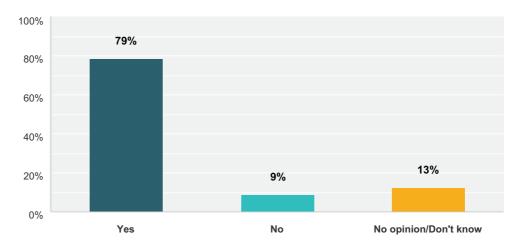
Q1 We assume that 3 major categories of allele function are needed for TPMT and DPYD. Do you agree (yes or no)? If no, please indicate how many you think are needed and why:

Answered: 56 Skipped: 2

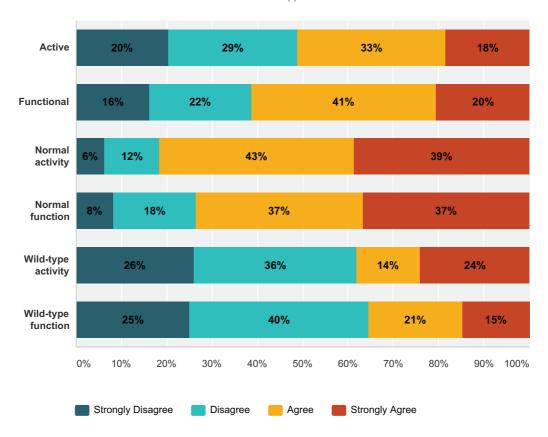


Answer Choices	Responses	
Yes	79%	44.00
No	9%	5.00
No opinion/Don't know	13%	7.00
Total		56

#	If No, please indicate how many you think are needed and why:	Date
1	Need an unknown allele function	2/20/2015 4:33 PM
2	Possibly 4 to include UM due to some literature suggesting increased activity associated with methylated products leading to clinical presentation. Although rare, it may be pertinent with advancement of technology and new SNPs?	2/19/2015 2:41 PM
3	Though I wonder if having a placeholder for increased function would always be useful.	2/19/2015 2:32 PM
4	Four, should include "unknown".	2/3/2015 10:27 AM
5	Unknown function alleles, particularly for novel variants identified by WGS/WES	2/3/2015 10:25 AM
6	4; need 'unknown'	2/2/2015 12:41 PM

Q2 Describe your degree of acceptance of the following terms to describe the allele function for a TPMT or DPYD allele with high/normal function/activity (e.g., TPMT*1 or DPYD*1):

Answered: 57 Skipped: 1

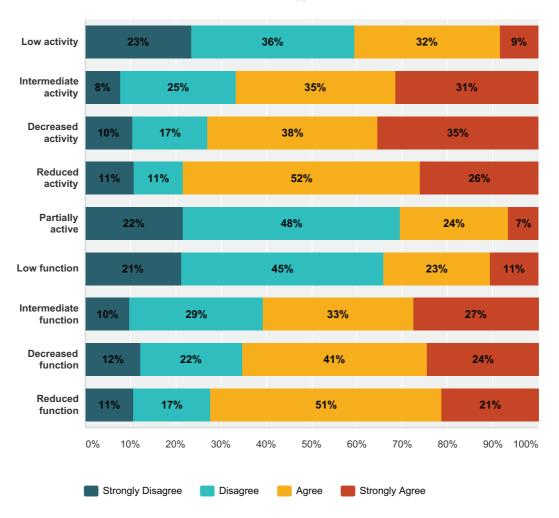


	Strongly Disagree	Disagree	Agree	Strongly Agree	Total	Weighted Average
Active	20%	29%	33%	18%		
	10.00	14.00	16.00	9.00	49	2.49
Functional	16%	22%	41%	20%		
	8.00	11.00	20.00	10.00	49	2.65
Normal activity	6%	12%	43%	39%		
	3.00	6.00	21.00	19.00	49	3.14
Normal function	8%	18%	37%	37%		
	4.00	9.00	18.00	18.00	49	3.02
Wild-type activity	26%	36%	14%	24%		
	13.00	18.00	7.00	12.00	50	2.36
Wild-type function	25%	40%	21%	15%		
	12.00	19.00	10.00	7.00	48	2.25

#	Other please specifiy	Date
1	Reference activity	2/20/2015 4:33 PM

2	normal enzyme activity	2/16/2015 8:03 AM
3	don't know	2/11/2015 12:25 PM

Q3 Describe your degree of acceptance of the following terms to describe the allele function for a TPMT or DPYD allele with medium/some function/activity (e.g., TPMT*8 or DPYD*3):

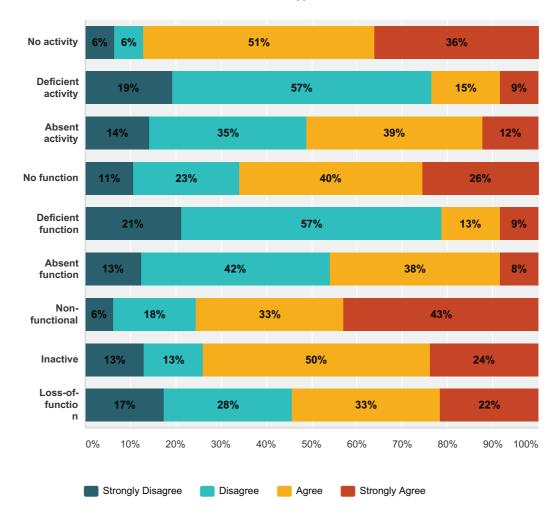


	Strongly Disagree	Disagree	Agree	Strongly Agree	Total	Weighted Average
Low activity	23%	36%	32%	9%		
	11.00	17.00	15.00	4.00	47	2.26
Intermediate activity	8%	25%	35%	31%		
	4.00	13.00	18.00	16.00	51	2.90
Decreased activity	10%	17%	38%	35%		
	5.00	8.00	18.00	17.00	48	2.98
Reduced activity	11%	11%	52%	26%		
	5.00	5.00	24.00	12.00	46	2.93
Partially active	22%	48%	24%	7%		
	10.00	22.00	11.00	3.00	46	2.15

Low function	21%	45%	23%	11%		
	10.00	21.00	11.00	5.00	47	2.23
Intermediate function	10%	29%	33%	27%		
	5.00	15.00	17.00	14.00	51	2.78
Decreased function	12%	22%	41%	24%		
	6.00	11.00	20.00	12.00	49	2.78
Reduced function	11%	17%	51%	21%		
	5.00	8.00	24.00	10.00	47	2.83

#	Other (please specify)	Date
1	intermediate/lower than normal enzyme activity	2/16/2015 8:03 AM
2	don't know	2/11/2015 12:25 PM

Q4 Describe your degree of acceptance of the following terms to describe the allele function for a TPMT or DPYD allele with no function/activity (e.g., TPMT*2 or DPYD*2A):



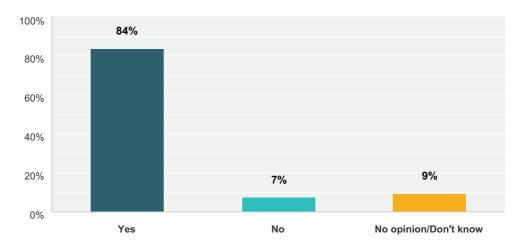
	Strongly Disagree	Disagree	Agree	Strongly Agree	Total	Weighted Average
No activity	6%	6%	51%	36%		
	3.00	3.00	24.00	17.00	47	3.17
Deficient activity	19%	57%	15%	9%		
	9.00	27.00	7.00	4.00	47	2.13
Absent activity	14%	35%	39%	12%		
	7.00	17.00	19.00	6.00	49	2.49
No function	11%	23%	40%	26%		
	5.00	11.00	19.00	12.00	47	2.81
Deficient function	21%	57%	13%	9%		
	10.00	27.00	6.00	4.00	47	2.09
Absent function	13%	42%	38%	8%		
	6.00	20.00	18.00	4.00	48	2.42

Non-functional	6%	18%	33%	43%		
	3.00	9.00	16.00	21.00	49	3.12
Inactive	13%	13%	50%	24%		
	6.00	6.00	23.00	11.00	46	2.85
Loss-of-function	17%	28%	33%	22%		
	8.00	13.00	15.00	10.00	46	2.59

#	Other (please specify)	Date
1	For this category, we need to differentiate between that caused by inactive protein and that caused by low protein level (but what is there has "normal" activity). The protein's phenotype is not necessarily the cellular/organismal phenotype.	2/20/2015 4:37 PM
2	undetectable activity	2/17/2015 5:33 PM
3	absent enzyme activity	2/16/2015 8:03 AM
4	don't know	2/11/2015 12:25 PM

Q5 We assume that 3 major categories of phenotypes are needed for TPMT or DPYD. Do you agree (yes or no)? If no, please indicate how many you think are needed and why:

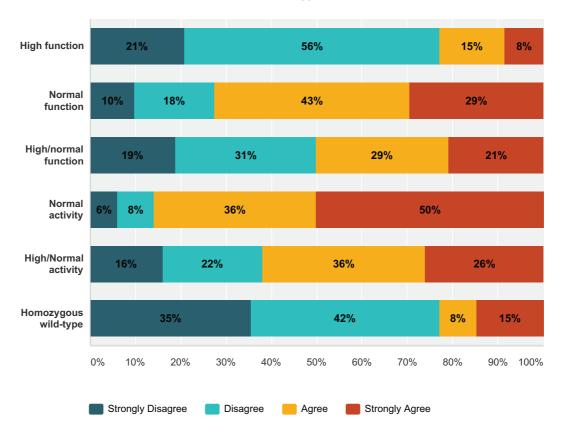
Answered: 55 Skipped: 3



Answer Choices	Responses	
Yes	84%	46.00
No	7%	4.00
No opinion/Don't know	9%	5.00
Total		55

#	If no, please indicate how many you think are needed and why:	Date
1	need an unknown phenotype	2/20/2015 4:37 PM
2	Possibly 4 to include UM due to some literature suggesting increased activity associated with methylated products leading to clinical presentation. Although rare, it may be pertinent with advancement of technology and new SNPs?	2/19/2015 2:44 PM
3	Should include Unknown.	2/3/2015 10:30 AM
4	category (ies) for diplotypes with alleles of unknown function	2/2/2015 12:41 PM

