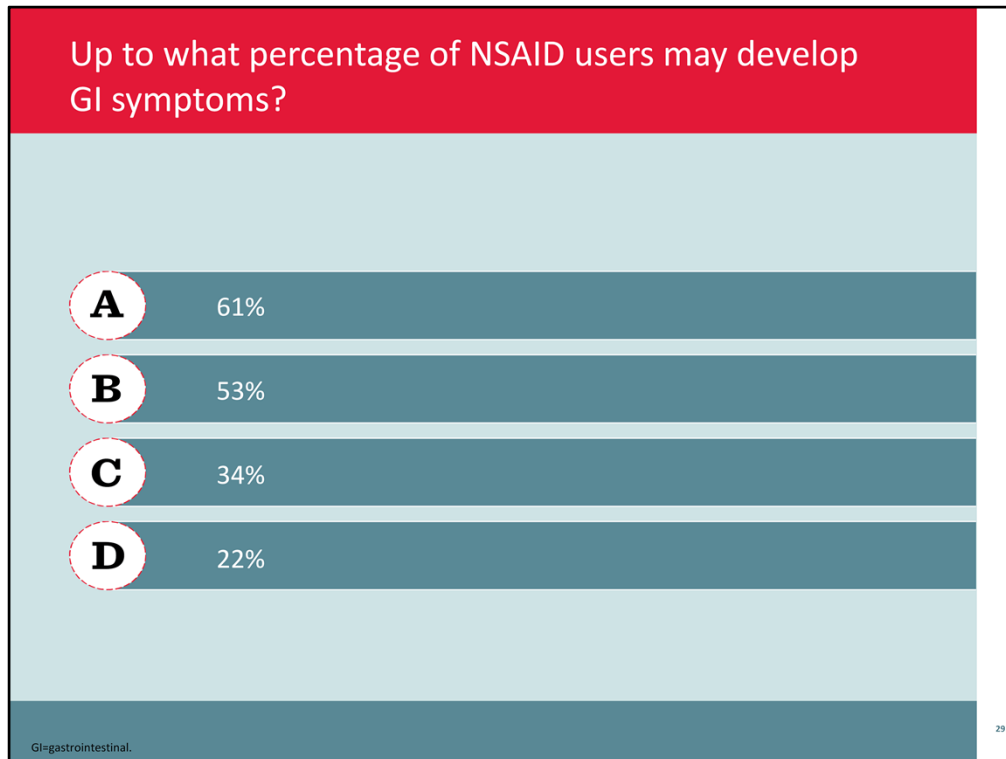
- ☐ Has cardiovascular disease?
- ☐ Has edema (due to congestive heart failure)?
- ☐ **Has an increased risk of gastrointestinal bleeding?**
- ☐ Has gastroesophageal reflux disease, dyspepsia, or peptic ulceration or a history of stomach problems?
- ☐ Has kidney disease?
- ☐ Has liver cirrhosis?
- ☐ Drinks 3 or more alcoholic beverages a day?
- ☐ Is 60 years of age or older?
- ☐ Takes prescription medications, such as NSAIDs, antihypertensive agents, diuretics, or anticoagulants?
- ☐ Takes OTC medications containing acetaminophen or NSAIDs, including cough and cold or allergy products, sleep aids, antipyretics, or analgesics?
- ☐ Takes aspirin for cardiovascular prophylaxis?

NSAIDs=nonsteroidal anti-inflammatory drugs.

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Speaker Notes:

It is important to consider gastrointestinal bleeding when making an OTC analgesic recommendation. We will review some of the challenges associated with pain management in this patient population.



Speaker Notes:

Up to what percentage of NSAID users may develop GI symptoms?

[Poll the audience and reveal the most common answer.]

Up to what percentage of NSAID users may develop GI symptoms?

- A** 61%
- B** 53%
- C** 34%
- D** 22%

GI=gastrointestinal.

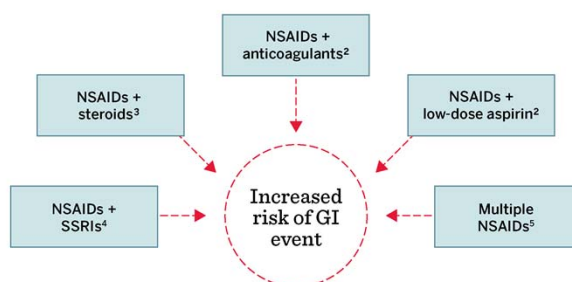
30

Speaker Notes:

The correct answer is 61%.

NSAID Use May Contribute to Gastrointestinal Issues in Some Individuals

- Up to 61% of NSAID users may develop GI symptoms¹
- There is an increased risk of GI events (such as ulcers and bleeding) in patients taking NSAIDs concomitant with other medications²⁻⁵



SSRIs=selective serotonin reuptake inhibitors.

1. McCarthy DM. *Best Pract Res Clin Gastroenterol*. 2001;15(5):755-773. 2. Bhatt DL, et al. *Circulation*. 2008;118(18):1894-1909. 3. García Rodríguez LA, et al. *Arthritis Res*. 2001;3(2):98-101. 4. de Jong JC, et al. *Br J Clin Pharmacol*. 2003;55(6):591-595. 5. Clinard F, et al. *Eur J Clin Pharmacol*. 2004;60(4):279-283.

