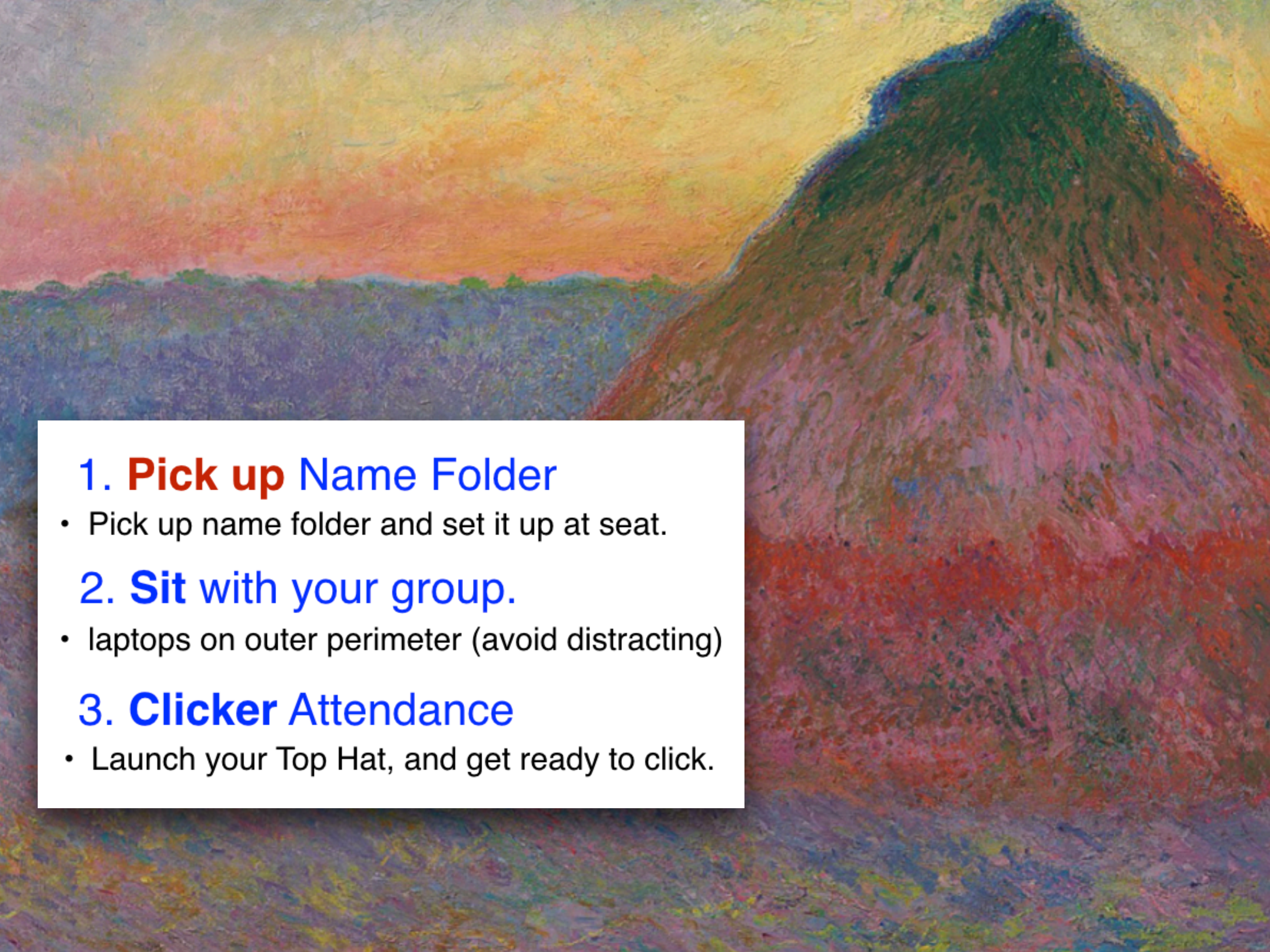

1. **Pick up** Name Folder

- Pick up name folder and set it up at seat.

2. **Sit** with your group.

- laptops on outer perimeter (avoid distracting)

3. **Clicker** Attendance

- Launch your Top Hat, and get ready to click.

Special Article

DIFFERING BIRTH WEIGHT AMONG INFANTS OF U.S.-BORN BLACKS, AFRICAN-BORN BLACKS, AND U.S.-BORN WHITES

RICHARD J. DAVID, M.D., AND JAMES W. COLLINS, JR., M.D., M.P.H.

ABSTRACT

Background In the United States, the birth weights of infants of black women are lower than those of infants of white women. The extent to which the lower birth weights among blacks are related to social or genetic factors is unclear.

Methods We used vital records for 1980 through 1995 from Illinois to determine the distribution of birth weights among infants born to three groups of women — U.S.-born blacks, African-born blacks, and U.S.-born whites.

Results The mean birth weight of 44,046 infants of U.S.-born white women was 3446 g, that of 3135 infants of African-born black women was 3333 g, and that of 43,322 infants of U.S.-born black women was 3089 g. The incidence of low birth weight

creases in both blacks and whites as the number of risk factors declines, the improvement is faster among whites, resulting in a wider birth-weight gap between blacks and whites among infants of low-risk women.[1,4] This has led some investigators to believe that genetic factors associated with race influence birth weight.[10-15] In the 1967 National Collaborative Perinatal Project, only 1 percent of the total variance in birth weight among 18,000 infants was accounted for by socioeconomic variables, leading the authors to conclude that "race behaves as a real biological variable in its effect on birth weight. This effect of race [is] presumably genetic."[10] The assumption that black women differ genetically from white women in their ability to bear normal or large

Number of Races Varied in Time

1749 the concept of race invented to empower land owners

1749: 6 races

1790: 3 races

1971: 33 races

Why so much variation?

Racial Disparities in America

	White Americans	Black Americans
age-adjusted death rate (2015)[1]		
prevalence of coronary heart disease (2010)[2]		
age-adjusted cancer deaths (2010-14)[3]		
infant mortality (2011-13)[4]		
pregnancy-related maternal deaths (2011-13)[5]		
diagnosed diabetes (2015)[6]		
obesity (≥ 20 yrs, 2011-12)[7]		
unemployment (≥ 20 years, 1st Q, 2018)[8]		

If race did not matter in America,
what would you predict for these 8 categories?

Table 6.2

original art

Racial Disparities in America

	White Americans	Black Americans
age-adjusted death rate (2015)[1]	753.2/100,000	876.1/100,000
prevalence of coronary heart disease (2010)[2]	5.8% (± 0.1%)	6.5% (± 0.4%)
age-adjusted cancer deaths (2010-14)[3]	166.2/100,000	194.2/100,000
infant mortality (2011-13)[4]	5.1/1,000	11.3/1,000
pregnancy-related maternal deaths (2011-13)[5]	12.7/100,000	43.5/100,000
diagnosed diabetes (2015)[6]		
obesity (≥ 20 yrs, 2011-12)[7]		
unemployment (≥ 20 years, 1st Q, 2018)[8]		

43.5/12.7 = 3.5 fold difference!

Table 6.2

original art

Racial Disparities in America

Is race real?
Does it have a biological impact on people?

	White Americans	Black Americans
age-adjusted death rate (2015)[1]	753.2/100,000	876.1/100,000
prevalence of coronary heart disease (2010)[2]	5.8% (± 0.1%)	6.5% (± 0.4%)
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infant mortality (2011-13)[4]	5.1/1,000	11.3/1,000
pregnancy-related maternal deaths (2011-13)[5]	12.7/100,000	43.5/100,000
diagnosed diabetes (2015)[6]	7.4%	12.7%
obesity (≥ 20 yrs, 2011-12)[7]	32.6% (± 4%)	47.8% (± 3.5%)
unemployment (≥ 20 years, 1st Q, 2018)[8]	3.6%	6.6%

Table 6.2

original art

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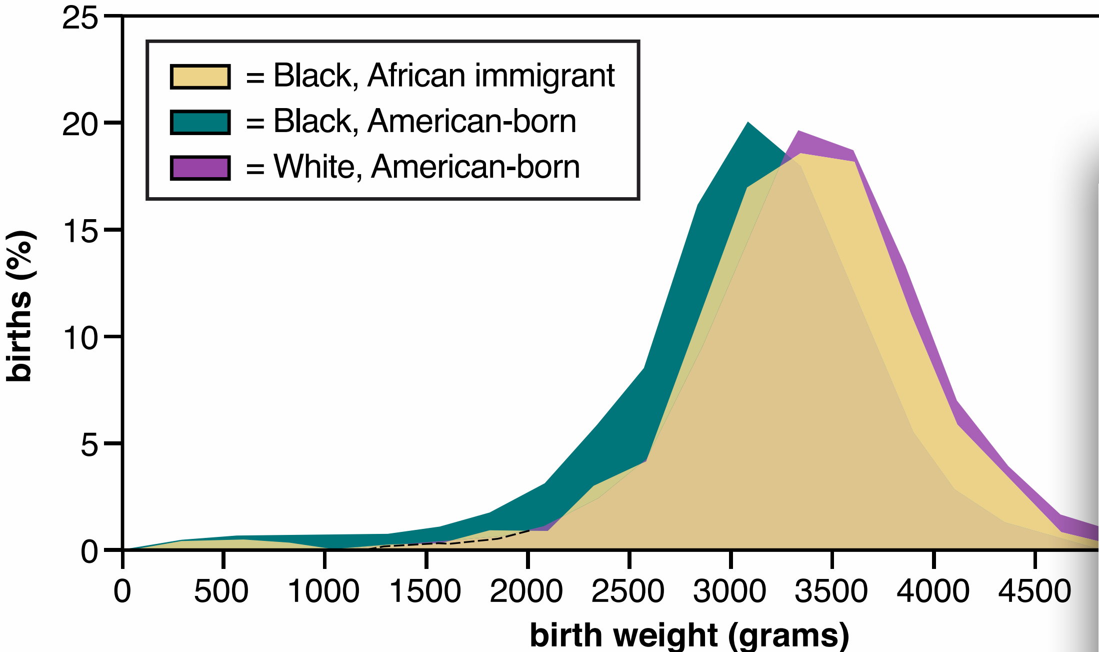
Birth Weight Differences by Race

What could cause differences in birth weights?