Q6 Describe your degree of acceptance of the following terms to describe the presumed phenotype for TPMT in an individual with high/normal TPMT or DPYD function/activity (e.g., TPMT*1/*1 or DPYD*1/*1):

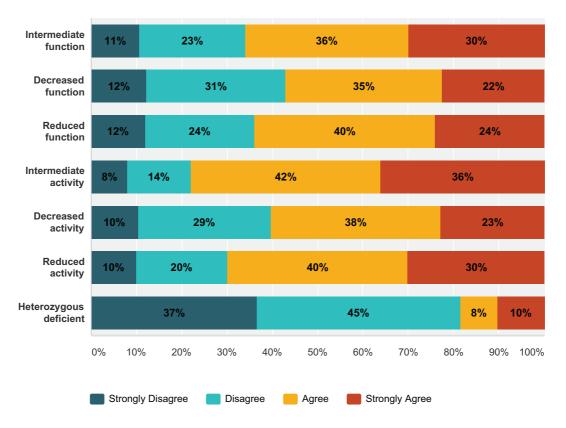


	Strongly Disagree	Disagree	Agree	Strongly Agree	Total	Weighted Average
High function	21%	56%	15%	8%		
	10.00	27.00	7.00	4.00	48	2.10
Normal function	10%	18%	43%	29%		
	5.00	9.00	22.00	15.00	51	2.9
High/normal function	19%	31%	29%	21%		
	9.00	15.00	14.00	10.00	48	2.5
Normal activity	6%	8%	36%	50%		
	3.00	4.00	18.00	25.00	50	3.3
High/Normal activity	16%	22%	36%	26%		
	8.00	11.00	18.00	13.00	50	2.7
Homozygous wild-type	35%	42%	8%	15%		
	17.00	20.00	4.00	7.00	48	2.0

#	Other (please specify)	Date

1	Reference function	2/20/2015 4:37 PM
2	normal metabolizer	2/16/2015 8:04 AM
3	don't know	2/11/2015 12:26 PM

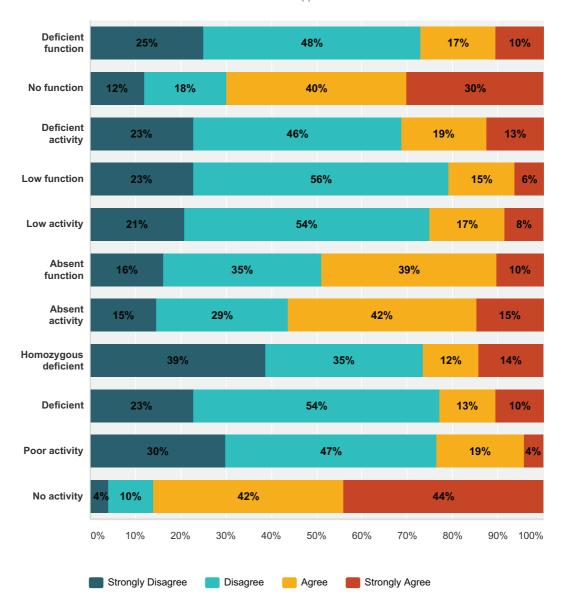
Q7 Describe your degree of acceptance of the following terms to describe the presumed phenotype for TPMT or DPYD in an individual with medium/some function/activity (e.g., TPMT*1/*3 or DPYD*1/*2A)):



	Strongly Disagree	Disagree	Agree	Strongly Agree	Total	Weighted Average
Intermediate function	11%	23%	36%	30%		
	5.00	11.00	17.00	14.00	47	2.85
Decreased function	12%	31%	35%	22%		
	6.00	15.00	17.00	11.00	49	2.67
Reduced function	12%	24%	40%	24%		
	6.00	12.00	20.00	12.00	50	2.76
Intermediate activity	8%	14%	42%	36%		
	4.00	7.00	21.00	18.00	50	3.06
Decreased activity	10%	29%	38%	23%		
	5.00	14.00	18.00	11.00	48	2.73
Reduced activity	10%	20%	40%	30%		
	5.00	10.00	20.00	15.00	50	2.90
Heterozygous deficient	37%	45%	8%	10%		
	18.00	22.00	4.00	5.00	49	1.92

#	Other (please specify)	Date
1	intermediate metabolizer	2/16/2015 8:04 AM
2	don't know	2/11/2015 12:26 PM

Q8 Describe your degree of acceptance of the following terms to describe the presumed phenotype for TPMT or DPYD in an individual with no function/activity (e.g., TPMT*3/*3 or DPYD*2A/*2A):



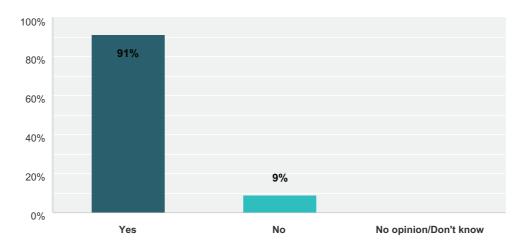
	Strongly Disagree	Disagree	Agree	Strongly Agree	Total	Weighted Average
Deficient function	25%	48%	17%	10%		
	12.00	23.00	8.00	5.00	48	2.13
No function	12%	18%	40%	30%		
	6.00	9.00	20.00	15.00	50	2.88
Deficient activity	23%	46%	19%	13%		
	11.00	22.00	9.00	6.00	48	2.21

Low function	23%	56%	15%	6%		
	11.00	27.00	7.00	3.00	48	2
Low activity	21%	54%	17%	8%		
	10.00	26.00	8.00	4.00	48	2
Absent function	16%	35%	39%	10%		
	8.00	17.00	19.00	5.00	49	
Absent activity	15%	29%	42%	15%		
	7.00	14.00	20.00	7.00	48	
Homozygous deficient	39%	35%	12%	14%		
	19.00	17.00	6.00	7.00	49	:
Deficient	23%	54%	13%	10%		
	11.00	26.00	6.00	5.00	48	
Poor activity	30%	47%	19%	4%		
	14.00	22.00	9.00	2.00	47	
No activity	4%	10%	42%	44%		
	2.00	5.00	21.00	22.00	50	;

#	Other (please specify)	Date
1	For this category, we need to differentiate between that caused by inactive protein and that caused by low protein level (but what is there has "normal" activity). The protein's phenotype is not necessarily the cellular/organismal phenotype.	2/20/2015 4:38 PM
2	Poor function	2/20/2015 4:37 PM
3	poor metabolizer	2/16/2015 8:04 AM
4	don't know	2/11/2015 12:26 PM

Q9 We assume that 4 or 5 major categories of allele function (depending on enzyme) are needed for CYP2C19, CYP2D6, and CYP2C9. Do you agree (yes or no)? If no, please indicate how many you think are needed and why:

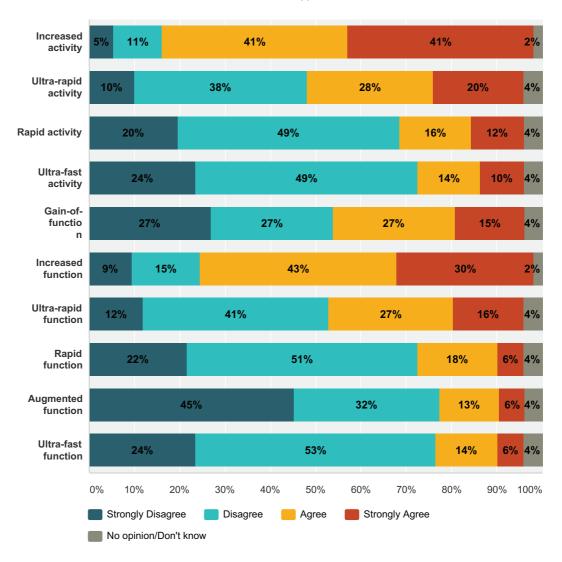
Answered: 56 Skipped: 2



Answer Choices	Responses	
Yes	91%	51.00
No	9%	5.00
No opinion/Don't know	0%	0.00
Total		56

#	If No, please indicate how many you think are needed and why:	Date
1	5 are needed because you need "unknown"	2/20/2015 4:44 PM
2	Again, I think this should be consitent across all PGx genes	2/19/2015 2:38 PM
3	For CYP2C9, only 3 categories are needed. There are no known alleles with increased or gain-of function.	2/9/2015 3:58 PM
4	I would favor 3 for 2C9. I don't think we should be cutting dosing recommendations for this CYP too finely. I would favor four for 2C19 and I am open to 4- 5 for 2D6 in view of all the activities described and since many of the substrates have CNS toxicity.	2/4/2015 12:53 PM
5	Stick with 4 categories here.	2/3/2015 12:58 PM
6	Unknown.	2/3/2015 10:34 AM
7	No convincing evidence of more than 3 phenotypes for CYP2C9	2/2/2015 12:46 PM
8	need categories for 'unknown'	2/2/2015 12:41 PM

Q10 Describe your degree of acceptance of the following terms to describe the allele function for a CYP2C19, CYP2D6, or CYP2C9 allele with high function/activity (e.g., CYP2C19*17):

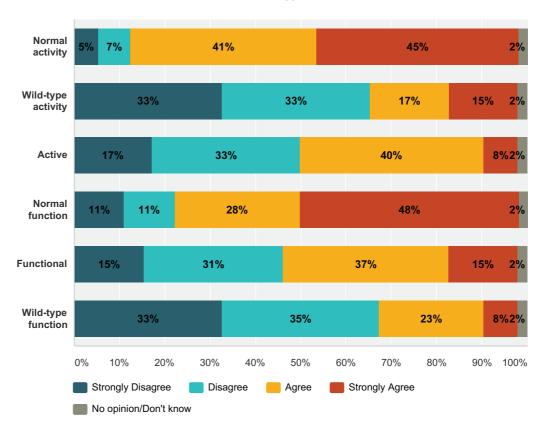


	Strongly Disagree	Disagree	Agree	Strongly Agree	No opinion/Don't know	Total	Weighted Average
Increased activity	5%	11%	41%	41%	2%		
	3.00	6.00	23.00	23.00	1.00	56	3.20
Ultra-rapid activity	10%	38%	28%	20%	4%		
	5.00	19.00	14.00	10.00	2.00	50	2.60
Rapid activity	20%	49%	16%	12%	4%		
	10.00	25.00	8.00	6.00	2.00	51	2.20
Ultra-fast activity	24%	49%	14%	10%	4%		
	12.00	25.00	7.00	5.00	2.00	51	2.10

Gain-of-function	27%	27%	27%	15%	4%		
	14.00	14.00	14.00	8.00	2.00	52	2.3
Increased function	9%	15%	43%	30%	2%		
	5.00	8.00	23.00	16.00	1.00	53	2.9
Ultra-rapid function	12%	41%	27%	16%	4%		
	6.00	21.00	14.00	8.00	2.00	51	2.
Rapid function	22%	51%	18%	6%	4%		
	11.00	26.00	9.00	3.00	2.00	51	2
Augmented function	45%	32%	13%	6%	4%		
	24.00	17.00	7.00	3.00	2.00	53	1.
Ultra-fast function	24%	53%	14%	6%	4%		
	12.00	27.00	7.00	3.00	2.00	51	2.

