



# G3C Cases and Pharmacogenomics

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# Global Genetics and Genomics Community (G3C)

- High Fidelity Simulated Online Unfolding Case Studies
  - Ethnically diverse
  - Focus on common public health issues
- Portable, web-based, open access
- Bilingual (English/Spanish)
- Interactive, self-paced, self-directed, unfolding case studies

<http://www.g-3-c.org>

# Global Genetics and Genomics Community (G3C)

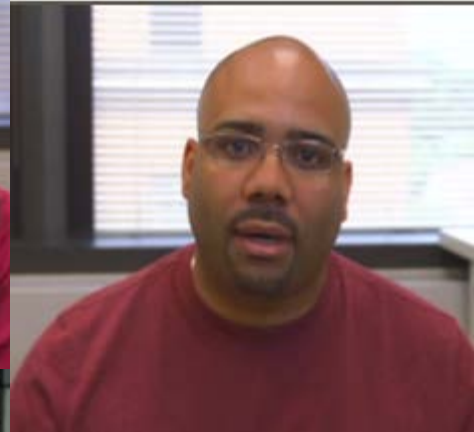
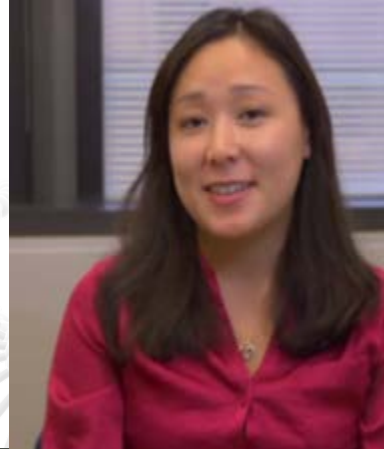
- Utilizing professional actors as simulated patients
- Incorporates student/learner education activities and resources
- Faculty support includes suggestions on how to use cases in the curriculum

<http://www.g-3-c.org>

# Cases

16 cases available  
Ethnically diverse  
In- and Out-patient  
Address

- Family history assessment
- Direct to consumer marketing/testing
- Family issues
- Personal values assessment
- Genetics/genomics of common diseases (diabetes, cardiovascular disease, psychiatric disorders, pharmacogenomics, prenatal testing)



# Continuing Education Platform

The screenshot displays the website for the Global Genetics and Genomics Community (GBC). At the top, the GBC logo and name are visible, along with navigation links for Home, Resources, About, and Login / Register. The main banner features a silhouette of a person's head with the text "YOU ASK THE QUESTIONS" inside, set against a background of healthcare professionals. Below this, a section titled "GENOMIC HEALTH CARE SIMULATIONS" lists several bullet points: "Interview 'patients' at your own pace", "Complete supplemental educational activities", "Assess your genomic competency", "Consider commentary about specific cases from genomic experts", and "Earn CNE or CME credit for each case".

Below the banner, a text prompt reads: "Recognize when your own attitudes and values may affect care provided to clients." This is followed by a "HOW IT WORKS" section on a corkboard background, consisting of three numbered steps:

- 1. Login or Register**  
Join the GBC Learning Portal for free and expand your genetic/genomic knowledge.
- 2. Choose from 15 Cases**  
Narrow your search based on topic and level of difficulty.
- 3. Start Seeing Patients**  
Apply what you learn today. Lead your "patients" to quality healthcare outcomes.

Below the flowchart, the text "Unfolding Case Studies for Genetics & Genomics Healthcare Education" is followed by a paragraph: "The GBC (Global Genetics and Genomics Community) learning portal presents a bilingual collection of interactive cases that demonstrate how genetics and genomics link to health and illness. GBC is free to all users and encourages students and practicing healthcare providers to address the multi-dimensional needs of patients through various self-guided, video-taped 'patient-provider' interview simulations." Another paragraph states: "Throughout each patient scenario, there are links to resources and supplemental educational activities to expand upon genetic/genomic learning concepts. At the end of each patient encounter, learners are prompted to make a recommendation to their 'patient' and are assessed across multiple domains such as risk assessment, family history, and patient medical history." A final paragraph notes: "All cases include educator support content that offers suggestions on how to utilize each case in the classroom, curriculum, or as part of continuing education."