Speaker Notes:

NSAID use may lead to GI complications, such as bleeding, perforation, obstruction, or ulcers, but the frequency of these complications varies, depending on the NSAID.¹ Among patients taking NSAIDs, between 8% and 61% experience GI symptoms at some point during therapy, and about 10% to 12% discontinue NSAID use because of such symptoms.¹ Use of NSAIDs, including COX-2–selective agents and OTC doses of traditional NSAIDs, in conjunction with aspirin substantially increases the risk of ulcer complications.² Increasing use of antiplatelet medications in combination with NSAIDs may also increase the risk of GI bleeding.²

Use of oral steroids increases the risk of upper GI complications associated with NSAIDs.³ This risk was more than 12 times higher in concomitant users of both steroids and NSAIDs compared with nonusers of either drug.³ Use of SSRIs also increases the risk of GI bleeding, especially in combination with NSAIDs.⁴ The risk of GI bleeding with SSRIs used in combination with NSAIDs was about 10 times higher than that with SSRIs alone and about 4 times higher than that with NSAIDs alone.⁴

The risk of GI bleeding, hepatic injury, and acute renal failure increases with the number of NSAIDs used.⁵ Compared with patients receiving only 1 NSAID, patients receiving 2 or more NSAIDs simultaneously demonstrated a roughly 2-fold increase in the risk of GI events (odds ratio 3.51 [95% CI: 2.20-5.60] and odds ratio 2.04 [95% CI: 1.63-2.56], respectively).⁵ HCPs should consider all of the medications that patients are taking and the increased GI risks associated with use of NSAIDs concomitantly with other medications.

1. McCarthy DM. *Best Pract Res Clin Gastroenterol*. 2001;15(5):755-773.

2. Bhatt DL, et al. *Circulation*. 2008;118(18):1894-1909.

3. García Rodríguez LA, et al. *Arthritis Res*. 2001;3(2):98-101.

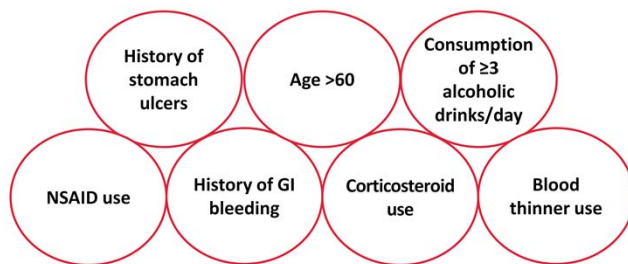
4. de Jong JC, et al. *Br J Clin Pharmacol*. 2003;55(6):591-595.

5. Clinard F, et al. *Eur J Clin Pharmacol*. 2004;60(4):279-283.

Various Factors May Increase an Individual's Gastrointestinal Bleeding Risk¹

- OTC NSAID labels include warnings to indicate the increased risk of stomach bleeding

Factors that contribute to increased risk include:



1. US Food and Drug Administration. *Fed Regist.* 2009;74(81):19385-19409.

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Speaker Notes:

The FDA issued a final rule, effective in 2010, requiring updated organ-specific warnings and related labeling for OTC internal analgesic drug products. This labeling informs patients of the risk of stomach bleeding when using NSAIDs.¹ Factors that may contribute to an increased risk of stomach bleeding are listed on the slide.¹

The warning statements also instruct patients who have any of these stomach bleeding risk factors to ask an HCP before using an NSAID.¹

1. US Food and Drug Administration. *Fed Regist.* 2009;74(81):19385-19409.

Consider Whether My Patient . . .

- ☐ Has cardiovascular disease?
- ☐ Has edema (due to congestive heart failure)?
- ☐ Has an increased risk of gastrointestinal bleeding?
- ☐ Has gastroesophageal reflux disease, dyspepsia, or peptic ulceration or a history of stomach problems?
- ☐ **Has kidney disease?**
- ☐ Has liver cirrhosis?
- ☐ Drinks 3 or more alcoholic beverages a day?
- ☐ Is 60 years of age or older?
- ☐ Takes prescription medications, such as NSAIDs, antihypertensive agents, diuretics, or anticoagulants?
- ☐ Takes OTC medications containing acetaminophen or NSAIDs, including cough and cold or allergy products, sleep aids, antipyretics, or analgesics?
- ☐ Takes aspirin for cardiovascular prophylaxis?

NSAIDs=nonsteroidal anti-inflammatory drugs.

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Speaker Notes:

It is important to consider kidney disease when making an OTC analgesic recommendation. We will review some of the challenges associated with pain management in this patient population.

Some Individuals Have Kidney-Related Risks That May Be Impacted by OTC Analgesics

- Patients who have renal insufficiencies may be at increased risk for acute renal failure if they use NSAIDs regularly^{1,2}
- In individuals with kidney disease, aspirin may increase the tendency to bleed³
- The National Kidney Foundation considers acetaminophen the OTC analgesic of choice for occasional use in patients with kidney disease³



1. Harirforoosh S, et al. *Expert Opin Drug Saf.* 2009;8(6):669-681. 2. Bush TM, et al. *West J Med.* 1991;155(1):39-42. 3. National Kidney Foundation. Pain medicines (analgesics). http://www.kidney.org/atoz/content/painMeds_Analgesics.cfm. Reviewed June 2009. Accessed May 26, 2015.