#	Other (please specify)	Date
1	higher than normal enzyme activity	2/16/2015 8:04 AM
2	don't know	2/11/2015 12:30 PM

Q11 Describe your degree of acceptance of the following terms to describe the allele function for a CYP2C19, CYP2D6 or CYP2C9 allele with normal function/activity (e.g., CYP2C19*1):

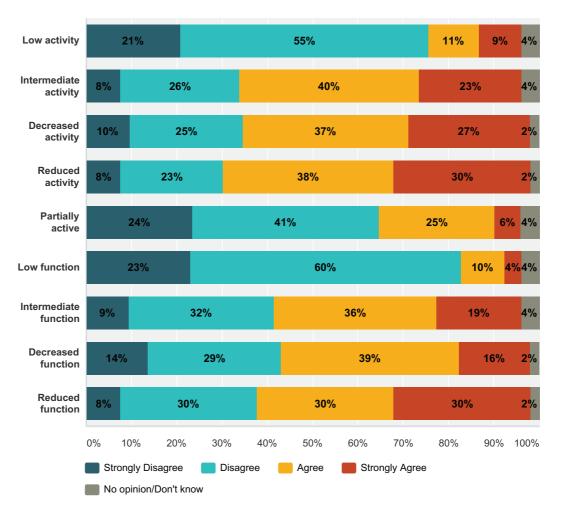


	Strongly Disagree	Disagree	Agree	Strongly Agree	No opinion/Don't know	Total	Weighted Average
Normal activity	5%	7%	41%	45%	2%		
	3.00	4.00	23.00	25.00	1.00	56	3.27
Wild-type activity	33%	33%	17%	15%	2%		
	17.00	17.00	9.00	8.00	1.00	52	2.16
Active	17%	33%	40%	8%	2%		
	9.00	17.00	21.00	4.00	1.00	52	2.39
Normal function	11%	11%	28%	48%	2%		
	6.00	6.00	15.00	26.00	1.00	54	3.15
Functional	15%	31%	37%	15%	2%		
	8.00	16.00	19.00	8.00	1.00	52	2.53
Wild-type function	33%	35%	23%	8%	2%		
	17.00	18.00	12.00	4.00	1.00	52	2.06

#	Other please specifiy	Date
1	Reference activity	2/20/2015 4:44 PM

2	normal enzyme activity	2/16/2015 8:04 AM
3	don't know	2/11/2015 12:30 PM

Q12 Describe your degree of acceptance of the following terms to describe the allele function for a CYP2C19, CYP2D6 or CYP2C9 allele with medium/some function/activity (e.g., CYP2C19*9 or CYP2D6*17):

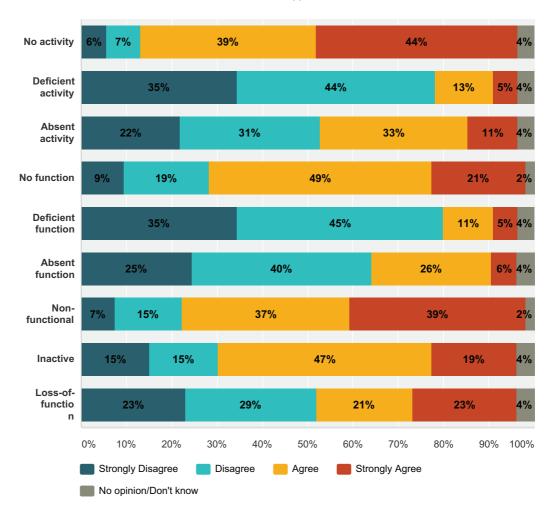


	Strongly Disagree	Disagree	Agree	Strongly Agree	No opinion/Don't know	Total	Weighted Average
Low activity	21%	55%	11%	9%	4%		
	11.00	29.00	6.00	5.00	2.00	53	2.10
Intermediate activity	8%	26%	40%	23%	4%		
	4.00	14.00	21.00	12.00	2.00	53	2.80
Decreased activity	10%	25%	37%	27%	2%		
	5.00	13.00	19.00	14.00	1.00	52	2.82
Reduced activity	8%	23%	38%	30%	2%		
·	4.00	12.00	20.00	16.00	1.00	53	2.92
Partially active	24%	41%	25%	6%	4%		
	12.00	21.00	13.00	3.00	2.00	51	2.14

Low function	23%	60%	10%	4%	4%		
	12.00	31.00	5.00	2.00	2.00	52	1.94
Intermediate function	9%	32%	36%	19%	4%		
	5.00	17.00	19.00	10.00	2.00	53	2.67
Decreased function	14%	29%	39%	16%	2%		
	7.00	15.00	20.00	8.00	1.00	51	2.58
Reduced function	8%	30%	30%	30%	2%		
	4.00	16.00	16.00	16.00	1.00	53	2.85

#	Other (please specify)	Date
1	intermediate/lower than normal enzyme activity	2/16/2015 8:04 AM
2	don't know	2/11/2015 12:30 PM

Q13 Describe your degree of acceptance of the following terms to describe the allele function for a CYP2C19, CYP2D6 or CYP2C9 allele with no function/activity (e.g., CYP2C19*2 or CYP2D6*4 or CYP2C9*6):



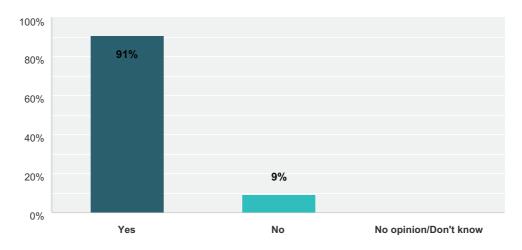
	Strongly Disagree	Disagree	Agree	Strongly Agree	No opinion/Don't know	Total	Weighted Average
No activity	6%	7%	39%	44%	4%		
	3.00	4.00	21.00	24.00	2.00	54	3.27
Deficient activity	35%	44%	13%	5%	4%		
	19.00	24.00	7.00	3.00	2.00	55	1.89
Absent activity	22%	31%	33%	11%	4%		
	12.00	17.00	18.00	6.00	2.00	55	2.34
No function	9%	19%	49%	21%	2%		
	5.00	10.00	26.00	11.00	1.00	53	2.83
Deficient function	35%	45%	11%	5%	4%		
	19.00	25.00	6.00	3.00	2.00	55	1.87

Absent function	25%	40%	26%	6%	4%		
	13.00	21.00	14.00	3.00	2.00	53	2.14
Non-functional	7%	15%	37%	39%	2%		
	4.00	8.00	20.00	21.00	1.00	54	3.09
Inactive	15%	15%	47%	19%	4%		
	8.00	8.00	25.00	10.00	2.00	53	2.73
Loss-of-function	23%	29%	21%	23%	4%		
	12.00	15.00	11.00	12.00	2.00	52	2.46

#	Other (please specify)	Date
1	For this category, we need to differentiate between that caused by inactive protein and that caused by low protein level (but what is there has "normal" activity). The protein's phenotype is not necessarily the cellular/organismal phenotype.	2/20/2015 4:42 PM
2	absent enzyme activity	2/16/2015 8:04 AM

Q14 We assume that 4 or 5 major categories of phenotype (depending on enzyme) are needed for CYP2C19, CYP2D6 and CYP2C9. Do you agree (yes or no)? If no, please indicate how many you think are needed and why:

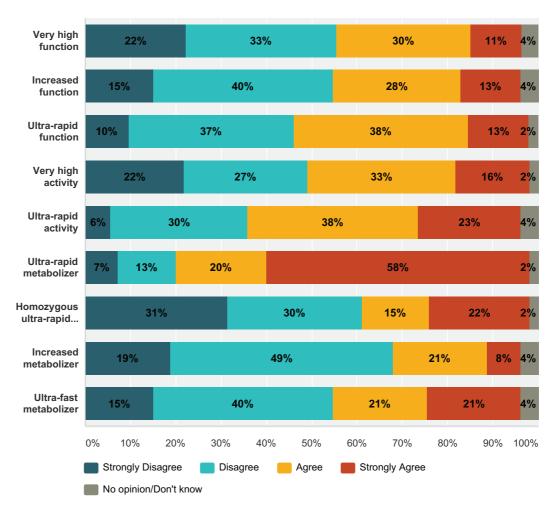
Answered: 53 Skipped: 5



Answer Choices	Responses	
Yes	91%	48.00
No	9%	5.00
No opinion/Don't know	0%	0.00
Total		53

#	If no, please indicate how many you think are needed and why:	Date
1	i just start pharmacogenetic project and I am still learning	2/11/2015 12:39 PM
2	4 categories. Difference between high and very high seems may not be clinically meaningful.	2/11/2015 12:36 PM
3	CYP2C9 does not have an ultrarapid metabolizer status, so would only have 3 major categories of phenotype (EM, IM, PM).	2/9/2015 4:01 PM
4	See my comments on the last screen.	2/4/2015 1:04 PM
5	I would stick with 4 categories (high/normal/low/none)	2/3/2015 12:58 PM
6	Should include unknown.	2/3/2015 10:37 AM
7	No convincing evidence for >3 phenotypes of clinical relevance for CYP2C9 or CYP2C19	2/2/2015 12:52 PM
8	need categories for genotypes with unknown alleles	2/2/2015 12:41 PM

Q15 Describe your degree of acceptance of the following terms to describe the presumed phenotype for CYP2C19, CYP2D6 and CYP2C9 in an individual with very high function/activity (e.g., CYP2C19*17/*17):