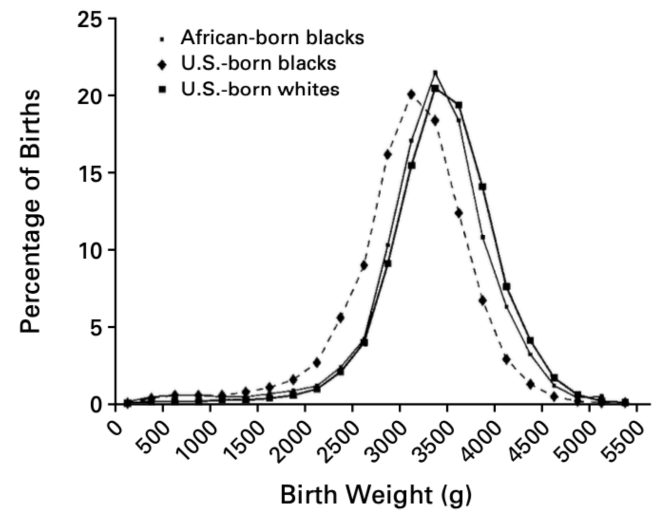


Figure 1. Distribution of Birth Weights among Infants of U.S.-Born White and Black Women and African-Born Black Women in Illinois, 1980–1995.

The calculation of frequencies was based on all singleton births in Illinois. The study population included the infants of 3135 black women born in sub-Saharan Africa, 43,322 black women born in the United States (a sample that included 7.5 percent of the total number of black women giving birth in Illinois), and 44,046 U.S.-born white women (2.5 percent of the total number of white women giving birth in Illinois).

environment? **genetics?**

Fig. 6.26 A

Panel A modified from David and Collins, 1997.

Birth Weight Differences by Race

TABLE 2. Infant birth weight in generation 2 and generation 3 females according to generation 1 race and nativity status, Illinois

Generation 1 (maternal grandmothers)	Generation 2 (1956–1975, mothers)			Generation 3 (1989–1991, daughters)		
	Mean birth weight (g)	1,500–2,499 g (%)	<1,500 g (%)	Mean birth weight (g)	1,500–2,499 g (%)	<1,500 g (%)
White						
US-born (n = 91,061)	3,309	5.5	0.2	3,374*	5.0†	0.8‡
European-born (n = 3,339)	3,347	4.2	—§	3,392*	4.5¶	0.6
African-American						
US-born (n = 31,699)	3,060	12.7	0.9	3,077*	12.5#	3.1**
African/Caribbean-born (n = 104)	3,249	6.7	—	3,192	9.6††	—

* $p < 0.001$, compares mean birth weight in generation 3 with that in generation 2 according to generation 1 race and nativity status.

Fig. 6.26 B

Panel A modified from David and Collins, 1997.

Birth Weight Differences by Race

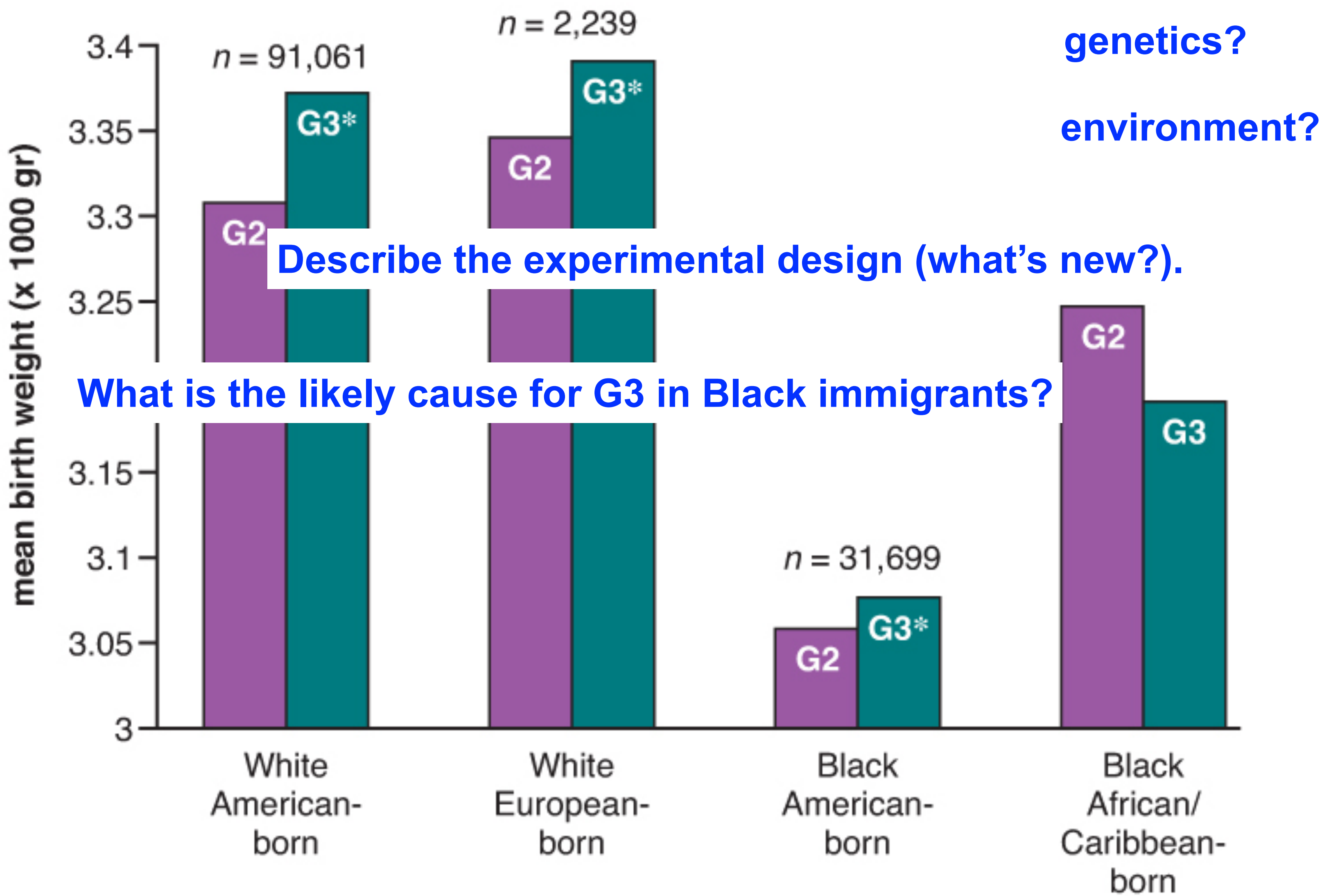
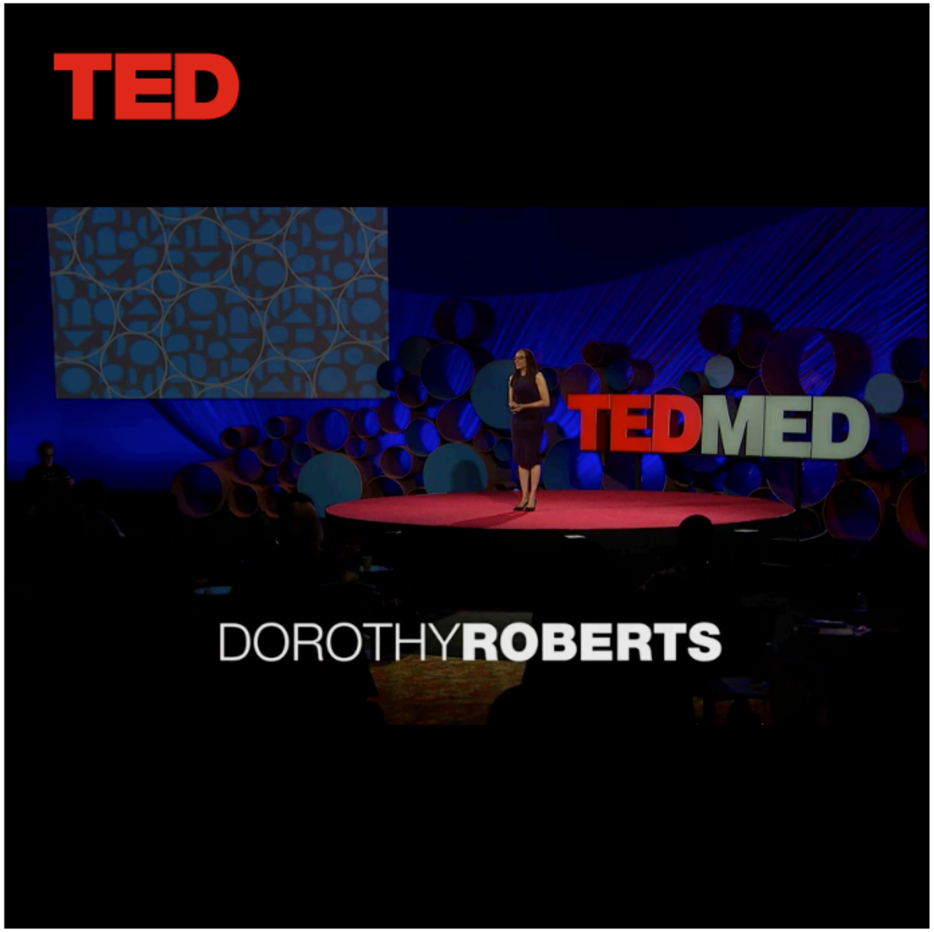


Fig. 6.26 B

Panel A modified from David and Collins, 1997.