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Speaker Notes:

Some patients may be at risk for acute renal failure associated with use of NSAIDs, including elderly patients and those with underlying volume depletion, renal insufficiency, congestive heart failure, diabetes, nephrosis, and cirrhosis.¹ Use of NSAIDs may interfere with renal function within the first few weeks of therapy, especially in patients with preexisting renal disease.² In fact, the incidence of renal toxicity due to use of NSAIDs can approach 20% in the high-risk patient population.²

Patients with kidney disease should talk to their doctor before using NSAIDs.³ NSAIDs may increase the risk of sudden kidney failure or progressive kidney damage.³ Stomach ulcers and GI bleeding are the most common side effects of taking NSAIDs and aspirin.³ The National Kidney Foundation considers acetaminophen the drug of choice for occasional use in patients with kidney disease because of bleeding complications that may occur when these patients take aspirin.³

1. Harirforoosh S, et al. *Expert Opin Drug Saf.* 2009;8(6):669-681.

2. Bush TM, et al. *West J Med.* 1991;155(1):39-42.

3. National Kidney Foundation. Pain medicines (analgesics).

http://www.kidney.org/atoz/content/painMeds_Analgesics.cfm. Reviewed June 2009. Accessed May 26, 2015.

Consider Whether My Patient . . .

- ☐ Has cardiovascular disease?
- ☐ Has edema (due to congestive heart failure)?
- ☐ Has an increased risk of gastrointestinal bleeding?
- ☐ Has gastroesophageal reflux disease, dyspepsia, or peptic ulceration or a history of stomach problems?
- ☐ Has kidney disease?
- ☐ Has liver cirrhosis?
- ☐ Drinks 3 or more alcoholic beverages a day?
- ☐ Is 60 years of age or older?
- ☐ Takes prescription medications, such as NSAIDs, antihypertensive agents, diuretics, or anticoagulants?
- ☐ Takes OTC medications containing acetaminophen or NSAIDs, including cough and cold or allergy products, sleep aids, antipyretics, or analgesics?
- ☐ Takes aspirin for cardiovascular prophylaxis?

NSAIDs=nonsteroidal anti-inflammatory drugs.

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Speaker Notes:

It is important to consider the unique characteristics of older patients when making an OTC analgesic recommendation. We will review some of the challenges associated with pain management in this patient population.

The American Geriatrics Society recommends which treatment option as a first-line analgesic in older patients?

A

Ibuprofen

B

Naproxen

C

Aspirin

D

Acetaminophen

Speaker Notes:

The American Geriatrics Society recommends which treatment option as a first-line analgesic in older patients?

[Poll the audience and reveal the most common answer.]

The American Geriatrics Society recommends which treatment option as a first-line analgesic in older patients?

A

Ibuprofen

B

Naproxen

C

Aspirin

D

Acetaminophen

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Speaker Notes:

The correct answer is acetaminophen.

Achieving Pain Relief in Patients Over 60 Years Old Can Be Challenging	
<p>Patients over 60 years old tend to take more medications</p> <p>Nearly 37% receive ≥ 5 prescription drugs¹</p>	<p>Risk of stomach bleeding is increased in patients over 60 years old taking OTC NSAIDs^{3,4}</p>
<p>Risk of developing hypertension or heart disease may be greater in older patients taking NSAIDs²</p>	<p>Acetaminophen is recommended by the American Geriatrics Society as a first line analgesic in older patients⁵</p>

1. Gu Q, et al. *NCHS Data Brief*. 2010;(42):1-8. 2. Barber JB, et al. *Drug Saf*. 2009;32(6):457-474. 3. US Food and Drug Administration. *Fed Regist*. 2009;74(81):19385-19409. 4. Motrin IB [product labeling]. Fort Washington, PA: McNeil Consumer Healthcare; 2015. 5. American Geriatrics Society Panel on Pharmacological Management of Persistent Pain in Older Persons. *J Am Geriatr Soc*. 2009;57(8):1331-1346.

Speaker Notes:

Managing pain in patients older than 60 years can be challenging. These patients tend to take more medications than younger patients. In fact, among Americans aged 60 years and over, more than 76% use ≥ 2 prescription drugs and nearly 37% use ≥ 5 .¹

NSAIDs warrant special care when used in older patients, as these drugs make a major contribution to the increasing incidence of adverse drug reactions in the elderly.² Specifically, the risk of developing hypertension or heart disease may be greater in older patients taking NSAIDs.²

NSAID labeling warns that the risk of stomach bleeding is increased in patients over 60 years old and in those who have had stomach ulcers or bleeding problems.^{3,4}

The American Geriatrics Society recommends acetaminophen as a first-line analgesic in older patients due to its greater safety than traditional NSAIDs.⁵ A maximum of 4000 mg/day of acetaminophen is considered safe in the geriatric population.⁵

1. Gu Q, et al. *NCHS Data Brief*. 2010;(42):1-8.

2. Barber JB, et al. *Drug Saf*. 2009;32(6):457-474.

3. US Food and Drug Administration. *Fed Regist*. 2009;74(81):19385-19409.

4. Motrin IB [product labeling]. Fort Washington, PA: McNeil Consumer Healthcare; 2015.

5. American Geriatrics Society Panel on Pharmacological Management of Persistent Pain in Older Persons. *J Am Geriatr Soc*. 2009;57(8):1331-1346.

Sheila's Medical History

- Type 2 diabetes
- Hyperlipidemia
- Hypertension



Speaker Notes:

Let us return to our patient, Sheila. In reviewing her medical history, we find that she has a number of chronic coexisting medical conditions, including type 2 diabetes, hyperlipidemia, and hypertension. We previously discussed how cardiovascular risks may impact a patient's treatment plan.

Sheila's Medical History

?

What medications is she currently taking?



Speaker Notes:

We should consider what medications Sheila is taking, including those related and unrelated to managing her coexisting medical conditions, to help determine an appropriate treatment for her pain.