At the bottom right, there is a "Register" form with fields for "First Name:", "Last Name:", and "E-mail Address:". Below the form is a red button labeled "CONTINUE REGISTRATION" with a right-pointing arrow.



# Track Your Case Progress or Resume A Case



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## In Progress

Sort by... ▼



Lisa

Questions Asked: 0/16  
Recommendation: 0/5

Continue Patient Interview



Stephanie

Questions Asked: 0/17  
Recommendation: 0/6

Continue Patient Interview

## Completed

Sort by... ▼



Dai

Questions Asked: 11/17  
Recommendation: 4/4

View Assessment

Certification

# Filter Cases Based on Topic and/or Difficulty

FILTER BY

Select a Category

Select a Difficulty

## Case Studies

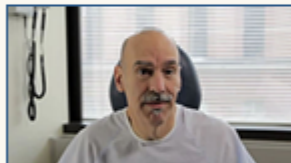


Start Case Study

View Case Notes

### Gabe ( [View Patient Info](#) )

Gabe Geller is a 55 year old Ashkenazi Jewish male who presents for evaluation of rectal bleeding and to receive his colonoscopy results. Several weeks ago he noticed a small amount of blood in the toilet bowl after a bowel movement. He thought it was just hemorrhoids and was not concerned. This happened a couple more times over the next few days and he mentioned this to his wife, who called to schedule him an appointment for evaluation about two weeks ago. He was referred to a gastroenterologist for a colonoscopy prior to this visit, which he had a few days ago. Eleven adenomatous polyps were found during the procedure, mostly on the right side of the colon. All polyps were successfully removed during the colonoscopy.



Start Case Study

View Case Notes

### Gabe #2 ( [View Patient Info](#) )

Gabe is a 56 year old Ashkenazi Jewish man who was recently admitted to the hospital for an arrhythmia. He is miserable having to stay in the hospital to be monitored and he is short with everyone. Work-up may indicate that he needs anticoagulation treatment and he is asking a lot of questions about what that means for him and his family.



Start Case Study

View Case Notes

### Grace ( [View Patient Info](#) )

Grace Washington is a 44 year old African American female who moved to the area about a year ago and was referred to our clinic for her annual well woman examination. She has not seen a health care provider since her move. She is married with three children, reports having a family history of breast cancer and wants a mammogram because she is very concerned about her breast cancer risk due to her family history. A brief health history was taken by phone when she called to schedule an appointment as a new patient. A family history questionnaire was emailed to her and she completed it and brought it with her to the clinic visit.

# Case Format



## Jeff & Maria

### Student Activity

What are the cancer risk management guidelines for men with a BRCA2 mutation?

[Resource 1](#)

[Resource 2](#)

[Resource 3](#)

[Resource 4](#)



**Jeff:** Well, I'm here for my yearly physical. And I completed the ACT for health and the WebHA, and found out that I'm at an increased risk for breast cancer. My dad, incidentally, was found to have the mutation BRCA2, which I was under the impression that could only be passed down by the mother's side of the family.

**Maria:** But we found out that is not true.

**Jeff:** Right.

**Maria:** And really I think the reason we are here today is - for me, it's primarily because I'm concerned about Jeff's health, and I guess I just



# Incorporation of Outcome Recommendations

## Make a Recommendation




### Are you ready to make a recommendation?

1 of 3

When you feel that you have gained enough insight into the patient's circumstance, choose a recommendation below that best fits the situation. If you answer incorrectly, you will be returned to the patient's case to gather further information. At any point you may then return and try again. Upon successfully making the best recommendations for each scenario, you will receive an assessment of your performance.

Grace's family history indicates that she is at an increased risk for breast cancer because she has two second degree relatives with breast cancer. My recommendation for Grace is that she begin increased breast cancer screening based on her increased risk for breast cancer.


Grace's family history indicates that she is at an increased risk for breast cancer because she has two second degree relatives with breast cancer. My recommendation for Grace is that she undergo genetic testing for breast cancer susceptibility.