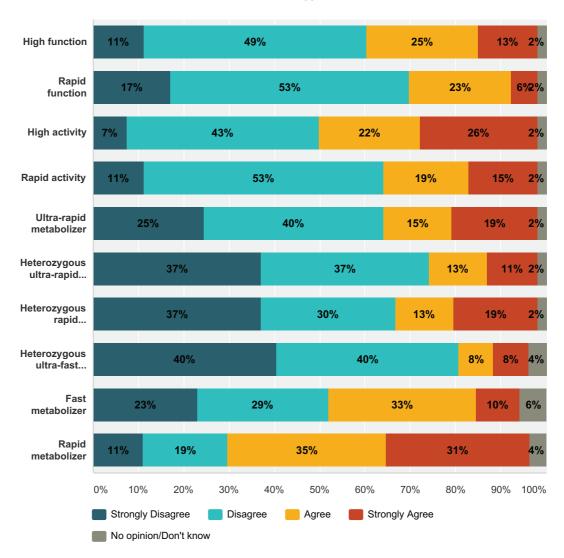


	Strongly Disagree	Disagree	Agree	Strongly Agree	No opinion/Don't know	Total	Weighted Average
Very high function	22%	33%	30%	11%	4%		
	12.00	18.00	16.00	6.00	2.00	54	2.31
Increased function	15%	40%	28%	13%	4%		
	8.00	21.00	15.00	7.00	2.00	53	2.41
Ultra-rapid function	10%	37%	38%	13%	2%		
	5.00	19.00	20.00	7.00	1.00	52	2.57
Very high activity	22%	27%	33%	16%	2%		
	12.00	15.00	18.00	9.00	1.00	55	2.44

Ultra-rapid activity	6%	30%	38%	23%	4%		
	3.00	16.00	20.00	12.00	2.00	53	2.80
Ultra-rapid metabolizer	7%	13%	20%	58%	2%		
	4.00	7.00	11.00	32.00	1.00	55	3.3
Homozygous ultra-rapid	31%	30%	15%	22%	2%		
metabolizer	17.00	16.00	8.00	12.00	1.00	54	2.2
Increased metabolizer	19%	49%	21%	8%	4%		
	10.00	26.00	11.00	4.00	2.00	53	2.1
Ultra-fast metabolizer	15%	40%	21%	21%	4%		
	8.00	21.00	11.00	11.00	2.00	53	2.4

#	Other (please specify)	Date
1	Very increased function	2/20/2015 4:54 PM
2	Homozygous increased metabolizer	2/18/2015 9:41 AM
3	don't know	2/11/2015 12:39 PM
4	I'd prefer "greatly increased function" or "greatly increased activity" to contrast "increased activity" for high function	2/3/2015 1:20 PM
5	Increased activity	2/2/2015 12:52 PM

Q16 Describe your degree of acceptance of the following terms to describe the presumed phenotype for CYP2C19, CYP2D6 and CYP2C9 in an individual with high function/activity (e.g., CYP2C19*1/*17):

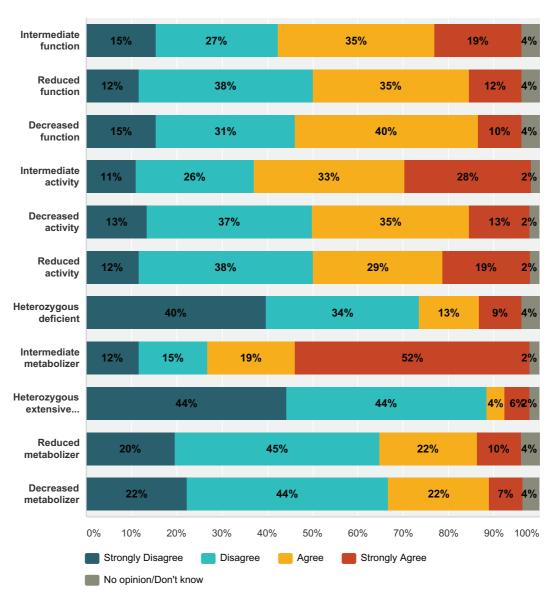


	Strongly Disagree	Disagree	Agree	Strongly Agree	No opinion/Don't know	Total	Weighted Average
High function	11%	49%	25%	13%	2%		
	6.00	26.00	13.00	7.00	1.00	53	2.40
Rapid function	17%	53%	23%	6%	2%		
	9.00	28.00	12.00	3.00	1.00	53	2.17
High activity	7%	43%	22%	26%	2%		
	4.00	23.00	12.00	14.00	1.00	54	2.68
Rapid activity	11%	53%	19%	15%	2%		
	6.00	28.00	10.00	8.00	1.00	53	2.38

Ultra-rapid metabolizer	25%	40%	15%	19%	2%		
	13.00	21.00	8.00	10.00	1.00	53	2.
Heterozygous ultra-rapid	37%	37%	13%	11%	2%		
metabolizer	20.00	20.00	7.00	6.00	1.00	54	1
Heterozygous rapid metabolizer	37%	30%	13%	19%	2%		
	20.00	16.00	7.00	10.00	1.00	54	2
Heterozygous ultra-fast	40%	40%	8%	8%	4%		
metabolizer	21.00	21.00	4.00	4.00	2.00	52	,
Fast metabolizer	23%	29%	33%	10%	6%		
	12.00	15.00	17.00	5.00	3.00	52	2
Rapid metabolizer	11%	19%	35%	31%	4%		
	6.00	10.00	19.00	17.00	2.00	54	2

#	Other (please specify)	Date
1	Increased function	2/20/2015 4:54 PM
2	Heterozygous increased metabolizer	2/18/2015 9:41 AM
3	"Increased function" or "increased activity" would differentiate from "normal" in a very clear way	2/3/2015 1:20 PM

Q17 Describe your degree of acceptance of the following terms to describe the presumed phenotype for CYP2C19, CYP2D6 and CYP2C9 in an individual with medium/some function/activity (e.g., CYP2C19*1/*2, CYP2D6*4/*17, CYP2C9*1/*3):

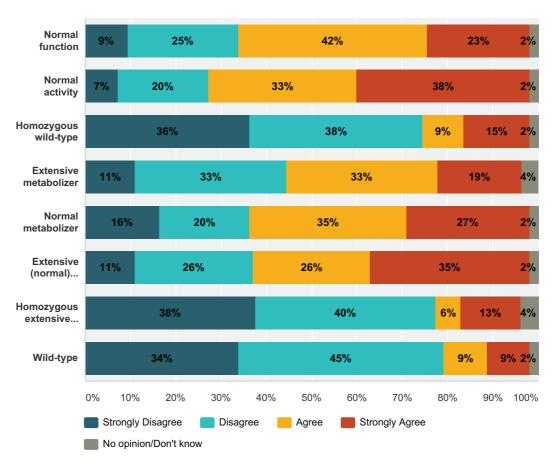


	Strongly Disagree	Disagree	Agree	Strongly Agree	No opinion/Don't know	Total	Weighted Average
Intermediate function	15% 8.00	27% 14.00	35% 18.00	19% 10.00	4% 2.00	52	2.60
Reduced function	12% 6.00	38% 20.00	35% 18.00	12% 6.00	4% 2.00	52	2.48

Decreased function	15%	31%	40%	10%	4%		
	8.00	16.00	21.00	5.00	2.00	52	2.
Intermediate activity	11%	26%	33%	28%	2%		
	6.00	14.00	18.00	15.00	1.00	54	2
Decreased activity	13%	37%	35%	13%	2%		
	7.00	19.00	18.00	7.00	1.00	52	2
Reduced activity	12%	38%	29%	19%	2%		
	6.00	20.00	15.00	10.00	1.00	52	2
Heterozygous deficient	40%	34%	13%	9%	4%		
	21.00	18.00	7.00	5.00	2.00	53	1
Intermediate metabolizer	12%	15%	19%	52%	2%		
	6.00	8.00	10.00	27.00	1.00	52	3
Heterozygous extensive	44%	44%	4%	6%	2%		
metabolizer	23.00	23.00	2.00	3.00	1.00	52	1
Reduced metabolizer	20%	45%	22%	10%	4%		
	10.00	23.00	11.00	5.00	2.00	51	2
Decreased metabolizer	22%	44%	22%	7%	4%		
	12.00	24.00	12.00	4.00	2.00	54	2

#	Other (please specify)	Date
1	heterozygous decreased metabolizer	2/18/2015 9:41 AM
2	don't know	2/11/2015 12:39 PM
3	Reduced metabolism; decreased metabolism	2/5/2015 7:07 AM

Q18 Describe your degree of acceptance of the following terms to describe the presumed phenotype for CYP2C19, CYP2D6 and CYP2C9 in an individual with normal function/activity (e.g., CYP2C19*1/*1, CYP2D6*1/*1, CYP2C9*1/*1):

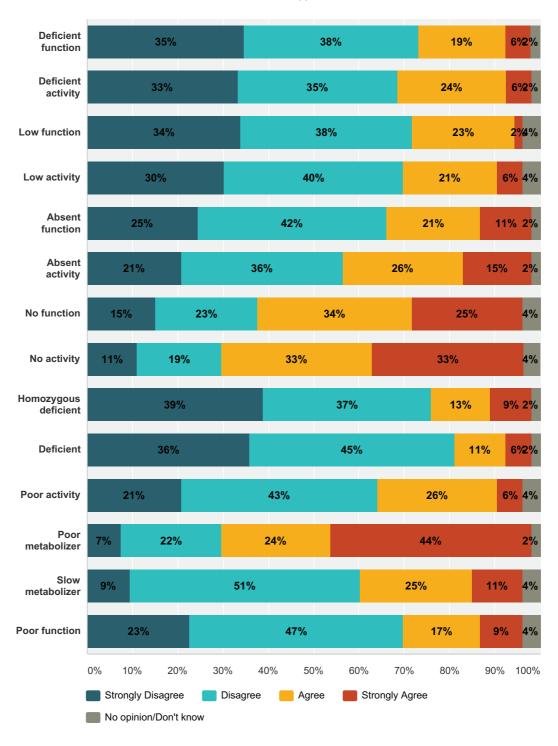


	Strongly Disagree	Disagree	Agree	Strongly Agree	No opinion/Don't know	Total	Weighted Average
Normal function	9% 5.00	25% 13.00	42% 22.00	23% 12.00	2% 1.00	53	2.79
Normal activity	7% 4.00	20% 11.00	33% 18.00	38% 21.00	2% 1.00	55	3.04
Homozygous wild-type	36% 20.00	38% 21.00	9% 5.00	15% 8.00	2% 1.00	55	2.02
Extensive metabolizer	11% 6.00	33% 18.00	33% 18.00	19% 10.00	4% 2.00	54	2.62
Normal metabolizer	16% 9.00	20% 11.00	35% 19.00	27% 15.00	2% 1.00	55	2.74
Extensive (normal) metabolizer	11% 6.00	26% 14.00	26% 14.00	35% 19.00	2% 1.00	54	2.87

