Solutions

Marking: **M1** a correct method, **A1** the correct answer, **B1** an independent mark.

Each answer shows the steps, then the **result**.

2.1

liability comes from many genes and the environment, and is normally distributed

disease appears only above a threshold

relatives share genes, so their curve is shifted and more of them are above the threshold

2.2

MZ concordance is higher than DZ, so genes play a part

MZ concordance is below 100%, so the environment also plays a part

2.3

$h^2 = 2(0.8 - 0.5)$

$= 0.6$

2.4

carbamazepine: **C, HLA-B*15:02**

abacavir: **B, HLA-B*57:01**

azathioprine: **A, TPMT**

3.1

(a) **CYP2D6**

(b) she is a poor metaboliser with little working CYP2D6, so little morphine is made

(c) he is an ultrarapid metaboliser, with extra copies of the gene, so morphine is made fast and builds up: toxicity with slow breathing

(d) paracetamol, an NSAID or morphine itself (not codeine or tramadol), because these do not need CYP2D6 to work

3.2

(a) **60**

(b) clopidogrel is a prodrug made active by CYP2C19; less active drug means platelets are less blocked, so stent clots are more likely

(c) **ticagrelor** or prasugrel

(d) a stent clot is serious and can kill, while the test is cheap and needed only once

3.3

(a) girls have a higher threshold, so an affected woman has more risk genes to pass on

(b) about **2–5%**

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(c) **5 mg** daily from before conception until 12 weeks

(d) **HLA-B*15:02**: carriers have a high risk of Stevens–Johnson syndrome on carbamazepine

(e) family members share many genes and much of their environment, such as diet