Grace's family history of breast cancer is older onset disease with only one second degree relative on her mothers side and one second degree relative on her fathers side. Grace's family history does not indicate an elevated risk for breast cancer above the average population. My recommendation for Grace is that she follow average risk population based guidelines if she has no other breast cancer risk factors. 

Correct! Please continue to the next recommendation.

CONTINUE

# Inclusion of Outcome Assessments

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## Your Assessment

There are 17 questions involved in completing this case study if the user takes the preferred path. Since this is an interactive case study, there are a number of possible paths which may vary in length depending on which question the user chooses at each of the screens. You completed 11 out of the 17 questions.

Points for Your Responses: 15  
Maximum Points for Your Path: 33  
Maximum Points for the Case: 51

### 45%

15 out of 33 points

[Claim Your Credit](#)

### Breakdown of Your Responses

The preferred follow-up question is worth three points, the next best choice is worth two points and the third choice is worth one point.

- 9%** of your responses followed the preferred path.
- 18%** of your responses followed the second best path.
- 73%** of your responses followed the less than optimal path.

The sum of percentages may not add up to 100% due to rounding.



[SAVE](#)

### Your Competencies by Domain

Hover over section titles & progress bars for descriptions

Chief complaint/Reason for encounter	<input type="text"/>	0 of 1 Correct
Personal and Psychosocial Assessment	<input type="text"/>	0 of 2 Correct
Management/Recommendations/Plans	<input type="text"/>	0 of 1 Correct
Current and Past Medical History	<input type="text"/>	0 of 1 Correct
Clinical Issues	<input type="text"/>	0 of 2 Correct
Education and Counseling	<input type="text"/>	1 of 1 Correct
Genetics	<input type="text"/>	0 of 2 Correct

# Expert Commentary



**Howard McLeod, PharmD**

Select a Question below to get started

 **About Expert**

 **Ask a question**

 **Closed Caption**

## Howard McLeod, PharmD

Medical Director, Personalized Medicine Institute

Moffitt Cancer Center

### Resources:

Scott, S.A., Sangkuhl, K., Stein, C.M., Hulot, J.S., Mega, J.L., Roden, D.M., Klein, T.E., Sabatine, M.S., Johnson, J.A., Shuldiner, A.R. (2013). Clinical Pharmacogenetics Implementation Consortium Guidelines for CYP2C19 Genotype and Clopidogrel Therapy: 2013 Update. *Clinical pharmacology & Therapeutics*, 94, 317-323.

<http://www.ncbi.nlm.nih.gov/pubmed/23698643>

# Adverse Drug Reactions



- Adverse Drug Reactions (ADRs) are defined as any untoward medical occurrence associated with a medication prescribed at the **recommended dose**



# Codeine Fatal ADRs

- Deaths have been reported in UMs given codeine for pain management post-tonsillectomy and/or adenoidectomy for obstructive sleep apnea
- 8/15/2012, FDA published a safety communication: Codeine use in certain children after tonsillectomy and/or adenoidectomy may lead to rare, but life-threatening adverse events or death

Ciżkowski, C., et al. (2009). Codeine, ultrarapid-metabolism genotype, and postoperative death. *New England Journal of Medicine*, 361(8), 827-8.

Kelly LE, et al. (2012). More codeine fatalities after tonsillectomy in North American children. *Pediatrics*. 129(5):e1343-7

# Codeine Fatal ADRs

- 2/20/2013, the FDA updated the safety communication to a new Black Box Warning and Contraindications related to codeine use, noting that codeine is no longer recommended for pain control in children undergoing a tonsillectomy and/or adenoidectomy.