Homozygous extensive metabolizer	38% 20.00	40% 21.00	6% 3.00	13% 7.00	4% 2.00	53	1.94
Wild-type	34%	45%	9%	9%	2%		
	18.00	24.00	5.00	5.00	1.00	53	1.94

#	Other (please specify)	Date
1	Reference function	2/20/2015 4:54 PM
2	homozygous normal metabolizer	2/18/2015 9:41 AM

Q19 Describe your degree of acceptance of the following terms to describe the presumed phenotype for CYP2C19, CYP2D6 and CYP2C9 in an individual with no function/activity (e.g., CYP2C19*2/*2, CYP2D6*4/*4, CYP2C9*6/*6):

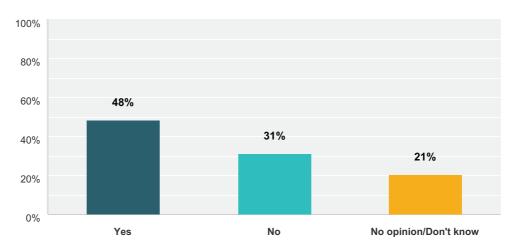


	Strongly Disagree	Disagree	Agree	Strongly Agree	No opinion/Don't know	Total	Weighted Average
Deficient function	35%	38%	19%	6%	2%		
	18.00	20.00	10.00	3.00	1.00	52	1.9
Deficient activity	33%	35%	24%	6%	2%		
	18.00	19.00	13.00	3.00	1.00	54	2.0
Low function	34%	38%	23%	2%	4%		
	18.00	20.00	12.00	1.00	2.00	53	1.9
Low activity	30%	40%	21%	6%	4%		
	16.00	21.00	11.00	3.00	2.00	53	2.0
Absent function	25%	42%	21%	11%	2%		
	13.00	22.00	11.00	6.00	1.00	53	2.1
Absent activity	21%	36%	26%	15%	2%		
	11.00	19.00	14.00	8.00	1.00	53	2.3
No function	15%	23%	34%	25%	4%		
	8.00	12.00	18.00	13.00	2.00	53	2.7
No activity	11%	19%	33%	33%	4%		
	6.00	10.00	18.00	18.00	2.00	54	2.9
Homozygous deficient	39%	37%	13%	9%	2%		
	21.00	20.00	7.00	5.00	1.00	54	1.9
Deficient	36%	45%	11%	6%	2%		
	19.00	24.00	6.00	3.00	1.00	53	1.8
Poor activity	21%	43%	26%	6%	4%		
	11.00	23.00	14.00	3.00	2.00	53	2.1
Poor metabolizer	7%	22%	24%	44%	2%		
	4.00	12.00	13.00	24.00	1.00	54	3.0
Slow metabolizer	9%	51%	25%	11%	4%		
	5.00	27.00	13.00	6.00	2.00	53	2.3
Poor function	23%	47%	17%	9%	4%		
	12.00	25.00	9.00	5.00	2.00	53	2.

#	Other (please specify)	Date
1	No metabolism	2/5/2015 7:07 AM

Q20 Scoring systems have been developed in an attempt to provide a uniform approach to quantitate the predicted functional status of CYP2D6 alleles as follows: 1 for normal function, 0.5 for decreased function, and 0 for no function alleles. The sum of the activity values for each allele of the diplotype provides a CYP2D6 activity score. Do you think the CYP2D6 scoring system is adequate in determining CYP2D6 phenotype?

Answered: 58 Skipped: 0



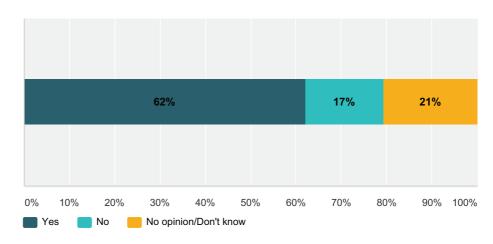
Answer Choices	Responses		
Yes	48% 28.00		
No	31% 18.00		
No opinion/Don't know	21% 12.00		
Total	58		

#	If No, please explain why:	Date
1	I'm admittedly not as educated as I need to be, but I suspect that intermediate alleles are not all equal in their degree of residual activity. I like a scoring system, but if there's sufficient data, perhaps it would be even more useful to assign a score that reflects the degree of allele activity on a scale from 0-1. Then the summary phenotype could be reflected as a quantitative scoreraw data would be a scale from 0-2, but that could be transformed back to a % or 0-1 scale. Qualitative assessments of phenotype could then be assigned based on score ranges, and reported along with the associated score. Of course, if the evidence refutes this idea, then it should not be pursued. The sticky situation would be if the evidence fails to support but also fails to refute this idea (i.e. lack of evidence for a quantitative score is not the same as evidence against a quantitative score).	2/21/2015 7:42 PM
2	How to deal with increased function alleles that are due to duplications. For example, consider PersonA with CYP2D6*1 CYP2D6*1 = 1 + 1 = 2 and PersonB with 3 CYP2D6 alleles composed of CYP2D6*9 CYP2D6*1x2 (2 copies of *1 on 1 chromosome) = 0.5 + 2 = 2.5. However, both persons are categorized (based on literature today) as extensive metabolizers. Thus, two different scores are yielding the same phenotype and that is confusing.	2/20/2015 5:05 PM

3	I like the idea of quantifying function, but I don't have enough experience with the gene to know that this is the right system.	2/19/2015 2:44 PM
4	Clinical labs are not consistently reporting copy numbers which is critical for calculating the score, therefore until that happens it cannot be a reliably used metric.	2/19/2015 2:42 PM
5	probably the 1 - 0.5 - 0 classification is too rough and requires refinement. Also the assigned value may be substrate specific	2/18/2015 3:47 PM
6	Drug-drug interactions need to be included in the scoring system as well	2/17/2015 11:01 AM
7	My "yes" answer is the the question of whether the 2D6 scoring system inadequate in DESCRIBING the phenotype. I'm not sure what you mean by DETERMINING the phenotype.	2/11/2015 12:59 PM
8	The CYP2D6 scoring system does not distinguish between more functional 'decreased function' alleles (*10) and less functional 'decreased function' alleles (*41). In the CYP2D6 scoring system, a *17/*17 would be considered an EM, but perhaps IM would be more appropriate.	2/9/2015 4:10 PM
9	I think it can be helpful for physicians, but not widely adopted, so not sure how well physicians understand.	2/9/2015 11:50 AM
10	The ultra rapid metabolizers will not be covered.	2/6/2015 7:36 AM
11	It may be useful for the time being but I would try to get information on the intrinsic clearance; also if you use the scoring system, need to include a score for the ultra-rapid metabolizers	2/4/2015 1:08 PM
12	For one thing it does not take into account the fact that for different drugs, the score could mean different things. Does not take into account location of the alleles relative to each other. Does not take into account whether having one functional allele actually confers normal function	2/3/2015 3:37 PM
13	This would seem to be an oversimplification. It may accurately predict a worthwhile course of action for a physician with the information we have now, but it doesn't take the extent of any decrease of activity into account, other than the drop to 0 for no activity. Also, some alleles may have substrate-dependent function. Practically, is it significantly easier for a physician to assign or use a function score of 1.5 than to simply think "one functional, one decreased allele?" However, once the activities of decreased-function alleles are better understood and assigned numbers other than 0.5, such a system could be very useful.	2/3/2015 1:20 PM
14	I would prefer a universal scoring system that includes HIGH function (that way it is not different for different genes). 0= no activity; 0.5 = reduced/low activity; 1 = normal activity (WT); 1.5 = high activity	2/3/2015 12:59 PM
15	Questionable utility, may lead to confusion (implies that activity is "exactly" 1/2 of the normal?)	2/3/2015 10:41 AM
16	You need to somehow score the multiple CYP2D6 copy alleles	2/3/2015 10:36 AM
17	Adequate on current knowledge, but ultimately needs to be fine-tuned	2/2/2015 12:41 PM
18	The gene-dose effect is not linear	2/2/2015 10:23 AM

Q21 To date, a scoring system (e.g., CYP2D6 activity scores) for CYP2C19 has not been developed. Do you think a scoring system should be developed for CYP2C19 and possibly other enzymes?

Answered: 58 Skipped: 0

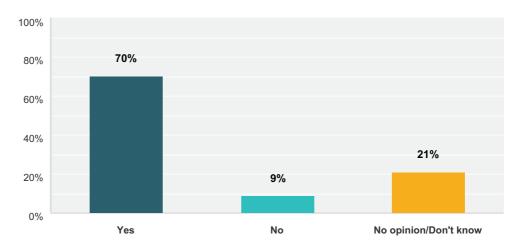


Answer Choices	Responses	
Yes	62%	36.00
No	17%	10.00
No opinion/Don't know	21%	12.00
Total		58

#	If No, please explain why:	Date
1	In reality, a quantitative scoring system would work if 1 lab produced all the cellular activity levels for each diplotype.	2/20/2015 5:05 PM
2	I would look to base it on the intrinsic clearance, because the drugs for these CYPs vary. It appears that you may need to involve Substrate effect with the enzyme activity.	2/4/2015 1:08 PM
3	For the same reasons listed above for 2D6 could be problematic	2/3/2015 3:37 PM
4	Questionable utility, may lead to confusion.	2/3/2015 10:41 AM
5	Given the lack of knowledge on the absolute function for many of the alleles, specifically in population outside of whites this would be difficult/ perhaps incorrect.	2/3/2015 10:40 AM
6	No evidence of clinical relevance for CYP2C19	2/2/2015 12:53 PM
7	The functional role of CYP2C19*17 requieres further analysis	2/2/2015 10:23 AM

Q22 We assume that 3 major categories of allele function are needed for CYP3A5. Do you agree (yes or no)? If no, please indicate how many you think are needed and why