Most Patients Are Already Taking Medications¹

- A 1998-1999 survey of 2590 adults showed that in the previous week:

81% had taken at least one medication

50%

had taken a prescription
medication

40%

had taken vitamins/
minerals

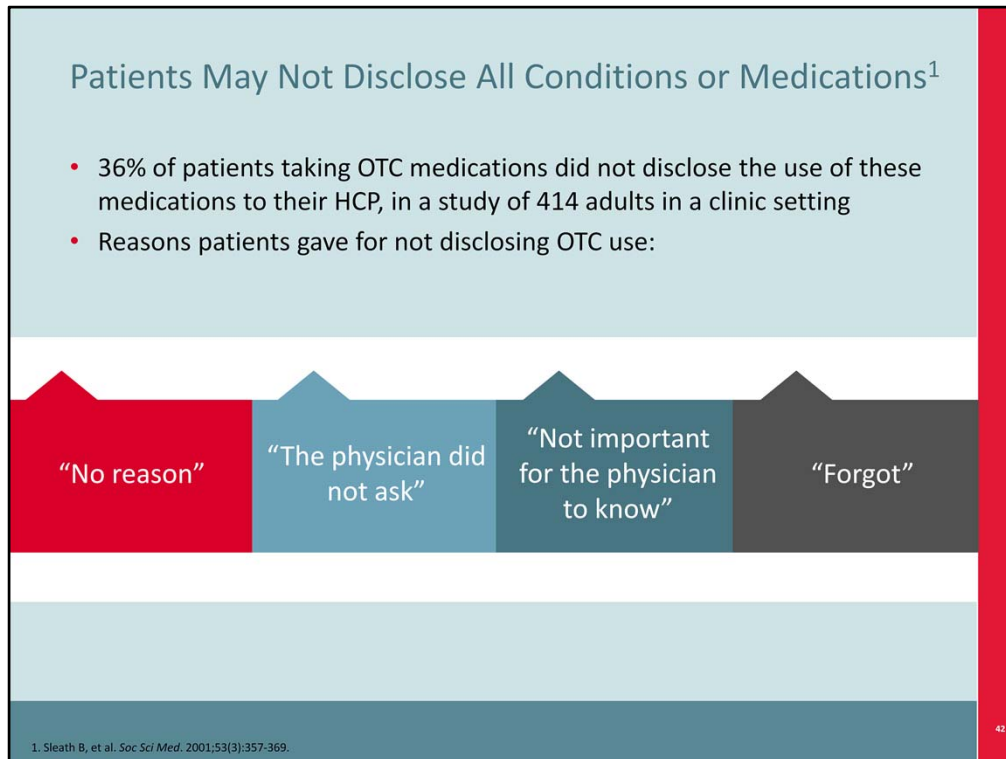
1. Kaufman DW, et al. JAMA. 2002;287(3):337-344.

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Speaker Notes:

A telephone survey of a random sample (N=2590) of the noninstitutionalized US ambulatory population was conducted between 1998 and 1999, and general patterns of medication use were examined.¹ During the preceding week, 81% of subjects had taken at least one medication (prescription or OTC drug, vitamin/mineral, or herbal/supplement); 50% had taken a prescription medication, while 40% had taken vitamins/minerals.¹

1. Kaufman DW, et al. JAMA. 2002;287(3):337-344.



Speaker Notes:

Patients may not disclose all conditions or medications to their HCP. Using data from audiotapes and transcripts of primary care medical visits, a study examined how physicians and patients discuss OTC medications.¹ Twenty-seven resident physicians and 414 of their adult patients participated.¹


The study found that 36% of patients who reported using an OTC medication in the past month did not tell their physician. Reasons patients gave for a lack of medication disclosure included¹:

- No reason stated (24%)
- The physician did not ask (23%)
- Not important for the physician to know (14%)
- Forgot (13%)

These data illustrate the need for improved physician/patient communication regarding medications. It is important for patients to tell their HCP about their use of OTC medications, as full disclosure can help prevent potential drug interactions and adverse effects.¹

1. Sleath B, et al. *Soc Sci Med*. 2001;53(3):357-369.

Sheila's Medications

- 
- Scheduled medications
 - Low-dose aspirin, sitagliptin, insulin glargine, atorvastatin, lisinopril, omeprazole
 - PRN medications
 - Multiple vitamins and mineral supplements, acetaminophen, ibuprofen, naproxen

PRN=as needed.

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Speaker Notes:

Our patient, Sheila, is taking several scheduled medications, which are listed on the slide. Additionally, she is taking PRN medications, including acetaminophen, ibuprofen, and naproxen.

Considerations for Sheila

- Cardiovascular disease
- Antihypertensive agents
- Multiple NSAIDs
- Ibuprofen together with low-dose aspirin



Speaker Notes:

When we consider Sheila's case as a whole, we see that she has several cardiovascular risk factors. She is taking antihypertensive agents and multiple NSAIDs. We previously discussed how each of these factors requires special considerations when developing a treatment plan and making an OTC analgesic recommendation.

Considerations for Sheila

?

What is an appropriate OTC analgesic to recommend to Sheila as part of her treatment plan?



Speaker Notes:

We will discuss the treatment recommendation made for Sheila based on her medical history.

