Case 8
Luca is a 12-year-old male who is excited to start 7th grade. During the first month of school, the teacher notices that Luca has trouble sitting still without fidgeting and is unable to concentrate on lessons. At home, Luca’s parents observe misplaced toys and incompletion of homework and weekly chores. Luca’s teacher and parents discuss his recent troubles at home and at school.

Luca’s parents decide to make an appointment with a psychiatrist. Upon meeting Luca and discussing his symptoms and school history, the psychiatrist diagnoses him with Attention-deficit/hyperactivity disorder (ADHD). Luca’s parents ask his psychiatrist what course of drug treatment and counseling would work best for Luca.
Case 8

• The psychiatrist is considering treating Luca with:

  Atomoxetine (Strattera)

• Question 1: How does this drug work to treat ADHD?

  Hint: pharmacodynamics; use https://www.pharmgkb.org/annotatedDrugs
Case 8

• Metabolism of Atomoxetine:

Atomoxetine $\xrightarrow{CYP2D6}$ Liver $\xrightarrow{4$-hydroxy atomoxetine}$ Increased neurotransmitter concentration

• Key pharmacogene for Atomoxetine: $CYP2D6$
Case 8

• You recommend preemptive testing of Luca’s *CYP2D6* genotype before initiating atomoxetine therapy. In the meantime, you have the genotypes of Luca’s parents in the electronic medical records.

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<thead>
<tr>
<th></th>
<th>Dad</th>
<th>Mom</th>
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<tbody>
<tr>
<td></td>
<td>*10/*1</td>
<td>*41/*1x2</td>
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*Dad: Male, *10/*1

*Mom: Female, *41/*1x2*
Question 2: What genotypes and phenotypes are possible for Luca (48 kg) based on mom and dad’s genotype?

<table>
<thead>
<tr>
<th>Possible Genotypes (*X/*X)</th>
<th>Phenotype (Poor/Normal/Intermediate/Ultrarapid Metabolizer)</th>
<th>Drug Therapy Recommendation (Use/Don’t Use/Change Dose)</th>
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Use This Website To Look Up Genotype-Based Dosing: https://www.pharmgkb.org/guidelineAnnotation/PA166181885
Case 8

• Luca underwent genotyping and you have received the results from the laboratory.

  **CYP2D6: *10/*41**

• Question 3: What is Luca’s phenotype?

• Question 4: What do you recommend for their treatment? Why (better or worse benefit/toxicity)?