Answered: 57 Skipped: 1

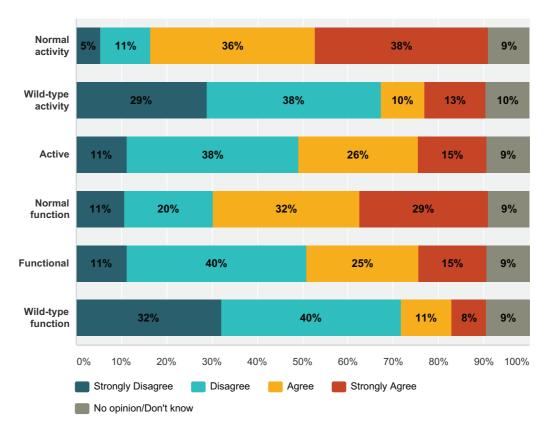


Answer Choices	Responses	
Yes	70%	40.00
No	9%	5.00
No opinion/Don't know	21%	12.00
Total		57

#	If No, please indicate how many you think are needed and why:	Date
1	Need unknown	2/20/2015 5:09 PM
2	I don't have any experience with this gene, but now having heard the unique issues that some have raised for this gene I don't think I am in a position to give specific responses.	2/19/2015 2:46 PM
3	As before, all terms should be consistent for every gene	2/19/2015 2:44 PM
4	Given the overlap with CYP3A4, it appears that for high risk drugs CYP3A adds extended activity or plays a role when CYP3A4 alone is inhibited.	2/4/2015 1:14 PM
5	I think categories should be uniform (4 categories for ALL allellic function)	2/3/2015 1:01 PM
6	4; need 'unknown'	2/2/2015 12:41 PM

Q23 Describe your degree of acceptance of the following terms to describe the allele function for a CYP3A5 allele with normal function/activity (e.g., CYP3A5*1):

Answered: 57 Skipped: 1



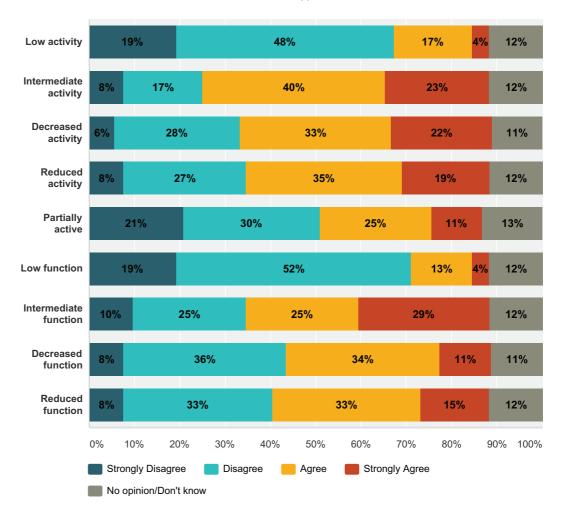
	Strongly Disagree	Disagree	Agree	Strongly Agree	No opinion/Don't know	Total	Weighted Average
Normal activity	5%	11%	36%	38%	9%		
	3.00	6.00	20.00	21.00	5.00	55	3.18
Wild-type activity	29%	38%	10%	13%	10%		
	15.00	20.00	5.00	7.00	5.00	52	2.09
Active	11%	38%	26%	15%	9%		
	6.00	20.00	14.00	8.00	5.00	53	2.50
Normal function	11%	20%	32%	29%	9%		
	6.00	11.00	18.00	16.00	5.00	56	2.86
Functional	11%	40%	25%	15%	9%		
	6.00	21.00	13.00	8.00	5.00	53	2.48
Wild-type function	32%	40%	11%	8%	9%		
	17.00	21.00	6.00	4.00	5.00	53	1.94

#	Other please specifiy	Date
1	Reference activity	2/20/2015 5:09 PM
2	most prevalent allele is 3A5*3 that should actually be renamed *1	2/18/2015 3:49 PM

3	normal enzyme activity	2/16/2015 8:05 AM
4	Normal metabolism	2/5/2015 7:10 AM
5	AF for *3 is higher than that of *1 in many groups; calling fully-functional 3A5 "normal" or "wild-type" is inaccurate.	2/3/2015 1:23 PM
6	high expression	2/2/2015 10:54 AM

Q24 Describe your degree of acceptance of the following terms to describe the allele function for a CYP3A5 allele with medium/some function/activity (e.g., CYP3A5*8):

Answered: 56 Skipped: 2



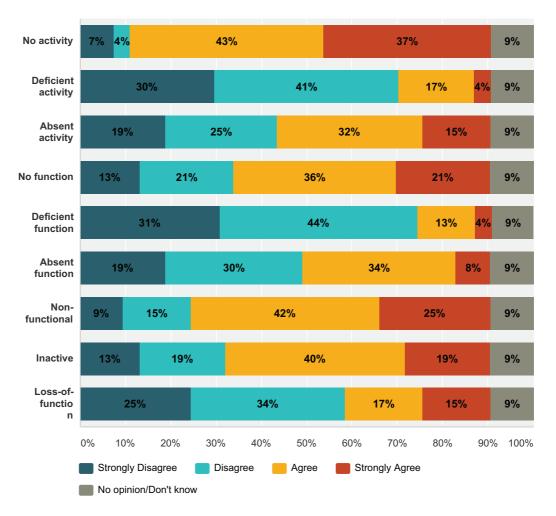
	Strongly Disagree	Disagree	Agree	Strongly Agree	No opinion/Don't know	Total	Weighted Average
Low activity	19%	48%	17%	4%	12%		
	10.00	25.00	9.00	2.00	6.00	52	2.07
Intermediate activity	8%	17%	40%	23%	12%		
	4.00	9.00	21.00	12.00	6.00	52	2.89
Decreased activity	6%	28%	33%	22%	11%		
	3.00	15.00	18.00	12.00	6.00	54	2.81
Reduced activity	8%	27%	35%	19%	12%		
	4.00	14.00	18.00	10.00	6.00	52	2.74
Partially active	21%	30%	25%	11%	13%		
•	11.00	16.00	13.00	6.00	7.00	53	2.30

Low function	19% 10.00	52% 27.00	13% 7.00	4% 2.00	12% 6.00	52	2.02
Intermediate function	10% 5.00	25% 13.00	25% 13.00	29% 15.00	12% 6.00	52	2.83
Decreased function	8% 4.00	36% 19.00	34% 18.00	11% 6.00	11% 6.00	53	2.55
Reduced function	8% 4.00	33% 17.00	33% 17.00	15% 8.00	12% 6.00	52	2.63

#	Other (please specify)	Date
1	intermediate (lower than normal) enzyme activity	2/16/2015 8:05 AM
2	decreased metabolism; reduced metabolism	2/5/2015 7:10 AM
3	Not sure that this is an important therapeutic/dosing distinction as of now	2/4/2015 1:14 PM
4	Expressor	2/2/2015 10:54 AM

Q25 Describe your degree of acceptance of the following terms to describe the allele function for a CYP3A5 allele with no function/activity (e.g., CYP3A5*3):

Answered: 57 Skipped: 1



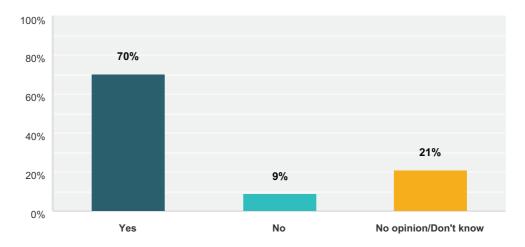
	Strongly Disagree	Disagree	Agree	Strongly Agree	No opinion/Don't know	Total	Weighted Average
No activity	7%	4%	43%	37%	9%		
	4.00	2.00	23.00	20.00	5.00	54	3.20
Deficient activity	30%	41%	17%	4%	9%		
	16.00	22.00	9.00	2.00	5.00	54	1.94
Absent activity	19%	25%	32%	15%	9%		
	10.00	13.00	17.00	8.00	5.00	53	2.48
No function	13%	21%	36%	21%	9%		
	7.00	11.00	19.00	11.00	5.00	53	2.71
Deficient function	31%	44%	13%	4%	9%		
	17.00	24.00	7.00	2.00	5.00	55	1.88
Absent function	19%	30%	34%	8%	9%		
	10.00	16.00	18.00	4.00	5.00	53	2.33

Non-functional	9%	15%	42%	25%	9%		
	5.00	8.00	22.00	13.00	5.00	53	2.90
Inactive	13%	19%	40%	19%	9%		
	7.00	10.00	21.00	10.00	5.00	53	2.71
Loss-of-function	25%	34%	17%	15%	9%		
	13.00	18.00	9.00	8.00	5.00	53	2.25

#	Other (please specify)	Date
1	absent enzyme activity	2/16/2015 8:05 AM
2	Non-expressor	2/2/2015 10:54 AM

Q26 We assume that 3 major categories of phenotype are needed for CYP3A5. Do you agree (yes or no)? If no, please indicate how many you think are needed and why:

Answered: 57 Skipped: 1

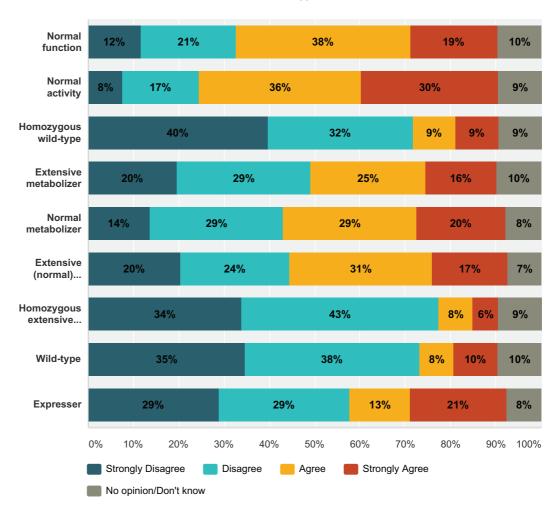


Answer Choices	Responses
Yes	70% 40.00
No	9% 5.00
No opinion/Don't know	21% 12.00
Total	57

#	If no, please indicate how many you think are needed and why:	Date
1	Need unknown	2/20/2015 5:11 PM
2	See last comment	2/19/2015 2:46 PM
3	I have not been convinced that more than 2 carries a dosing distinction at this point.	2/4/2015 1:20 PM
4	Keep the number of categories UNIVERSAL (4 - LOF; reduced; WT; high)	2/3/2015 1:03 PM
5	need categories for genotypes with unknown alleles	2/2/2015 12:43 PM