Treatment Recommendation for Sheila



- Physical therapy
- First-line therapy: acetaminophen, not to exceed 4000 mg/day
- Follow-up if insufficient pain relief



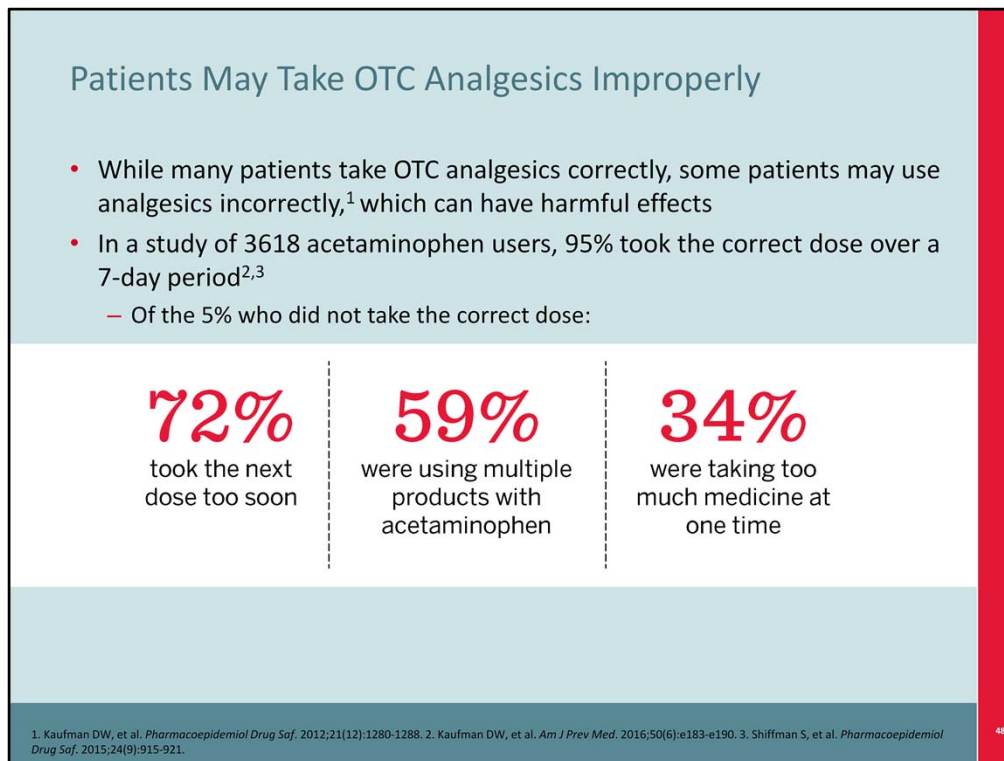
Speaker Notes:

The treatment recommended for Sheila involves nonpharmacologic and pharmacologic approaches. Physical therapy, which may include performing exercises at home, can help relieve her pain. Acetaminophen is an appropriate choice for first-line pharmacologic therapy, considering her comorbidities. Follow-up appointments will be important to monitor treatment efficacy, as measured by pain relief.



Speaker Notes:

Now that we have made a treatment recommendation, let us discuss how patient education can help ensure appropriate OTC analgesic use.



Speaker Notes:

Patients may take OTC analgesics improperly. A 1-week daily diary study of acetaminophen users conducted in 2010 assessed acetaminophen knowledge, attitudes, and dosing practices.¹ A total of 163 (5%) of 3618 acetaminophen users exceeded 4 g on at least one day in a week.¹ Label reading, knowledge that acetaminophen was an ingredient in all products taken, and knowledge of the maximum recommended OTC dose were inversely associated with use of >4 g.¹ However, the view that a user can choose the dose, regardless of recommendations, was positively associated with use of >4 g.¹ This study reinforces the importance of patient education to help ensure understanding of the recommended OTC analgesic dose.

Another report on this study showed that exceeding the correct dose was more likely on days that users deviated from label directions in other ways, with each deviation independently contributing to the likelihood of excess dosing (multivariate odds ratio 5.4-7.6).² Seventy-two percent of users took the next dose too soon, 59% were using multiple products with acetaminophen, and 34% were taking too much medicine at one time.²

A 2016 study explored health literacy and its correlation with exceeding the maximum recommended daily dose of acetaminophen.³ In that study, low health literacy was particularly likely among individuals with limited education and has been linked to poor comprehension of medication directions.³

1. Kaufman DW, et al. *Pharmacoepidemiol Drug Saf.* 2012;21(12):1280-1288.

2. Shiffman S, et al. *Pharmacoepidemiol Drug Saf.* 2015;24(9):915-921.

3. Kaufman DW, et al. *Am J Prev Med.* 2016;50(6):e183-e190.

Which OTC analgesic medication is associated with liver failure when taken in quantities above the maximum recommended dose?

A

Ibuprofen

B

Naproxen

C

Aspirin

D

Acetaminophen

Speaker Notes:

Which OTC analgesic medication is associated with liver failure when taken in quantities above the maximum recommended dose?

[Poll the audience and reveal the most common answer.]

Which OTC analgesic medication is associated with liver failure when taken in quantities above the maximum recommended dose?

A

Ibuprofen

B

Naproxen

C

Aspirin

D

Acetaminophen

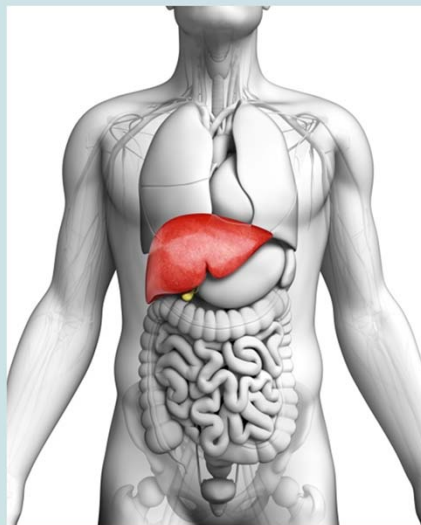
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Speaker Notes:

The correct answer is acetaminophen.