Required Viewing for All Health Providers



The problem with race-based medicine, by Dorothy Roberts, JD. Closed captioning available.

https://www.ted.com/talks/dorothy_roberts_the_problem_with_race_based_medicine?language=en

New Drugs and Technologies

Ethnic Differences in Cardiovascular Drug Response

Potential Contribution of Pharmacogenetics

Julie A. Johnson, PharmD

In the early 1980s, clinical differences in response to the blood pressure (BP)–lowering effects of β-blockers and, to a lesser extent, diuretics were noted between ethnic groups. The most convincing evidence at that time came from a Veterans Affairs (VA) Cooperative Trial,[1] which, along with other smaller studies, suggested that whites (those of European ancestry) had a better antihypertensive response to β-blockers than blacks (those of African ancestry), whereas blacks had a slight better response to diuretics than whites. Shortly after the first angiotensin-converting enzyme (ACE) inhibitor was approved in the mid-1980s, it was also recognized that whites responded more favorably to ACE inhibitors than did blacks. Over time, these differences in response became well accepted, such that ethnicity began to be used in helping to guide selection of antihypertensive drug therapy.[2,3] Although the ethnic differences in response between β-blockers and ACE inhibitors in hypertension are perhaps the mostly widely recognized examples of ethnic differences

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Ethnic differences in the warfarin dose required for an international normalized ratio (INR) between 2 and 3 are well documented in the literature but do not appear to be widely appreciated by clinicians. For example, the anticoagulation consensus guidelines that relate specifically to warfarin do not mention the influence of ethnicity on the typical maintenance dose,[5] a fact that may result from trials conducted predominantly in white populations. Figure 1 depicts average warfarin dose requirements for Asians, Hispanics, whites, and blacks to maintain an INR of 2 to 3.[6] Although these data were derived from a relatively small sample, average daily doses of 3.4 mg in Asians, 5.1 mg in whites, and 6.1 mg in blacks are representative of the literature for these ethnic groups. Given that most dosing algorithms recommend initiating therapy at 5 mg daily, it is apparent from Figure 1 that this is a reasonable estimate of the starting dose in whites but

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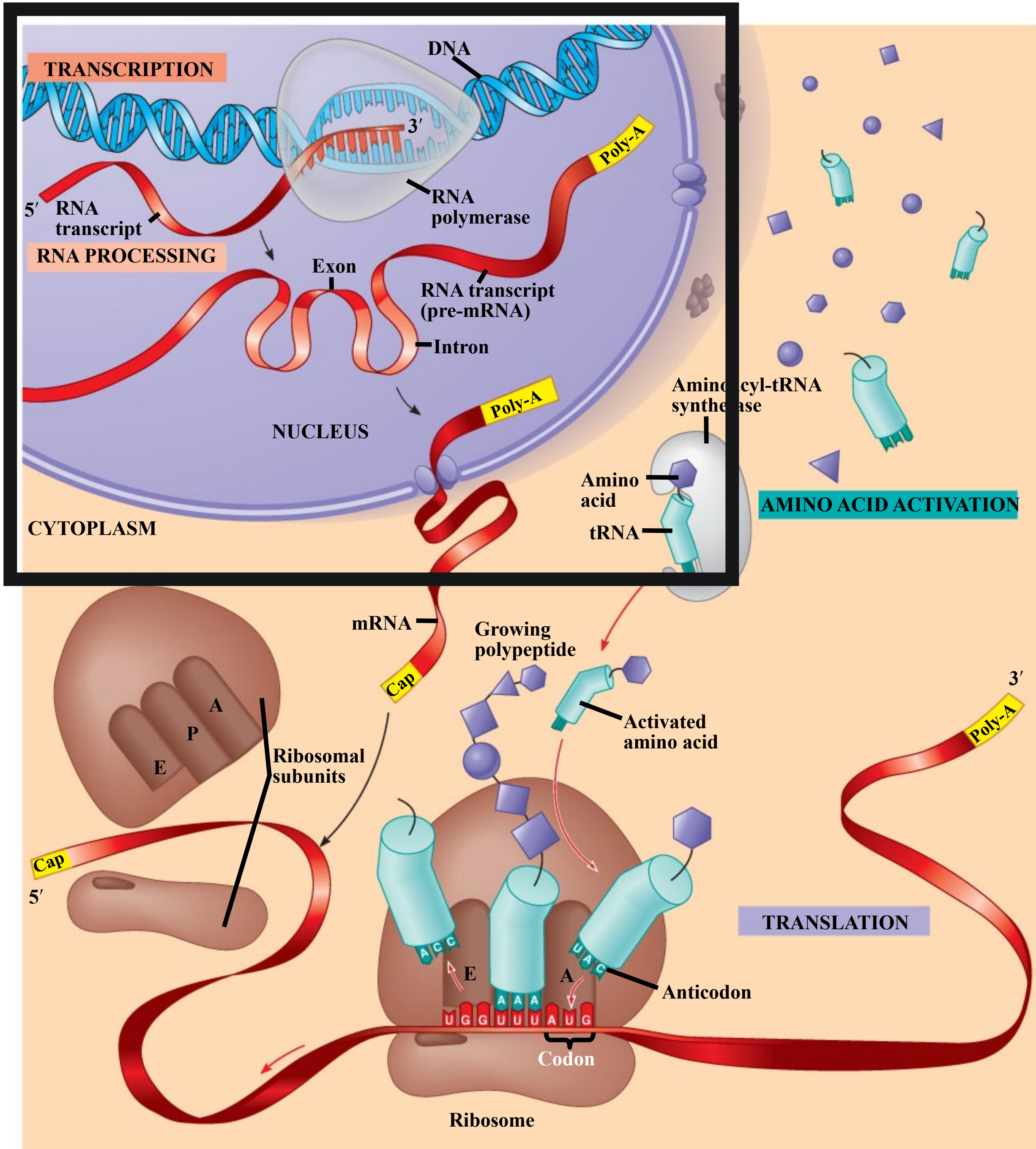
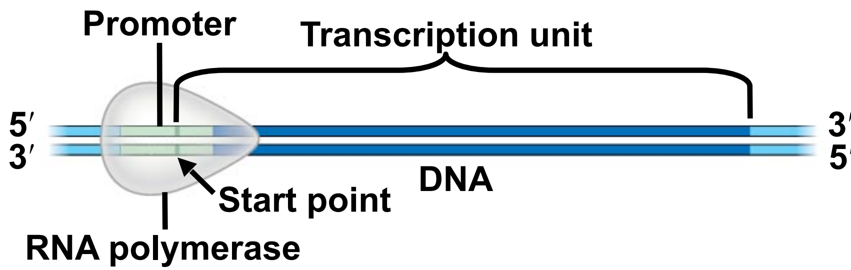
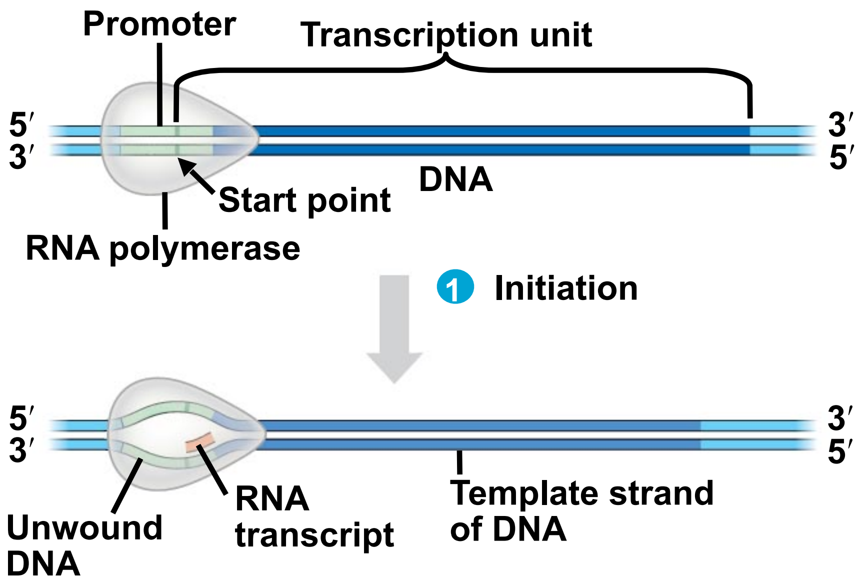
(*Circulation*. 2008;118:1383-1393.)

Transcription



- **What happens when a gene is transcribed?**


Promoter
Transcription unit
5′
3′
3′
5′
Start point
DNA
RNA polymerase


Promoter
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DNA
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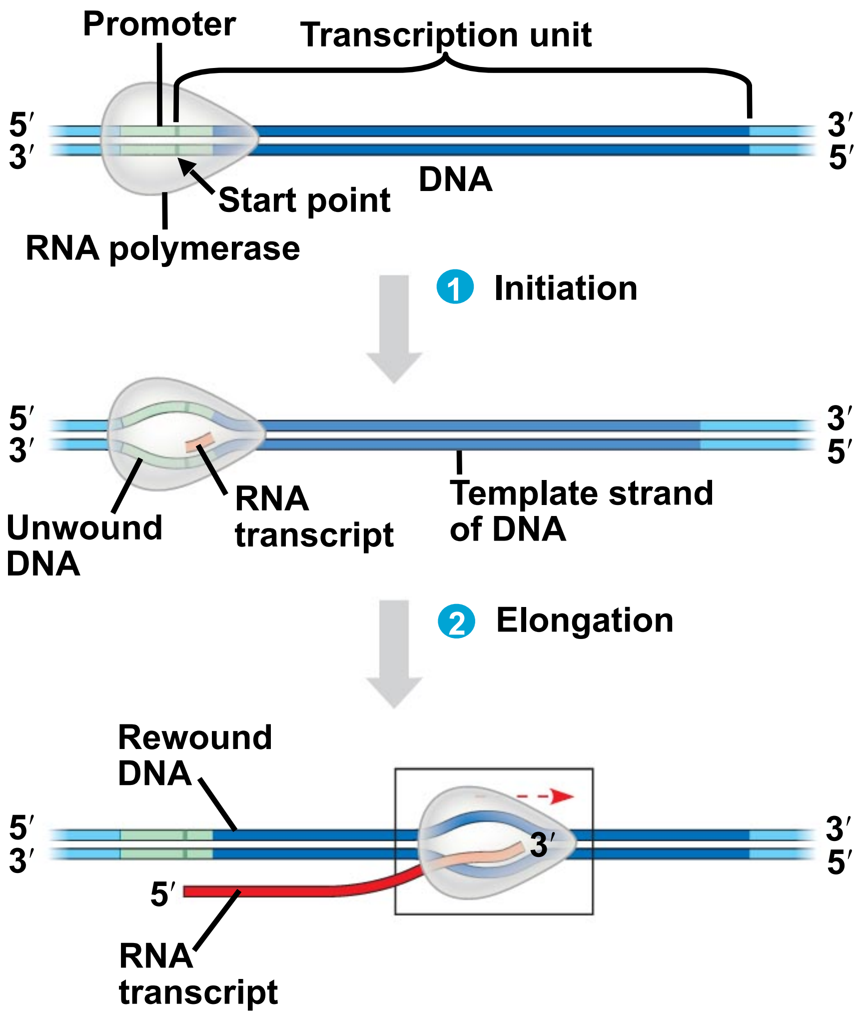
Unwound DNA
RNA transcript
Template strand of DNA