FDA codeine 08/2012 Safety Communication

<http://www.fda.gov/Drugs/DrugSafety/ucm313631.htm>

FDA codeine 02/2013 Boxed Warning and Contraindication on use after tonsillectomy and/or adenoidectomy

<http://www.fda.gov/Drugs/DrugSafety/ucm339112.htm>

FDA Drug Safety Podcast: Safety review update of codeine use in children

<http://www.fda.gov/Drugs/DrugSafety/DrugSafetyPodcasts/ucm340524.htm>

# CPIC Dosing Guidelines

- April 2014 there were updates to the existing CPIC CYP2D6 and codeine dosing guidelines
- The guideline update addresses the current FDA warning of codeine use in children as well as other opioids CYP2D6 metabolizes
- August 2015 the guideline was further updated with a supplemental table providing the association between allelic variants and CYP2D6 enzyme activity)

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Stephanie

[View Patient Info](#)

Name: Stephanie

Age: 25

## Background

Stephanie is a 25-year old female who presents to the otolaryngologist to discuss post-tonsillectomy pain management for her youngest daughter, given her older daughter's prior adverse reaction to codeine.

## Health Record



[Case Notes](#)



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# Clopidogrel Pharmacogenomic Phenotype

- Prodrug that works primarily by conversion to its active form in the liver, mediated by the liver enzyme CYP2C19
- Extensive metabolizer (normal) \*1/\*1
  - normal platelet inhibition
- Intermediate metabolizer \*1/\*2-<sup>8</sup> or \*17/\*2-<sup>8</sup>
  - Reduced platelet inhibition
  - Increased residual platelet aggregation
  - Increased risk for adverse cardiovascular events

# Clopidogrel Pharmacogenomic Phenotype

- Poor metabolizer  $*2/*2$ - $*8$ 
  - Significantly reduced platelet inhibition
  - increased residual platelet aggregation
  - increased risk for adverse cardiovascular events
- Ultrarapid metabolizer  $*17/*17$  and  $*1/*17$ 
  - Increased platelet inhibition
  - Decreased residual platelet aggregation

# CPIC Dosing Guidelines

- In September 2013 there were updates to the existing CPIC CYP2C19 and Clopidogrel dosing guidelines
- The guideline update is more focused on patients with acute coronary syndromes undergoing percutaneous coronary intervention and refined recommendations for variant and novel CYP2C19 alleles beyond \*2
- The full text guidelines and update are provided on PharmGKB as well as a genotype specific dosing guidelines table

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Larry

[View Patient Info](#)

Name: Larry  
Age: 55  
Height: 6'0"  
Weight: 205 lbs.  
BP: 130/85  
Pulse: 78  
Temp: 97.5

#### Background

Larry is a 55-year old African American who presents to the ED for moderate chest pain and a nosebleed a few days after he stopped taking clopidogrel (Plavix®).