Patients Taking Acetaminophen Inappropriately May Experience Hepatic Risks¹

- When the maximum daily dose is exceeded, acetaminophen has been associated with increased hepatic risks
- In adults, severe liver damage may occur with:
 - Use of over 4000 mg of acetaminophen in 24 hours
 - Consumption of 3 or more alcoholic drinks every day while using acetaminophen



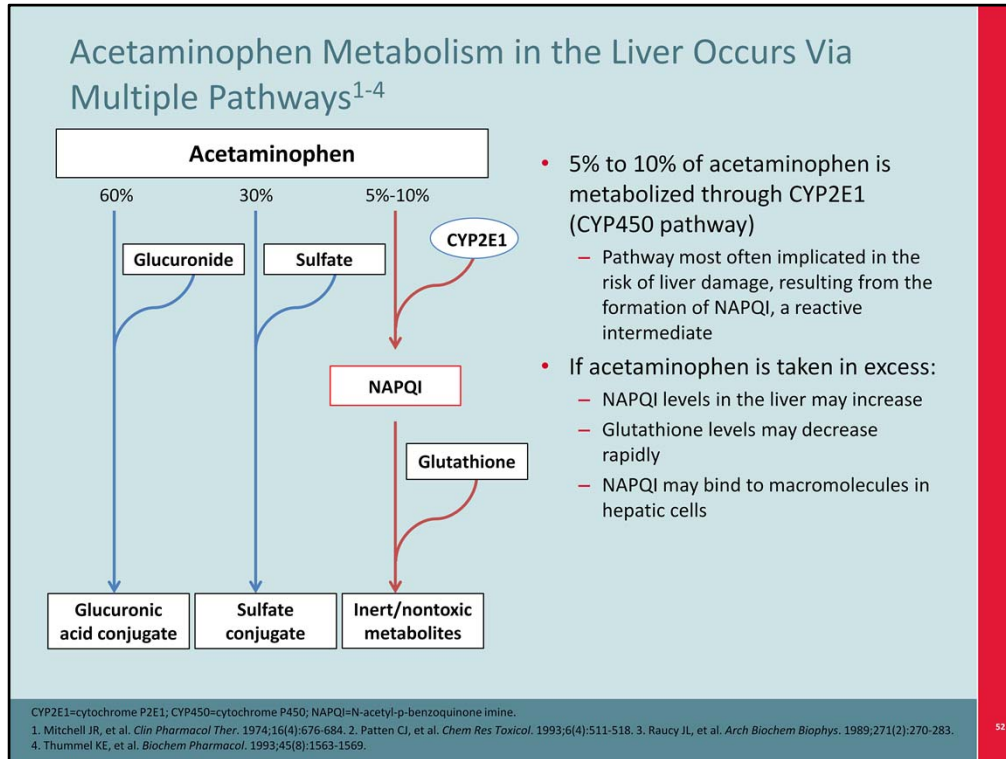
1. US Food and Drug Administration. *Fed Regist.* 2009;74(81):19385-19409.

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Speaker Notes:

Patients taking acetaminophen inappropriately may experience hepatic risks. Acetaminophen labeling includes warnings indicating that severe liver damage may occur if patients take more than the maximum recommended daily dose in 24 hours, take the drug with other drugs containing acetaminophen, or consume 3 or more alcoholic drinks every day while using acetaminophen.¹

1. US Food and Drug Administration. *Fed Regist.* 2009;74(81):19385-19409.



Speaker Notes:

To evaluate hepatic risks, it is helpful to understand how acetaminophen is metabolized in the liver.

Acetaminophen is metabolized via 3 separate hepatic pathways. The majority of acetaminophen, up to 90%, is processed through 2 pathways, conjugating the acetaminophen to either glucuronide or sulfate, to form nontoxic conjugates that are excreted in the urine.¹

The third pathway is responsible for the metabolism of 5% to 10% of acetaminophen.¹ This portion of acetaminophen is metabolized via the CYP450 pathway, resulting in the formation of NAPQI, a reactive intermediate that is thought to be responsible for liver damage associated with toxicity.^{2,3,4} Toxicity is avoided under typical conditions through binding of NAPQI to glutathione to form inert metabolites, which are excreted in the urine.⁵

When acetaminophen is taken at doses above 7.5 to 10 g over a period of ≤8 hours, NAPQI may accumulate in the liver, as short-term glutathione levels are depleted faster than the body can replenish them.⁵ Accumulating NAPQI may bind to macromolecules in hepatic cells, leading to liver injury.

1. Mitchell JR, et al. *Clin Pharmacol Ther.* 1974;16(4):676-684.
2. Patten CJ, et al. *Chem Res Toxicol.* 1993;6(4):511-518.

3. Raucy JL, et al. *Arch Biochem Biophys*. 1989;271(2):270-283
4. Thummel KE, et al. *Biochem Pharmacol*. 1993;45(8):1563-1569.
5. *Tylenol Professional Product Information*. Fort Washington, PA: McNeil Consumer Healthcare; 2015.

On the Drug Facts label for OTC ibuprofen, what is the maximum recommended dose?

A 2400 mg/day

B 2000 mg/day

C 1800 mg/day

D 1200 mg/day

Speaker Notes:

On the Drug Facts label for OTC ibuprofen, what is the maximum recommended dose?

[Poll the audience and reveal the most common answer.]

On the Drug Facts label for OTC ibuprofen, what is the maximum recommended dose?