Promoter
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RNA polymerase
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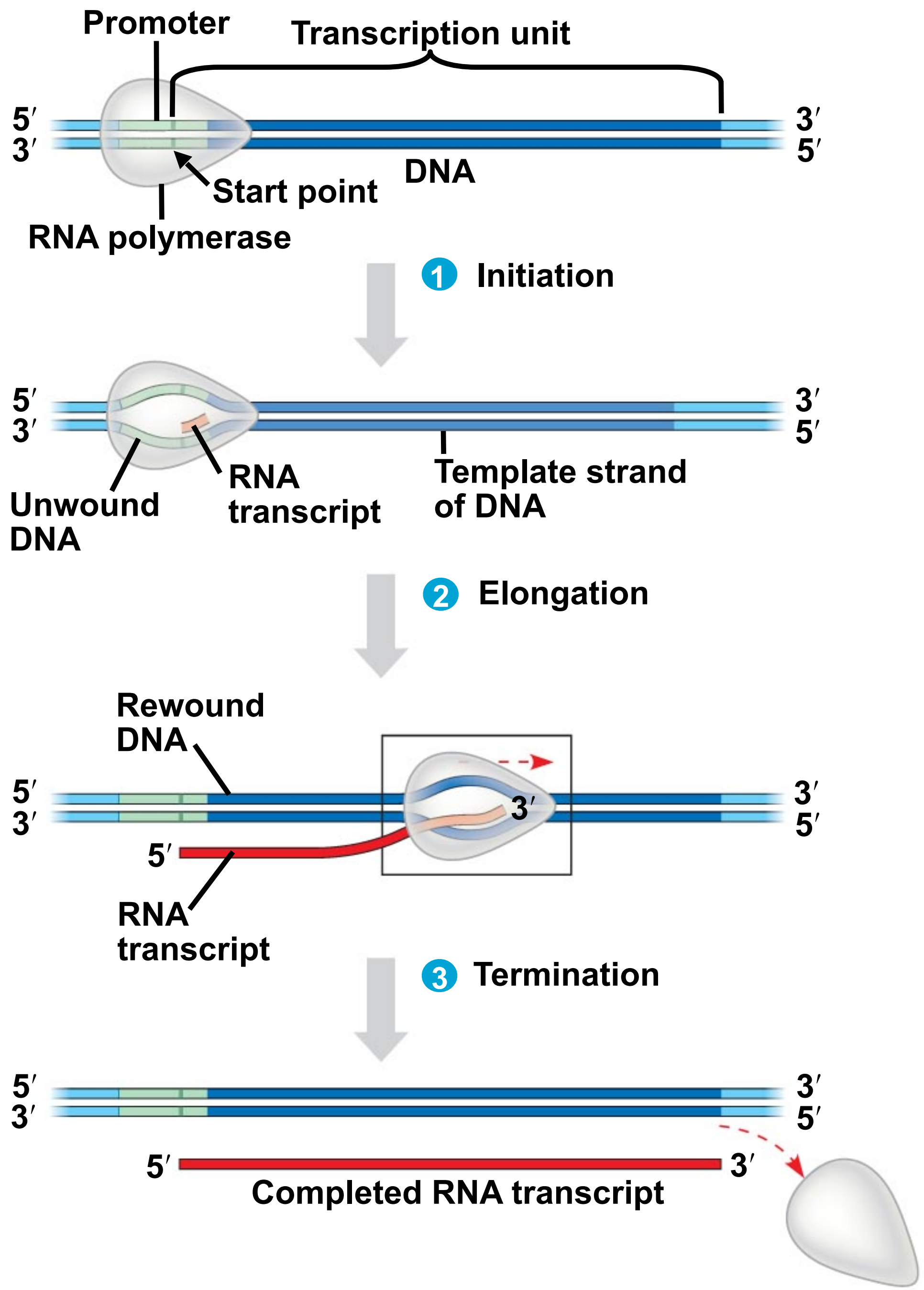
RNA transcript



Promoter
Transcription unit
5′
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Start point
DNA
RNA polymerase
1 Initiation
5′
3′
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Unwound DNA
RNA transcript
Template strand of DNA
2 Elongation
Rewound DNA
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RNA transcript
3 Termination
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Completed RNA transcript

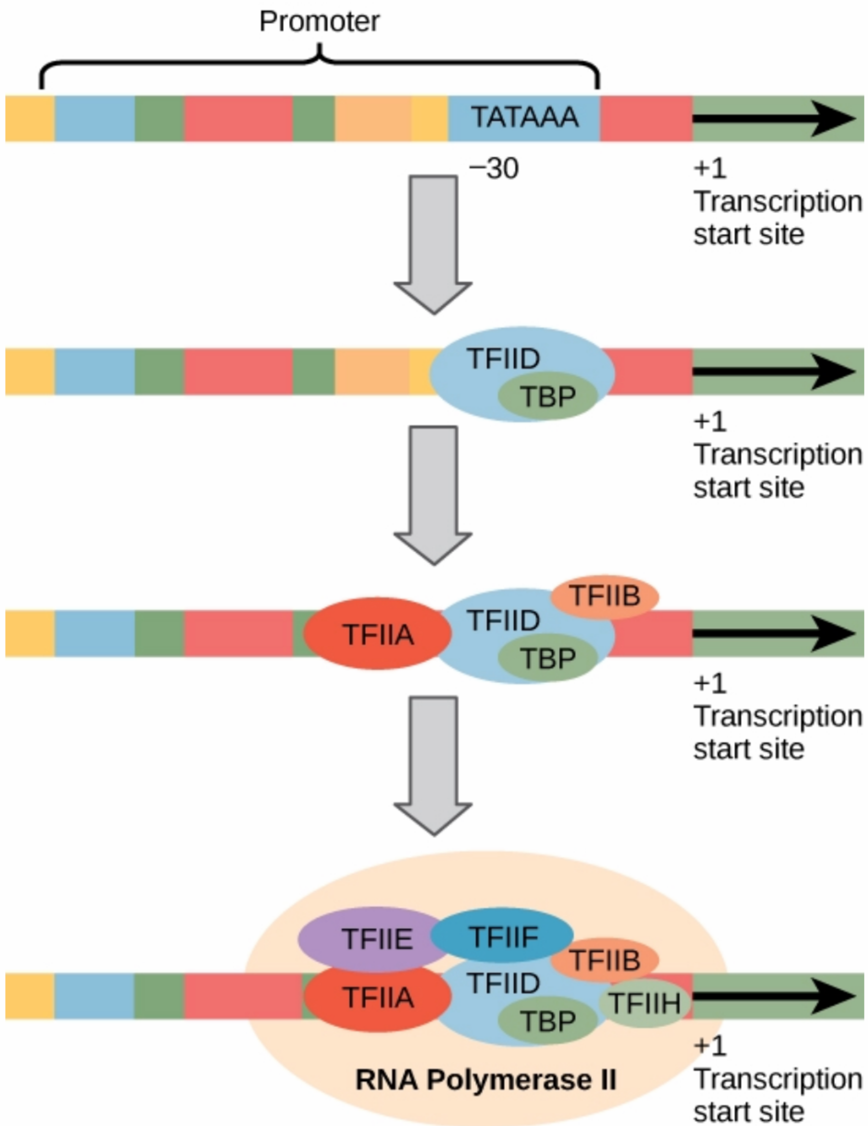

Figure 1: A generalized promoter of a gene transcribed by RNA polymerase II is shown. Transcription factors recognize the promoter. RNA polymerase II then binds and forms the transcription initiation complex.

New Drugs and Technologies

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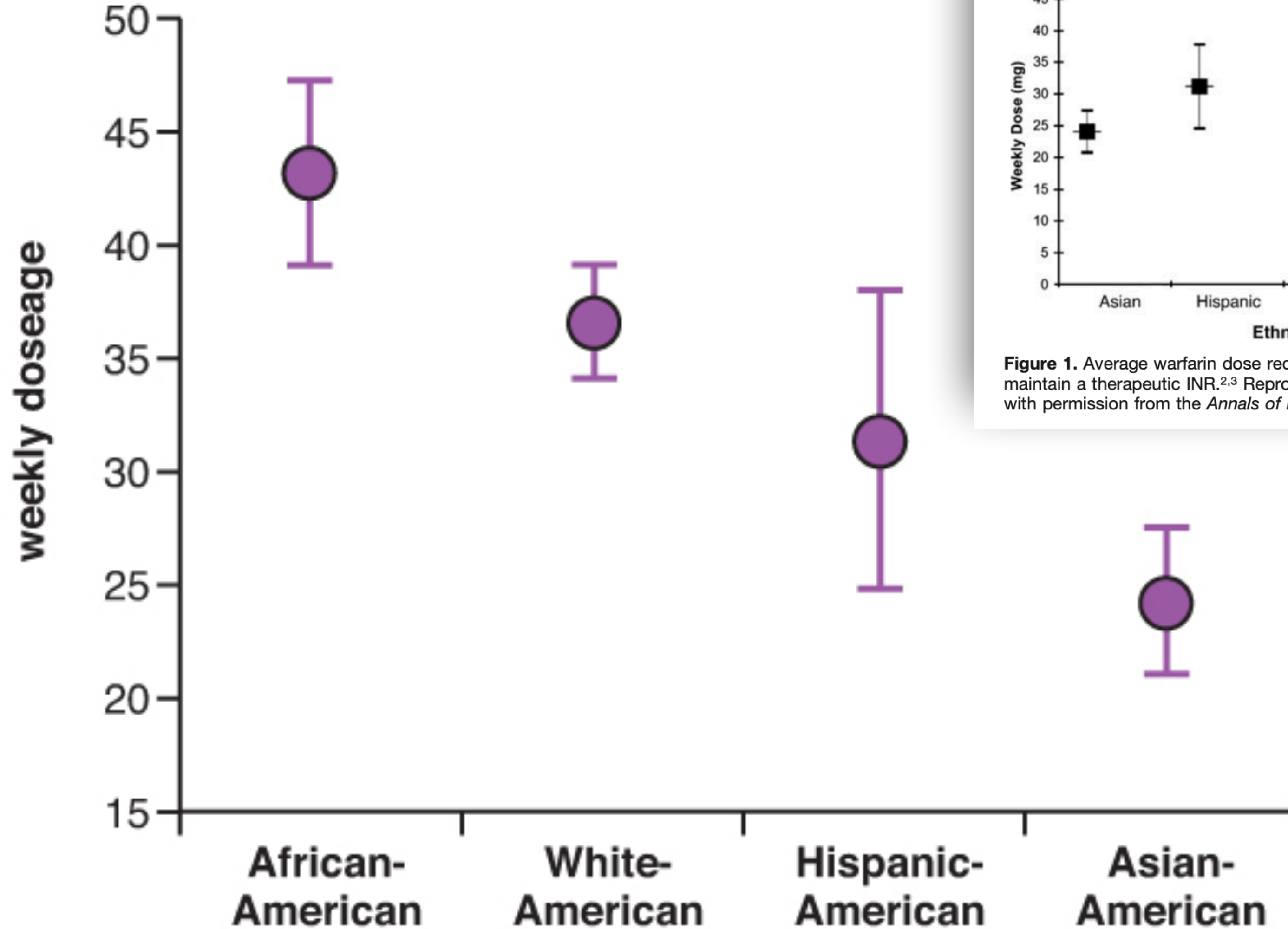
Warfarin Dosage by Race