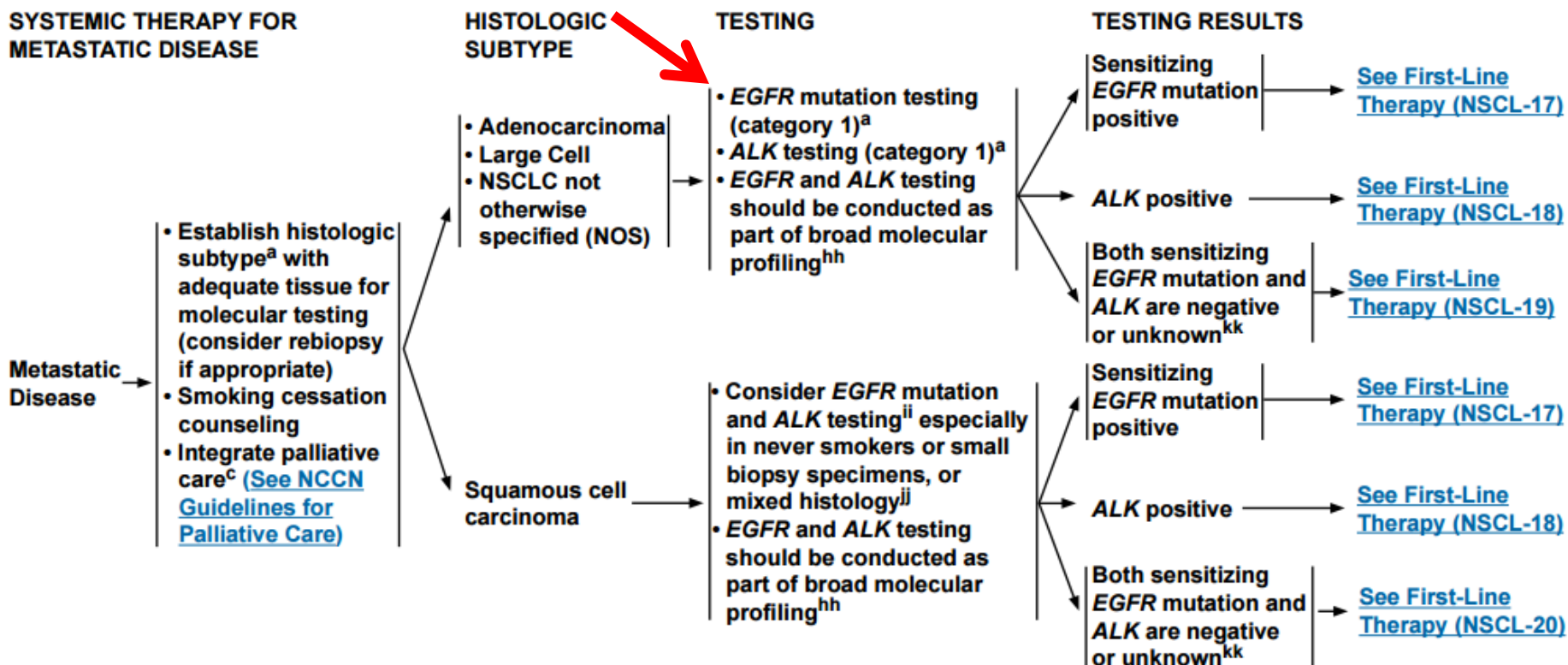
#### Health Record

[Case Notes](#)



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SYSTEMIC THERAPY FOR  
METASTATIC DISEASE

<sup>a</sup>See [Principles of Pathologic Review \(NSCL-A\)](#).

<sup>c</sup>Temel JS, Greer JA, Muzikansky A, et al. Early palliative care for patients with metastatic non-small-cell lung cancer. *N Engl J Med* 2010;363:733-742.

<sup>hh</sup>The NCCN NSCLC Guidelines Panel strongly endorses broader molecular profiling with the goal of identifying rare driver mutations for which effective drugs may already be available, or to appropriately counsel patients regarding the availability of clinical trials. Broad molecular profiling is a key component of the improvement of care of patients with NSCLC. See [Emerging Targeted Agents for Patients With Genetic Alterations \(NSCL-H\)](#).

<sup>ii</sup>In patients with squamous cell carcinoma, the observed incidence of EGFR mutations is 2.7% with a confidence that the true incidence of mutations is less than 3.6%. This frequency of EGFR mutations does not justify routine testing of all tumor specimens. Forbes SA, Bharna G, Bamford S, et al. The catalogue of somatic mutations in cancer (COSMIS). *Curr Protoc Hum Genet* 2008;chapter 10:unit 10.11.

<sup>jj</sup>Paik PK, Varghese AM, Sima CS, et al. Response to erlotinib in patients with EGFR mutant advanced non-small cell lung cancers with a squamous or squamous-like component. *Mol Cancer Ther* 2012;11:2535-2540.

<sup>kk</sup>Consider ROS1 testing; if positive, may treat with crizotinib. Shaw AT, Ou S-HI, Bang Y-J, et al. Crizotinib in ROS1-rearranged non-small cell lung cancer. *N Engl J Med* 2014;371:1963-1971.

**Note:** All recommendations are category 2A unless otherwise indicated.

**Clinical Trials:** NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

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Tom

[View Patient Info](#)

Name: Tom  
Age: 52 years old  
Height: 6'4"  
Weight: 187 lbs  
BP: 148/70  
Pulse: 80  
Temp: 97.9

## Background

Insurance salesman, male, age 52, lifetime non-smoker, diagnosed with non-small cell lung cancer within the past 6 weeks. This is his first visit since he received his first chemotherapy treatment. He...

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Health Record

[Case Notes](#)



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# Questions/Discussion

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