A

2400 mg/day

B

2000 mg/day

C

1800 mg/day

D

1200 mg/day

Speaker Notes:

The correct answer is 1200 mg/day. We will now cover dosing in more detail.

Ensure That Patients Understand the Recommended OTC Analgesic Dose

- The maximum dose listed on the box label may not reflect the maximum dose that an HCP can recommend
 - The maximum dose of acetaminophen that an HCP can recommend is **4000 mg/24 hours**

Ingredient	Maximum Dose Listed on the OTC Drug Facts Box Label	
	Box Directions on Maximum Dose	Maximum Dose Received
Acetaminophen ¹	Ten 325-mg tablets	3250 mg/day
	Six 500-mg caplets	3000 mg/day
	Six 650-mg bilayer caplets	3900 mg/day

- Labeled maximum daily doses vary among acetaminophen-containing products
 - There are 500 different acetaminophen-containing prescription and OTC medications²

1. Dart RC. Safety of acetaminophen during therapeutic use [PowerPoint presentation]. <http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/DrugSafetyandRiskManagementAdvisoryCommittee/UCM176819.pdf>. Accessed April 26, 2016. 2. Acetaminophen Awareness Coalition. Common medicines. <http://www.knowyourdose.org/common-medicines/>. Accessed April 26, 2016.

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Speaker Notes:

Labeled maximum daily doses vary among acetaminophen-containing products, and the maximum dose that an HCP can recommend may differ from that on the label.

For example, an HCP can safely recommend up to 4000 mg/24 hours of acetaminophen. However, as shown in the table, the dose listed on the OTC label may be lower.¹ HCPs should clearly explain to patients the specific dose recommended to meet their individual needs. This discussion is especially important given that 500 different acetaminophen-containing prescription and OTC medications are available.²

It is essential to ensure that patients understand the recommended OTC analgesic dose so that they can use the product safely and achieve the maximum possible efficacy.

1. Dart RC. Safety of acetaminophen during therapeutic use [PowerPoint presentation]. <http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/DrugSafetyandRiskManagementAdvisoryCommittee/UCM176819.pdf>. Accessed April 26, 2016.

2. Acetaminophen Awareness Coalition. Common medicines. <http://www.knowyourdose.org/common-medicines/>. Accessed April 26, 2016.

Ensure That Patients Understand the Recommended OTC Analgesic Dose

- The maximum dose listed on the box label may not reflect the maximum dose that an HCP can recommend

Ingredient	Maximum Dose Listed on the OTC Drug Facts Box Label	
	Box Directions on Maximum Dose	Maximum Dose Received
Acetaminophen ¹	Ten 325-mg tablets	3250 mg/day
	Six 500-mg caplets	3000 mg/day
	Six 650-mg bilayer caplets	3900 mg/day
Aspirin ²	Twelve 325-mg tablets	3900 mg/day
Ibuprofen ³	Six 200-mg caplets	1200 mg/day
Naproxen ⁴	Three 220-mg tablets	660 mg/day

1. Dart RC. Safety of acetaminophen during therapeutic use [PowerPoint presentation]. <http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/DrugSafetyandRiskManagementAdvisoryCommittee/UCM176819.pdf>. Accessed April 26, 2016. 2. Aspirin. <http://www.nsaid-list.com/nsaid-list/aspirin>. Accessed March 14, 2016. 3. Ibuprofen. <http://www.nsaid-list.com/nsaid-list/ibuprofen>. Accessed March 14, 2016. 4. Naproxen. <http://www.nsaid-list.com/nsaid-list/naproxen>. Accessed March 14, 2016.

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Speaker Notes:

It is also essential to ensure that patients understand the recommended OTC analgesic dose of products containing aspirin, ibuprofen, or naproxen.

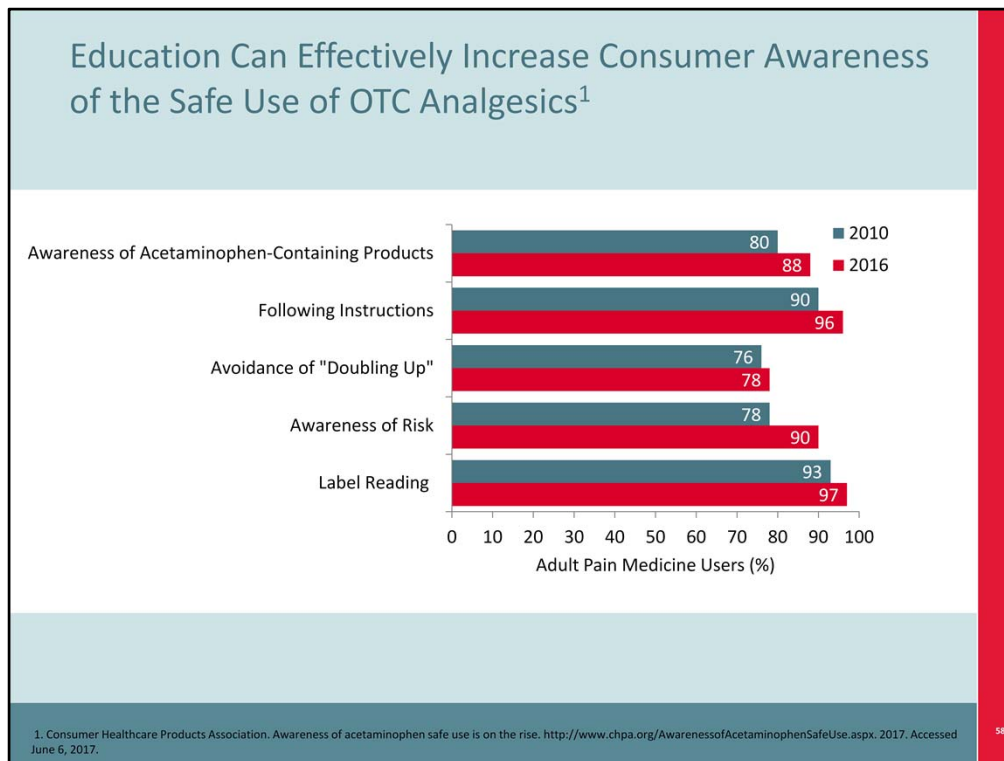
As with acetaminophen, HCPs should clearly explain to patients the specific dose recommended to meet their individual needs.