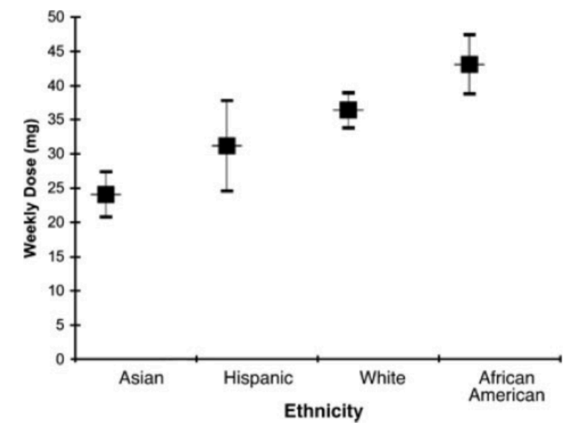
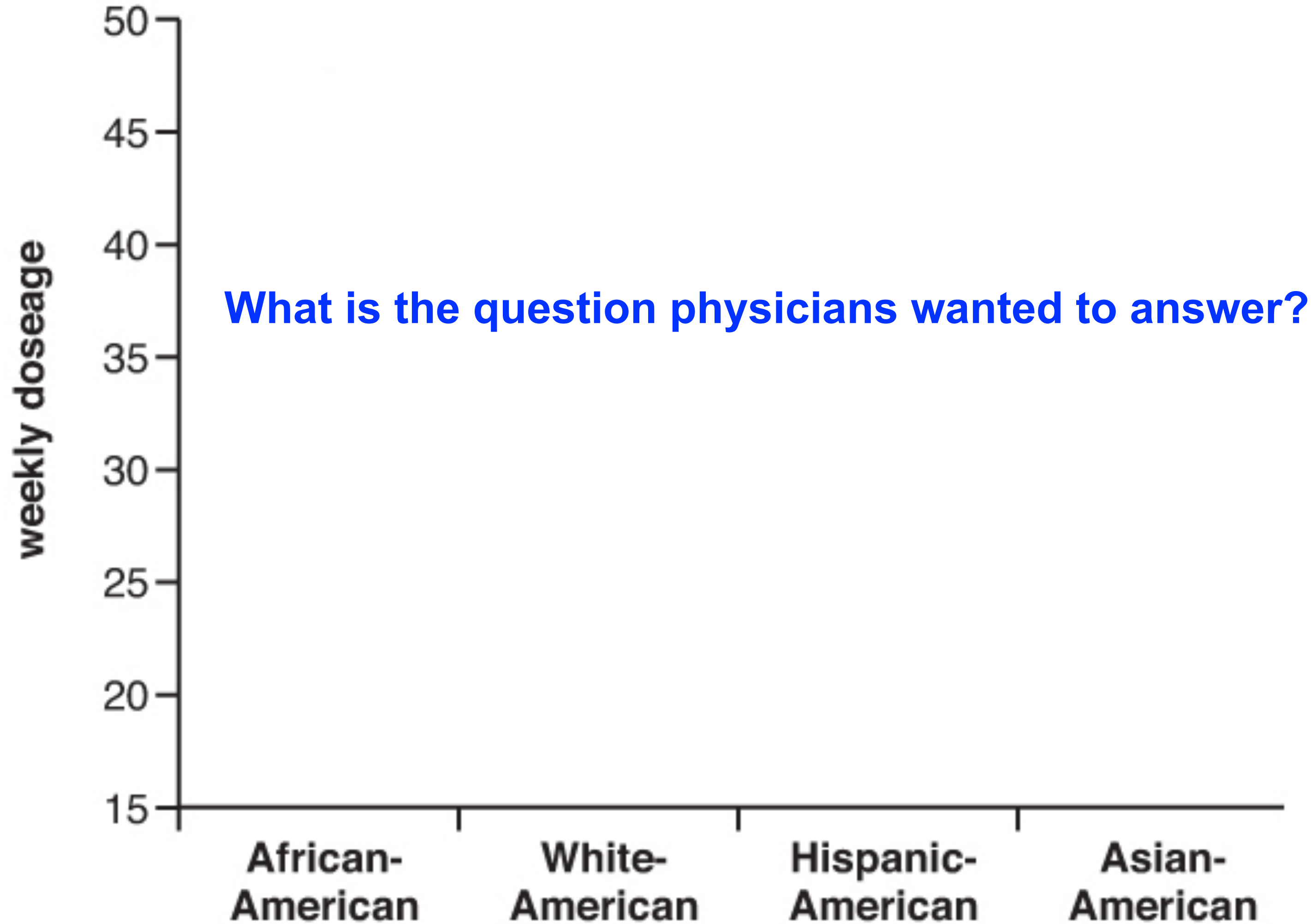


Figure 1. Average warfarin dose requirements, by ethnicity, to maintain a therapeutic INR.[2,3] Reproduced from Dang et al,[6] with permission from the *Annals of Pharmacotherpy*.

Fig. 6.27

Adapted from Dang *et al.*, 2005.

Warfarin Dosage by Race

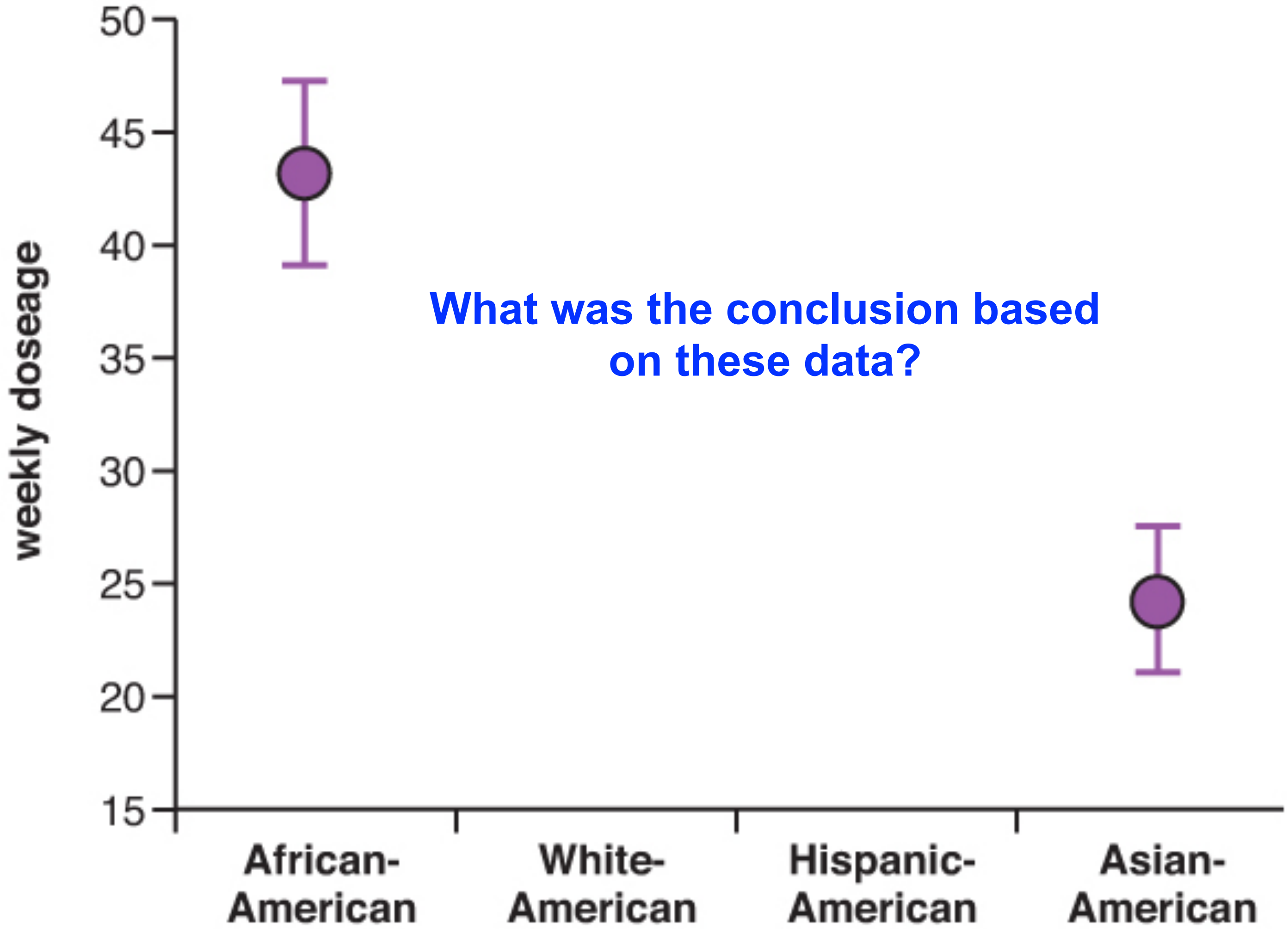


What is the question physicians wanted to answer?

Fig. 6.27

Adapted from Dang *et al.*, 2005.

Warfarin Dosage by Race

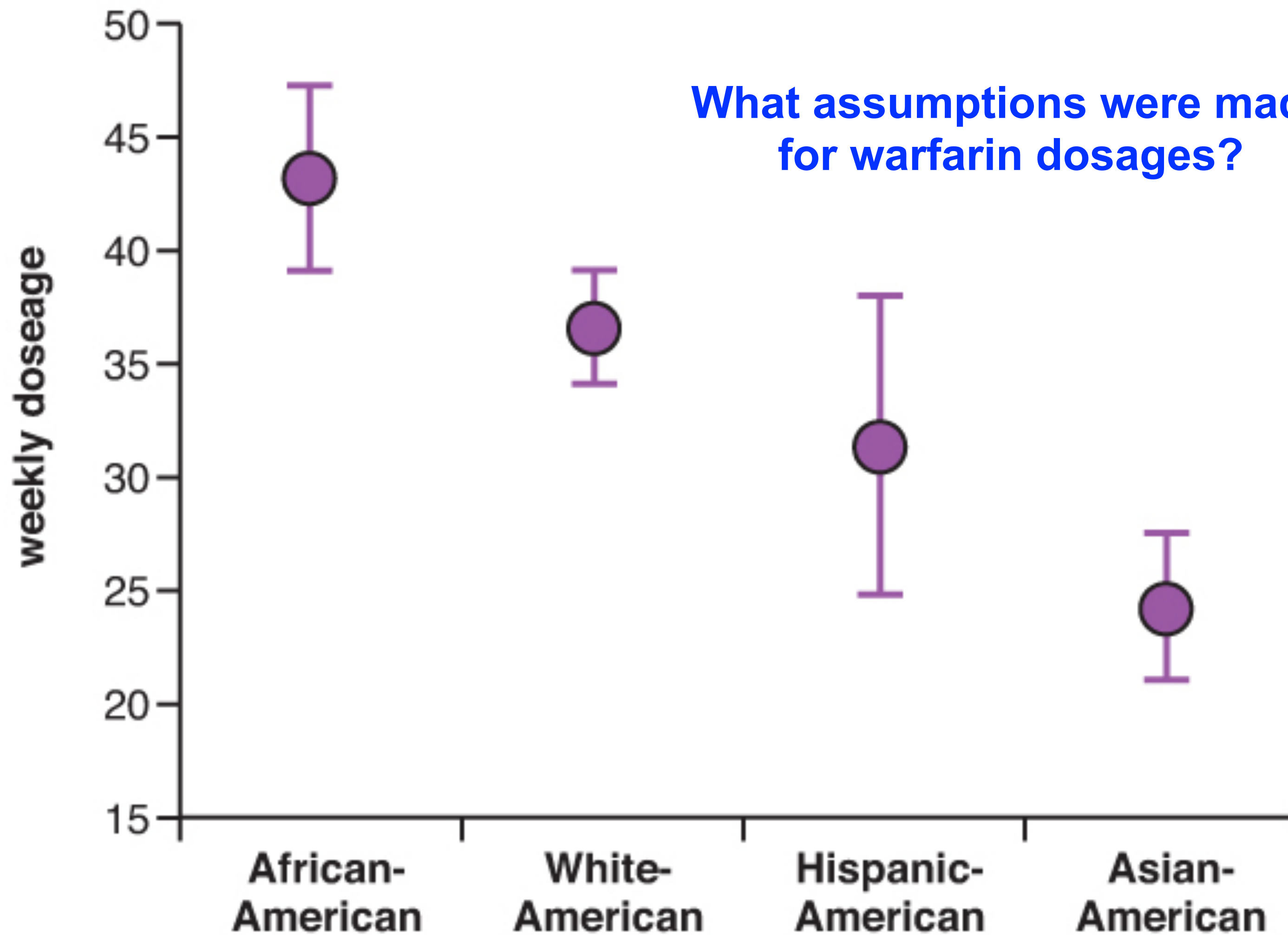


What was the conclusion based on these data?

Fig. 6.27

Adapted from Dang *et al.*, 2005.

Warfarin Dosage by Race



What assumptions were made for warfarin dosages?

Fig. 6.27

Adapted from Dang *et al.*, 2005.

Pathway Affected by Warfarin

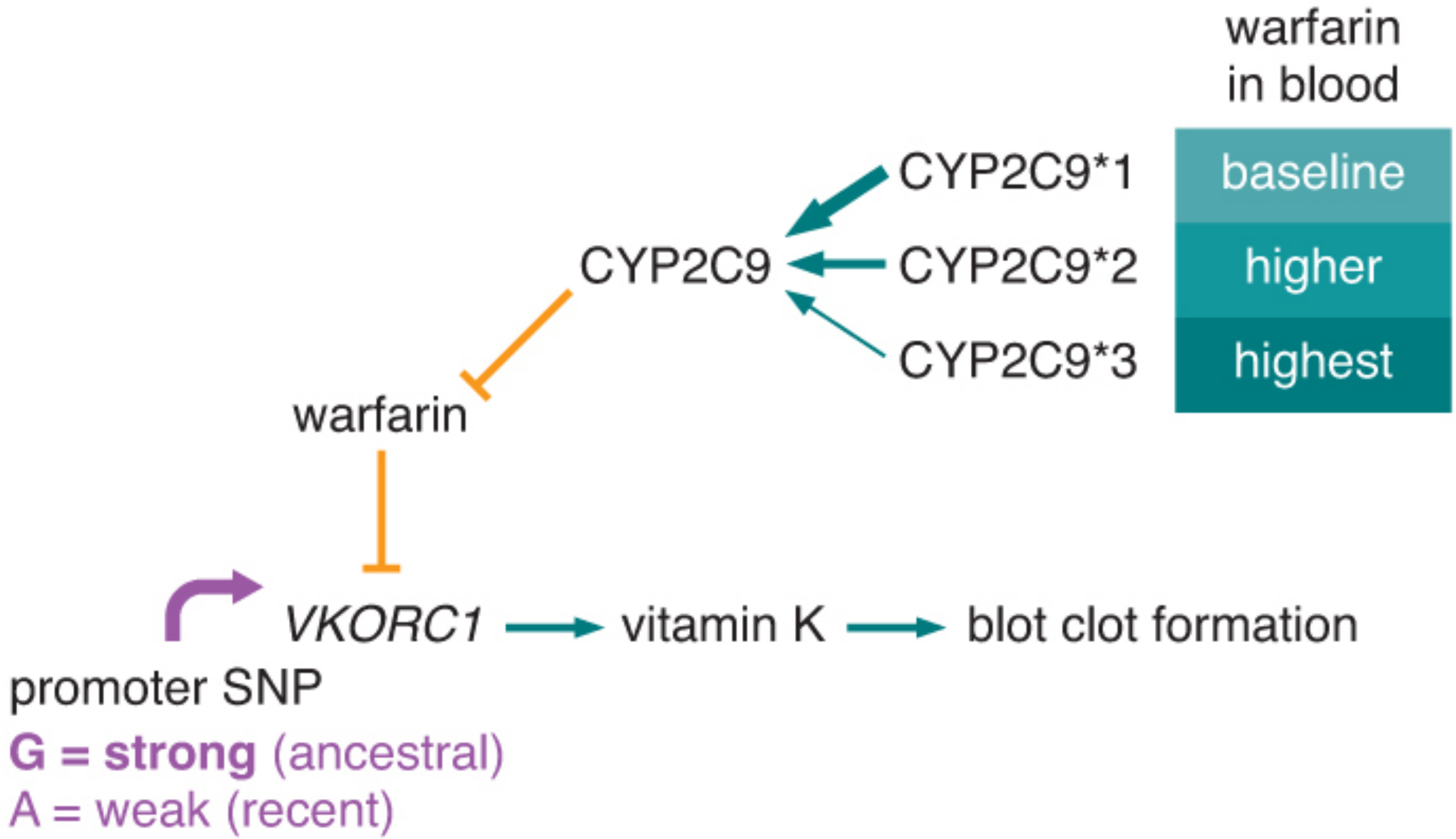


Fig. 6.28

Pathway Affected by Warfarin

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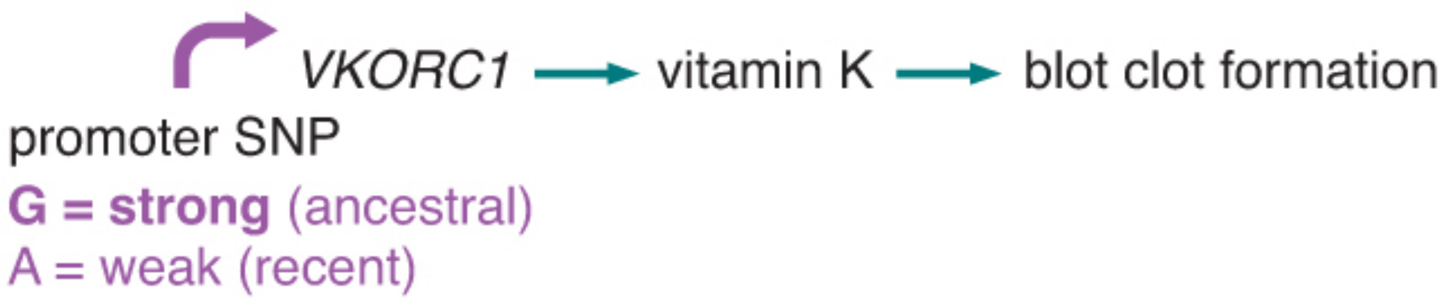
Pathway Affected by Warfarin



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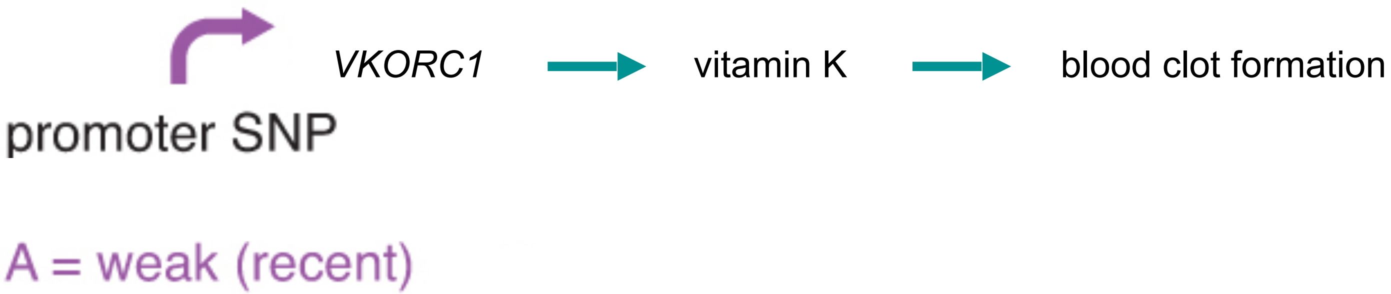