Patients Should Understand Their Individualized Treatment Plan

- Patients should understand that their OTC analgesic recommendation is specific and individualized for them
- Patients should be educated on the label directions and how they relate to their individual medical history
- HCPs should always ask about OTC analgesics that patients are taking and educate patients on the importance of disclosing their full medical history

Speaker Notes:

As we have discussed, it is essential to ensure that patients understand their individualized treatment plan and why a specific OTC analgesic was recommended for them. We can help patients understand our recommendations by being very specific about ingredients and appropriate dosages each time we recommend. HCPs should review the label directions with patients and explain how the recommended dose was tailored to their individual medical history. It is also important to ask patients about other OTC analgesics that they may be taking, as this discussion can help prevent misuse and drug interactions.



Speaker Notes:

Recent research indicates that more consumers know how to safely use medications with acetaminophen and avoid accidental overdose and liver damage.¹ These data reflect the results of a nationwide survey of 2000 US adult pain medicine users.¹ Overall, the results show that awareness of risk increased over a 6-year period (78%-90% from 2010-2016).¹ The percentage of consumers who reported following dosing instructions, avoiding “doubling up” on medication, being aware of medication risks, and reading the label also increased from 2010 to 2016.¹

Through educational initiatives such as the *Know Your Dose* campaign, more consumers know that acetaminophen can be found in many OTC and prescription pain medicines. Increases were also seen in the percentage of consumers who²:

- Agree that it is “important not to exceed the dosing directions on the label” of pain relievers
- Understand that “it is possible to exceed the maximum daily dose when taking an OTC acetaminophen product at the same time as a prescription pain medicine”
- Agree that it is “important to check the label to find out the maximum daily dose” of medicines
- Understand that “exceeding the recommended daily dose of acetaminophen may lead to liver damage”

There is hope that NSAID educational programs will be equally successful.

1. Consumer Healthcare Products Association. Awareness of acetaminophen safe use is on the rise. <http://www.chpa.org/AwarenessofAcetaminophenSafeUse.aspx>. 2017. Accessed June 6, 2017.

2. Acetaminophen Awareness Coalition. Acetaminophen: how it’s used, preventing overdose and what we can do to promote safe use. <http://www.knowyourdose.org/wpcontent/uploads/2015/05/Acetaminophen-Report.pdf>. 2014. Accessed April 26, 2016.

Patient Educational Initiatives on the Safe Use of OTC Analgesics

- Patients who are more knowledgeable about active ingredients and appropriate dosing are less likely to exceed the recommended dose of acetaminophen¹
- Patient educational initiatives include:

KnowYourDose.org
Acetaminophen Awareness Coalition



Gut Check:
Know Your Medicine

 Alliance for Rational
Use of NSAIDs
A Public Health Coalition

Get Relief Responsibly®
GetReliefResponsibly.com

1. Kaufman DW, et al. *Pharmacoepidemiol Drug Saf.* 2012;21(12):1280-1288.

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Speaker Notes:

Patients who are more knowledgeable about active ingredients and appropriate dosing are less likely to exceed the recommended dose of acetaminophen.¹ As discussed previously, a 1-week daily diary study demonstrated that knowledge of product ingredients and OTC label instructions for the maximum dose of acetaminophen at one time and in 24 hours was inversely associated with use of >4 g (odds ratio 0.5-0.6 [95% CI: 0.8-0.9]).¹

As the healthcare landscape continues to evolve, educating patients on safe use of prescription and OTC medications will remain a top priority. HCPs play an important role in ensuring that patients read and follow the instructions on product labels and become familiar with the active ingredients in their medicine.²

The Acetaminophen Awareness Coalition's *Know Your Dose* campaign is one of many ongoing, coordinated educational initiatives that target appropriate acetaminophen use and help prevent overdose.² Other educational initiatives, including the *Get Relief Responsibly®* campaign from Johnson & Johnson Consumer Inc, are listed on the slide.

1. Kaufman DW, et al. *Pharmacoepidemiol Drug Saf.* 2012;21(12):1280-1288.

2. Acetaminophen Awareness Coalition. Acetaminophen: how it's used, preventing overdose and what we can do to promote safe use. <http://www.knowyourdose.org/wp-content/uploads/2015/05/Acetaminophen-Report.pdf>. 2014. Accessed April 26, 2016.

An Individualized Approach to Managing Pain



Review the impact on quality of life



Consider medical history and coexisting conditions



Assess concomitant medications, including OTC medicines



Educate on safe and appropriate use of the recommended OTC analgesic



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Speaker Notes:

In summary:

- Pain can impact patient quality of life
- Certain considerations need to be taken into account when recommending an OTC analgesic:
 - Presence of coexisting medical conditions
 - Concomitant use of other medications
- Patient education is important to help ensure safe and appropriate OTC analgesic use

Question-and-Answer Session