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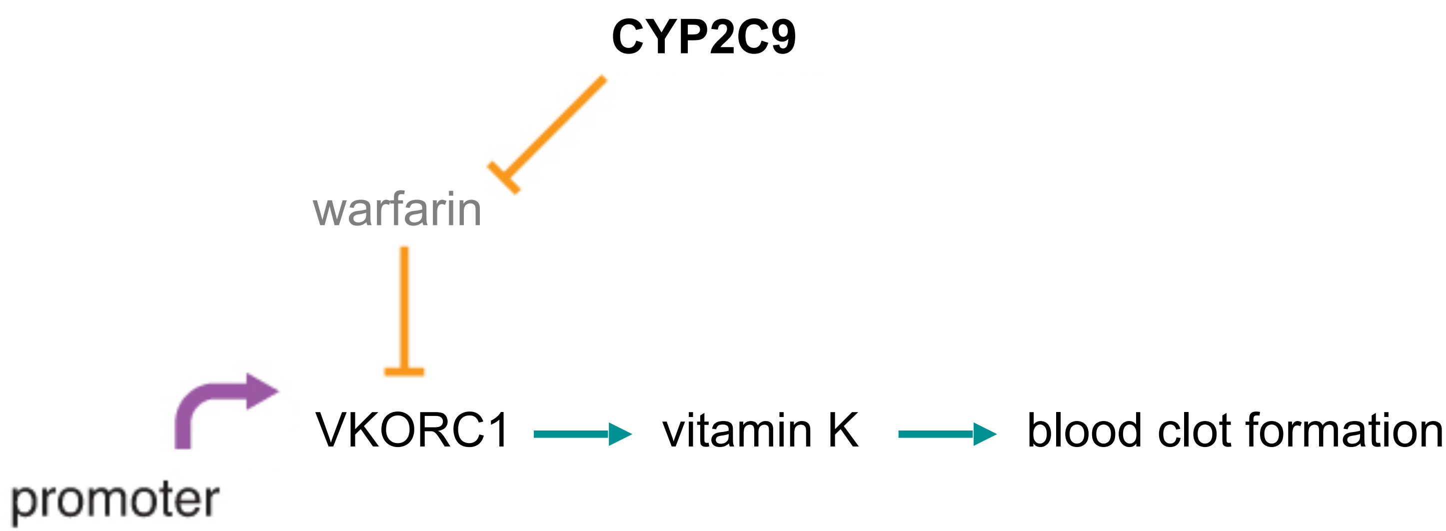

Fig. 6.28

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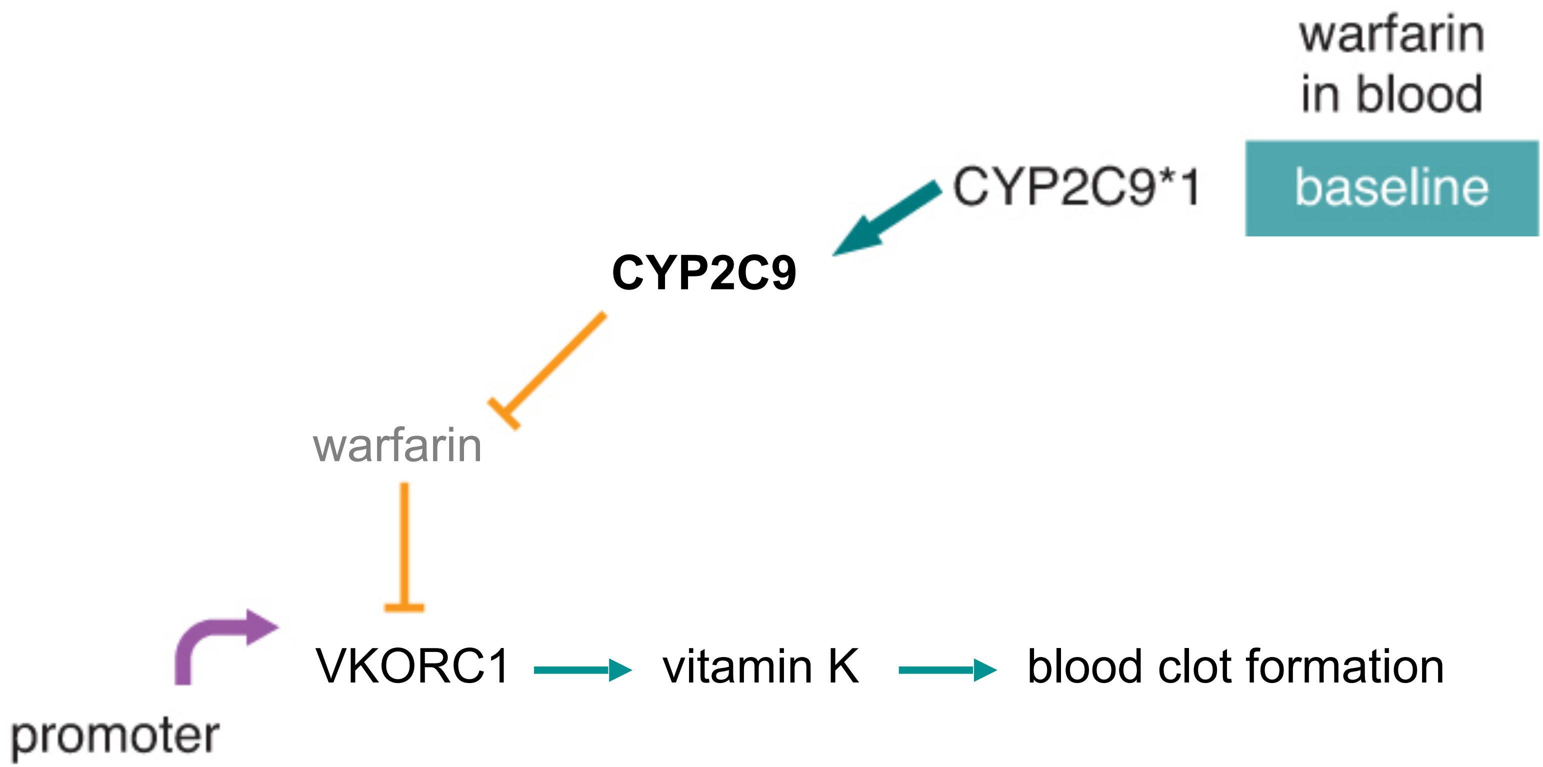
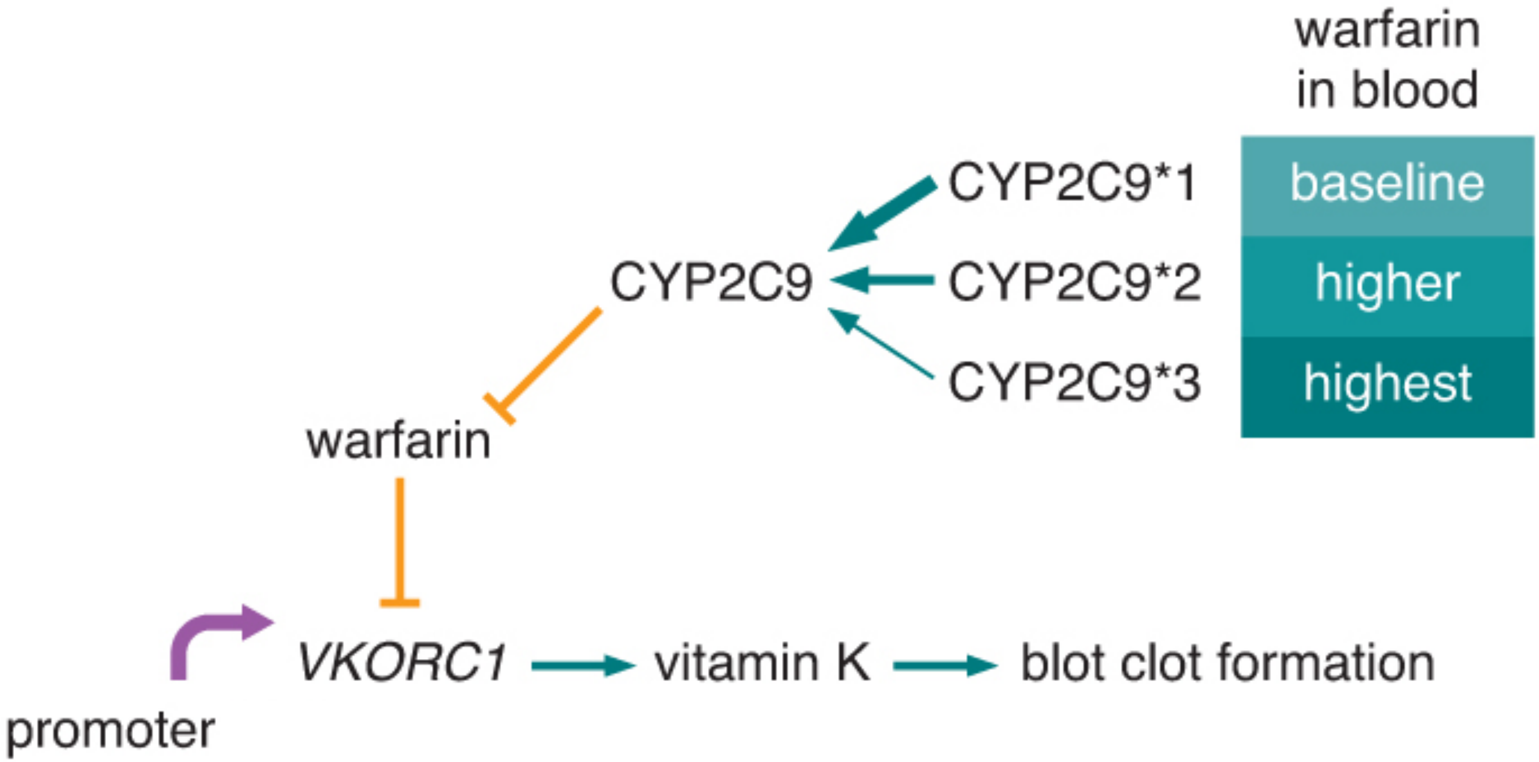


Fig. 6.28

Pathway Affected by Warfarin

CYP2C9 genotype influences warfarin blood levels



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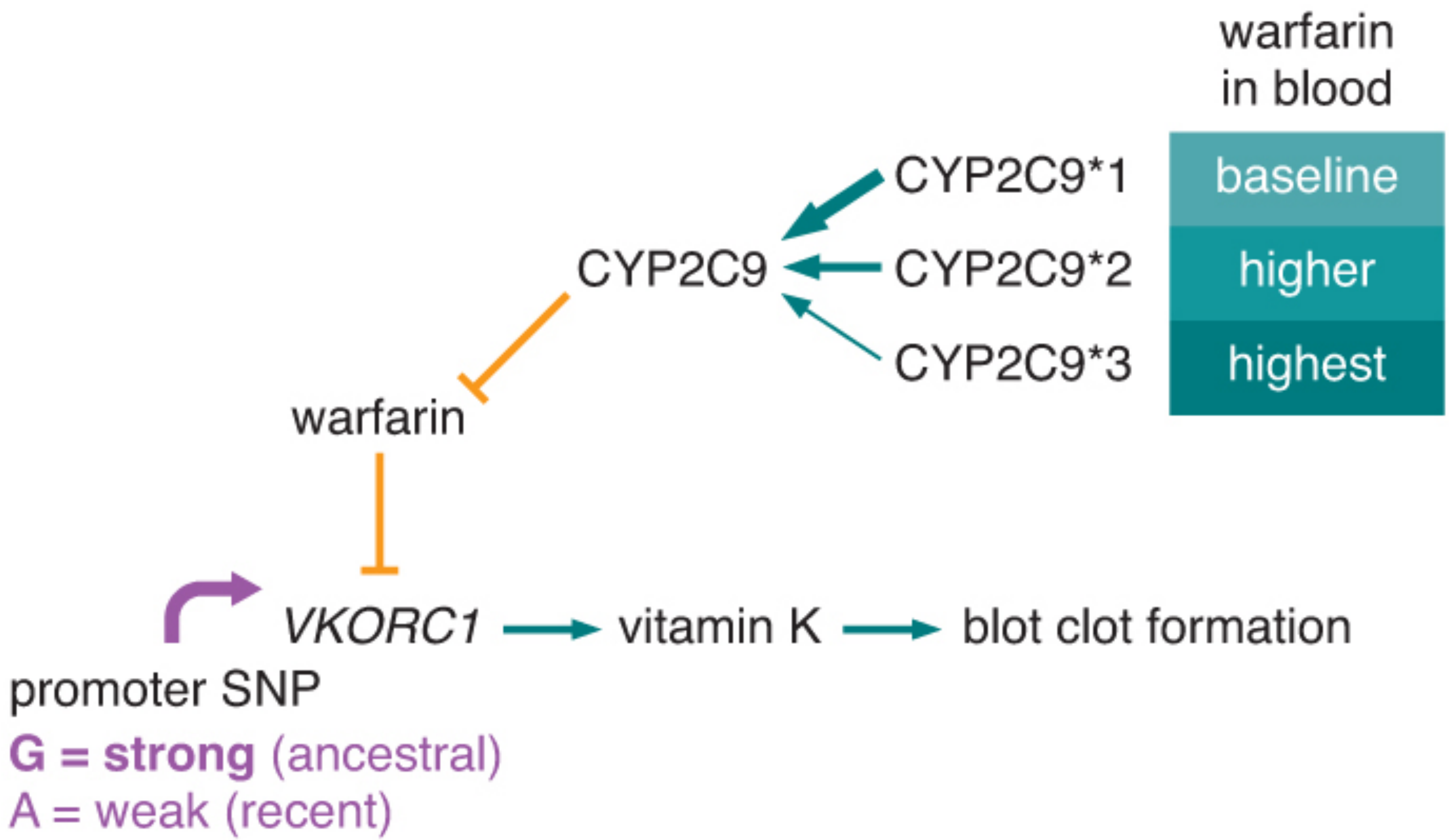

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New Drugs and Technologies

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Genotype Frequencies by Race

variants	Blacks	Whites	Asians
CYP2C9*2	rare	8-18%	rare
CYP2C9*3	1-2%	5-13%	2-5%
-1639 G→A	8-10%	35-45%	90-95%

Table 1. Ethnic Differences in Variant Allele Frequencies for Genes Important to Variable Warfarin Dose/Response (*CYP2C9* and *VKORC1*)

Variant	Whites	Blacks	Asians
CYP2C9*2	8% to 18%	Rare	Rare
CYP2C9*3	5% to 13%	1% to 2%	2% to 5%
Others†	Rare/absent	2% to 4%	Rare/absent
VKORC1 variant‡	35% to 45%	8% to 10%	90% to 95%

Data derived from various sources.[14,16–18]

Table 6.3

Genotype Frequencies by Race

Do allele frequencies correlate with dosage data?

variants	Blacks	Whites	Asians
CYP2C9*2	rare	8-18%	rare
CYP2C9*3	1-2%	5-13%	2-5%
-1639 G→A			

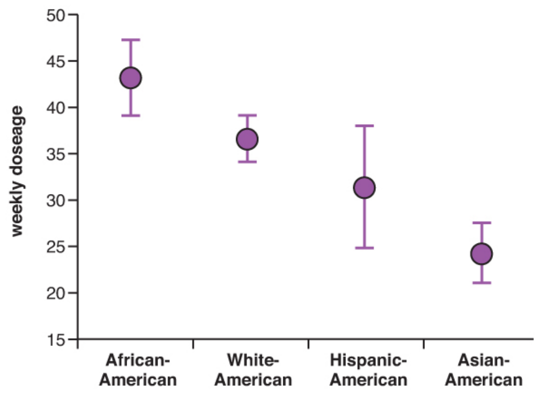


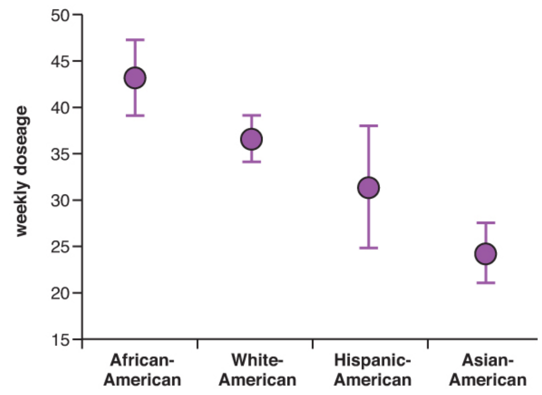
Table 6.3

data from Johnson, 2008.

Genotype Frequencies by Race

Which variant correlates best with warfarin dosage?

variants	Blacks	Whites	Asians
CYP2C9*2	rare	8-18%	rare
CYP2C9*3	1-2%	5-13%	2-5%
-1639 G→A	8-10%	35-45%	90-95%



data from Johnson, 2008.

Table 6.3

Genotype Frequencies by Race

What information should be used to determined warfarin dosage?

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CYP2C9*3	1-2%	5-13%	2-5%
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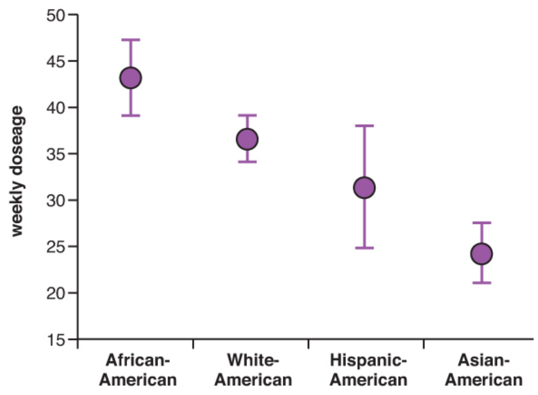

Table 6.3

data from Johnson, 2008.

Warfarin Doses by Genotype

Effective Weekly Doses				
SNP genotypes	Blacks	Whites	Hispanics	Asians
GG	39.9 mg	42.7 mg	43.1 mg	42.7 mg
GA	31.5 mg	31.5 mg	32.0 mg	31.7 mg
AA	21.7 mg	21.0 mg	20.8 mg	19.6 mg

Table 6.4

Warfarin Doses by Genotype

Does "race" OR promoter SNP correlate with effective dosage?

Effective Weekly Doses				
SNP genotypes	**Blacks**	**Whites**	**Hispanics**	**Asians**
GG	39.9 mg	42.7 mg	43.1 mg	42.7 mg
GA				
AA				

Table 6.4

Warfarin Doses by Genotype

Does "race" OR promoter SNP correlate with effective dosage?

Effective Weekly Doses				
SNP genotypes	**Blacks**	**Whites**	**Hispanics**	**Asians**
GG				
GA				
AA	21.7 mg	21.0 mg	20.8 mg	19.6 mg

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Warfarin Doses by Genotype

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Effective Weekly Doses				
SNP genotypes	**Blacks**	**Whites**	**Hispanics**	**Asians**
GG	39.9 mg	42.7 mg	43.1 mg	42.7 mg
GA	31.5 mg	31.5 mg	32.0 mg	31.7 mg
AA	21.7 mg	21.0 mg	20.8 mg	19.6 mg

Table 6.4

Genotype Frequencies by Race

What information should be used to determined warfarin dosage?

variants
CYP2C9*2
CYP2C9*3
-1639 G→A

Effective Weekly Doses				
SNP genotypes	Blacks	Whites	Hispanics	Asians
GG	39.9 mg	42.7 mg	43.1 mg	42.7 mg
GA	31.5 mg	31.5 mg	32.0 mg	31.7 mg
AA	21.7 mg	21.0 mg	20.8 mg	19.6 mg

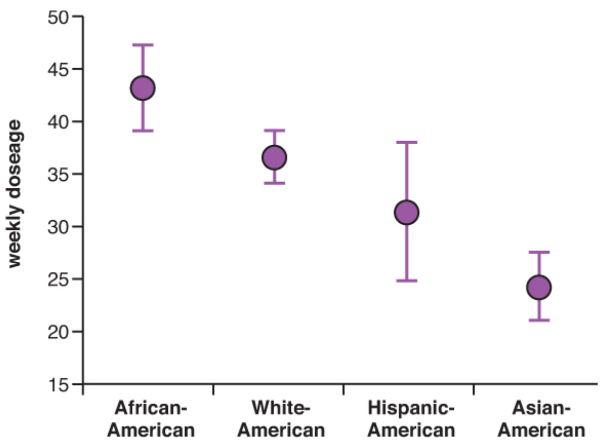

Table 6.3

data from Johnson, 2008.