Q27 Describe your degree of acceptance of the following terms to describe the presumed phenotype for CYP3A5 in an individual with normal CYP3A5 function/activity (e.g., CYP3A5*1/*1):

Answered: 56 Skipped: 2



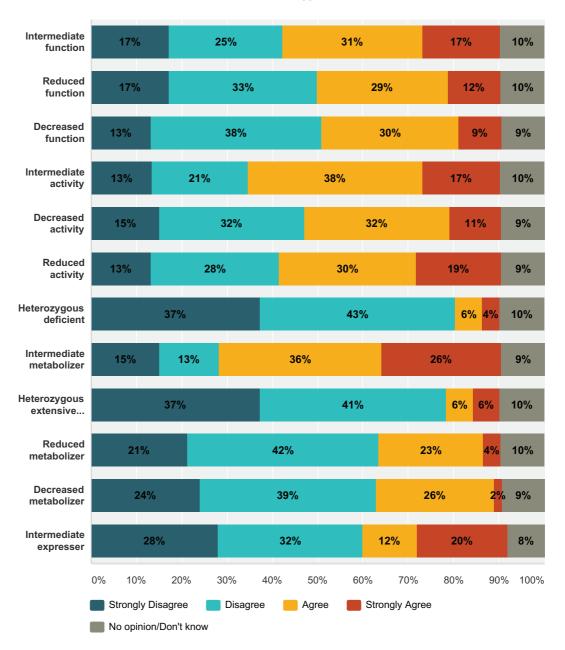
	Strongly Disagree	Disagree	Agree	Strongly Agree	No opinion/Don't know	Total	Weighted Average
Normal function	12%	21%	38%	19%	10%		
	6.00	11.00	20.00	10.00	5.00	52	2.72
Normal activity	8%	17%	36%	30%	9%		
	4.00	9.00	19.00	16.00	5.00	53	2.98
Homozygous wild-type	40%	32%	9%	9%	9%		
	21.00	17.00	5.00	5.00	5.00	53	1.88
Extensive metabolizer	20%	29%	25%	16%	10%		
	10.00	15.00	13.00	8.00	5.00	51	2.41
Normal metabolizer	14%	29%	29%	20%	8%		
	7.00	15.00	15.00	10.00	4.00	51	2.60

Extensive (normal) metabolizer	20%	24%	31%	17%	7%		
	11.00	13.00	17.00	9.00	4.00	54	2.48
Homozygous extensive	34%	43%	8%	6%	9%		
metabolizer	18.00	23.00	4.00	3.00	5.00	53	1.83
Wild-type	35%	38%	8%	10%	10%		
	18.00	20.00	4.00	5.00	5.00	52	1.91
Expresser	29%	29%	13%	21%	8%		
	15.00	15.00	7.00	11.00	4.00	52	2.29

#	Other (please specify)	Date
1	Reference function	2/20/2015 5:11 PM
2	Homozygous normal metabolizer	2/18/2015 10:24 AM
3	"Full function" would also work. Just not "normal" or "wild-type."	2/3/2015 1:41 PM
4	there should be a caveat on this descriptor that states that this is low frequency (not common) in white and more frequent in blacks ect	2/3/2015 10:48 AM

Q28 Describe your degree of acceptance of the following terms to describe the presumed phenotype for CYP3A5 in an individual with medium/some CYP3A5 function/activity (e.g., CYP3A5*1/*3):

Answered: 56 Skipped: 2



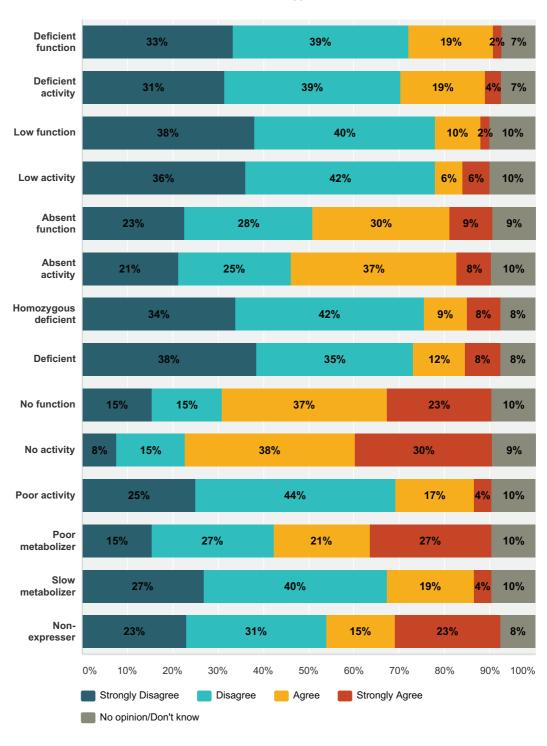
	Strongly Disagree	Disagree	Agree	Strongly Agree	No opinion/Don't know	Total	Weighted Average
Intermediate function	17% 9.00	25% 13.00	31% 16.00	17% 9.00	10% 5.00	52	2.53
Reduced function	17% 9.00	33% 17.00	29% 15.00	12% 6.00	10% 5.00	52	2.38

Decreased function	13%	38%	30%	9%	9%		
	7.00	20.00	16.00	5.00	5.00	53	2.
Intermediate activity	13%	21%	38%	17%	10%		
	7.00	11.00	20.00	9.00	5.00	52	2.
Decreased activity	15%	32%	32%	11%	9%		
	8.00	17.00	17.00	6.00	5.00	53	2
Reduced activity	13%	28%	30%	19%	9%		
	7.00	15.00	16.00	10.00	5.00	53	2
Heterozygous deficient	37%	43%	6%	4%	10%		
	19.00	22.00	3.00	2.00	5.00	51	1
Intermediate metabolizer	15%	13%	36%	26%	9%		
	8.00	7.00	19.00	14.00	5.00	53	2
Heterozygous extensive	37%	41%	6%	6%	10%		
metabolizer	19.00	21.00	3.00	3.00	5.00	51	1
Reduced metabolizer	21%	42%	23%	4%	10%		
	11.00	22.00	12.00	2.00	5.00	52	2
Decreased metabolizer	24%	39%	26%	2%	9%		
	13.00	21.00	14.00	1.00	5.00	54	2
Intermediate expresser	28%	32%	12%	20%	8%		
	14.00	16.00	6.00	10.00	4.00	50	2

#	Other (please specify)	Date
1	heterozygous expresser	2/18/2015 3:52 PM
2	Heterozygous decreased metabolizer	2/18/2015 10:24 AM
3	intermediate (less than normal) metabolizer	2/16/2015 8:05 AM
4	decreased metabolism; reduced metabolism	2/5/2015 7:12 AM
5	Partially Decreased Metabolizer	2/4/2015 2:22 PM
6	"reduced" or "decreased" make little sense here, when average activity is so low	2/3/2015 1:41 PM

Q29 Describe your degree of acceptance of the following terms to describe the presumed phenotype for CYP3A5 in an individual with no CYP3A5 function/activity (e.g., CYP3A5*3/*3):

Answered: 56 Skipped: 2



Agree

Strongly Agree

No opinion/Don't know

Total

Weighted Average

Strongly Disagree

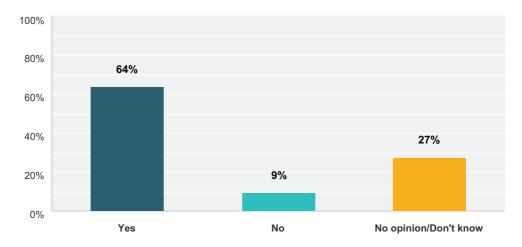
Disagree

Deficient function	33%	39%	19%	2%	7%		
	18.00	21.00	10.00	1.00	4.00	54	
Deficient activity	31%	39%	19%	4%	7%		
	17.00	21.00	10.00	2.00	4.00	54	
Low function	38%	40%	10%	2%	10%		
	19.00	20.00	5.00	1.00	5.00	50	
Low activity	36%	42%	6%	6%	10%		
	18.00	21.00	3.00	3.00	5.00	50	
Absent function	23%	28%	30%	9%	9%		
	12.00	15.00	16.00	5.00	5.00	53	
Absent activity	21%	25%	37%	8%	10%		
	11.00	13.00	19.00	4.00	5.00	52	
Homozygous deficient	34%	42%	9%	8%	8%		
	18.00	22.00	5.00	4.00	4.00	53	
Deficient	38%	35%	12%	8%	8%		
	20.00	18.00	6.00	4.00	4.00	52	
No function	15%	15%	37%	23%	10%		
	8.00	8.00	19.00	12.00	5.00	52	
No activity	8%	15%	38%	30%	9%		
	4.00	8.00	20.00	16.00	5.00	53	
Poor activity	25%	44%	17%	4%	10%		
	13.00	23.00	9.00	2.00	5.00	52	
Poor metabolizer	15%	27%	21%	27%	10%		
	8.00	14.00	11.00	14.00	5.00	52	
Slow metabolizer	27%	40%	19%	4%	10%		
	14.00	21.00	10.00	2.00	5.00	52	
Non-expresser	23%	31%	15%	23%	8%		
	12.00	16.00	8.00	12.00	4.00	52	

#	Other (please specify)	Date
1	wild type	2/18/2015 3:52 PM
2	No metabolism; non-metabolizer	2/5/2015 7:12 AM
3	Decreased Metabolizer	2/4/2015 2:22 PM

Q30 We assume that 4 major categories of allele function are needed for UGT1A1. Do you agree (yes or no)? If no, please indicate how many you think are needed and why:

Answered: 55 Skipped: 3

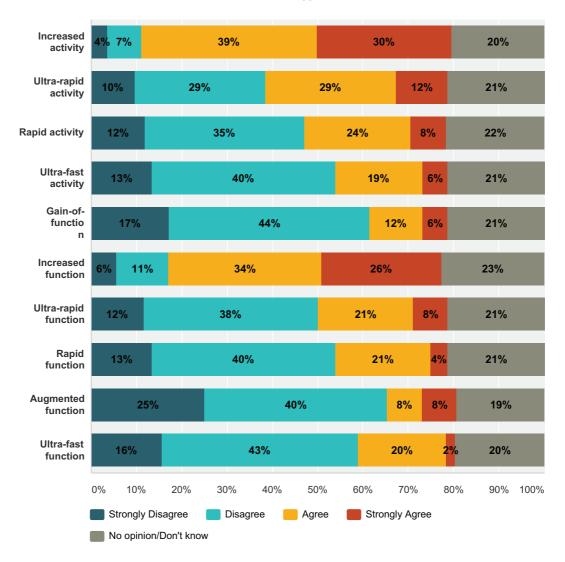


Answer Choices	Responses	
Yes	64%	35.00
No	9%	5.00
No opinion/Don't know	27%	15.00
Total		55

#	If No, please indicate how many you think are needed and why:	Date
1	There is also UGT1A1 *37. We include it in the AGI assay.	2/3/2015 3:45 PM
2	This doesn't account for rare deleterious variants.	2/3/2015 1:36 AM
3	NO convinving evidence of clinical relevance of 4 categories	2/2/2015 12:58 PM
4	need category for unknown	2/2/2015 12:45 PM

Q31 Describe your degree of acceptance of the following terms to describe the allele function for a UGT1A1 allele with high function/activity (e.g., UGT1A1*36 (5 TA repeats)):

Answered: 55 Skipped: 3



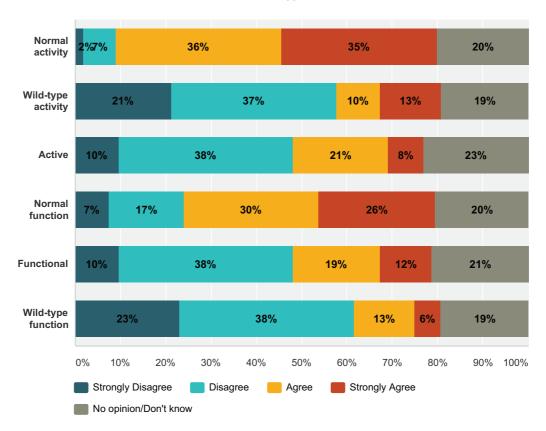
	Strongly Disagree	Disagree	Agree	Strongly Agree	No opinion/Don't know	Total	Weighted Average
Increased activity	4%	7%	39%	30%	20%		
	2.00	4.00	21.00	16.00	11.00	54	3.19
Ultra-rapid activity	10%	29%	29%	12%	21%		
	5.00	15.00	15.00	6.00	11.00	52	2.54
Rapid activity	12%	35%	24%	8%	22%		
	6.00	18.00	12.00	4.00	11.00	51	2.35
Ultra-fast activity	13%	40%	19%	6%	21%		
	7.00	21.00	10.00	3.00	11.00	52	2.22

Gain-of-function	17%	44%	12%	6%	21%		
	9.00	23.00	6.00	3.00	11.00	52	2.0
Increased function	6%	11%	34%	26%	23%		
	3.00	6.00	18.00	14.00	12.00	53	3.0
Ultra-rapid function	12%	38%	21%	8%	21%		
	6.00	20.00	11.00	4.00	11.00	52	2.
Rapid function	13%	40%	21%	4%	21%		
	7.00	21.00	11.00	2.00	11.00	52	2
Augmented function	25%	40%	8%	8%	19%		
	13.00	21.00	4.00	4.00	10.00	52	1.
Ultra-fast function	16%	43%	20%	2%	20%		
	8.00	22.00	10.00	1.00	10.00	51	2

#	Other (please specify)	Date
1	increased enzyme activity	2/16/2015 8:05 AM
2	High activity	2/3/2015 10:49 AM

Q32 Describe your degree of acceptance of the following terms to describe the allele function for a UGT1A1 allele with normal function/activity (e.g., UGT1A1*1 (6 TA repeats)):

Answered: 55 Skipped: 3



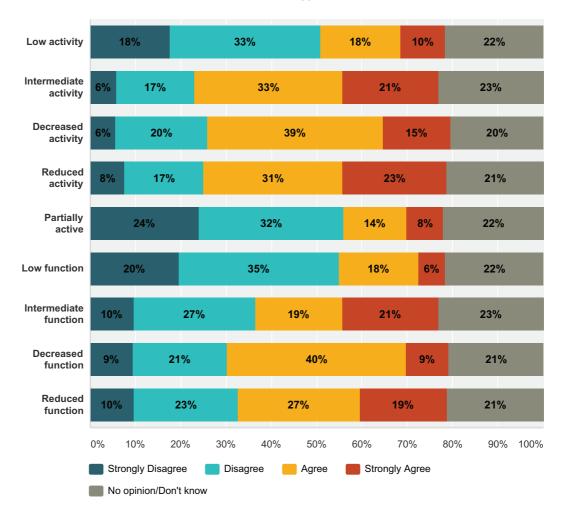
	Strongly Disagree	Disagree	Agree	Strongly Agree	No opinion/Don't know	Total	Weighted Average
Normal activity	2%	7%	36%	35%	20%		
	1.00	4.00	20.00	19.00	11.00	55	3.3
Wild-type activity	21%	37%	10%	13%	19%		
	11.00	19.00	5.00	7.00	10.00	52	2.1
Active	10%	38%	21%	8%	23%		
	5.00	20.00	11.00	4.00	12.00	52	2.3
Normal function	7%	17%	30%	26%	20%		
	4.00	9.00	16.00	14.00	11.00	54	2.9
Functional	10%	38%	19%	12%	21%		
	5.00	20.00	10.00	6.00	11.00	52	2.4
Wild-type function	23%	38%	13%	6%	19%		
	12.00	20.00	7.00	3.00	10.00	52	2.0

#	Other please specifiy	Date
1	Reference activity	2/20/2015 5:16 PM

2	normal enzyme activity	2/16/2015 8:05 AM

Q33 Describe your degree of acceptance of the following terms to describe the allele function for a UGT1A1 allele with medium/some function/activity (e.g., UGT1A1*28 (7 TA repeats)):

Answered: 55 Skipped: 3



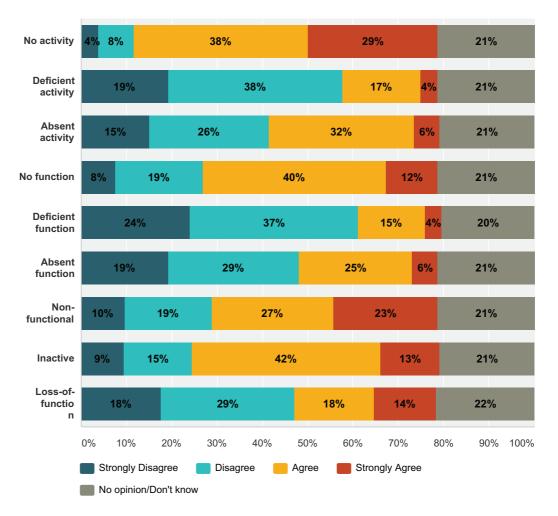
	Strongly Disagree	Disagree	Agree	Strongly Agree	No opinion/Don't know	Total	Weighted Average
Low activity	18%	33%	18%	10%	22%		
	9.00	17.00	9.00	5.00	11.00	51	2.25
Intermediate activity	6%	17%	33%	21%	23%		
	3.00	9.00	17.00	11.00	12.00	52	2.90
Decreased activity	6%	20%	39%	15%	20%		
	3.00	11.00	21.00	8.00	11.00	54	2.79
Reduced activity	8%	17%	31%	23%	21%		
	4.00	9.00	16.00	12.00	11.00	52	2.88
Partially active	24%	32%	14%	8%	22%		
-	12.00	16.00	7.00	4.00	11.00	50	2.08

Low function	20%	35%	18%	6%	22%		
	10.00	18.00	9.00	3.00	11.00	51	2.13
Intermediate function	10%	27%	19%	21%	23%		
	5.00	14.00	10.00	11.00	12.00	52	2.67
Decreased function	9%	21%	40%	9%	21%		
	5.00	11.00	21.00	5.00	11.00	53	2.62
Reduced function	10%	23%	27%	19%	21%		
	5.00	12.00	14.00	10.00	11.00	52	2.71

#	Other (please specify)	Date
1	intermediate (less than normal) enzyme activity	2/16/2015 8:05 AM

Q34 Describe your degree of acceptance of the following terms to describe the allele function for a UGT1A1 allele with no function/activity (e.g., UGT1A1*15):

Answered: 55 Skipped: 3



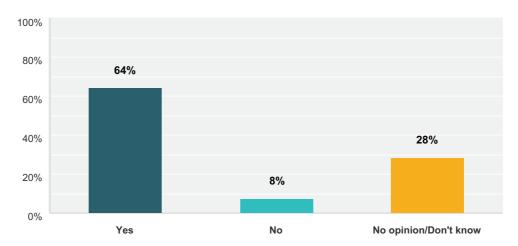
	Strongly Disagree	Disagree	Agree	Strongly Agree	No opinion/Don't know	Total	Weighted Average
No activity	4%	8%	38%	29%	21%		
	2.00	4.00	20.00	15.00	11.00	52	3.17
Deficient activity	19%	38%	17%	4%	21%		
	10.00	20.00	9.00	2.00	11.00	52	2.07
Absent activity	15%	26%	32%	6%	21%		
	8.00	14.00	17.00	3.00	11.00	53	2.36
No function	8%	19%	40%	12%	21%		
	4.00	10.00	21.00	6.00	11.00	52	2.71
Deficient function	24%	37%	15%	4%	20%		
	13.00	20.00	8.00	2.00	11.00	54	1.98
Absent function	19%	29%	25%	6%	21%		
	10.00	15.00	13.00	3.00	11.00	52	2.22

Non-functional	10%	19%	27%	23%	21%		
	5.00	10.00	14.00	12.00	11.00	52	2.80
Inactive	9%	15%	42%	13%	21%		
	5.00	8.00	22.00	7.00	11.00	53	2.74
Loss-of-function	18%	29%	18%	14%	22%		
	9.00	15.00	9.00	7.00	11.00	51	2.35

#	Other (please specify)	Date
1	absent enzyme activity	2/16/2015 8:05 AM

Q35 We assume that 4 major categories of phenotype are needed for UGT1A1. Do you agree (yes or no)? If no, please indicate how many you think are needed and why:

Answered: 53 Skipped: 5

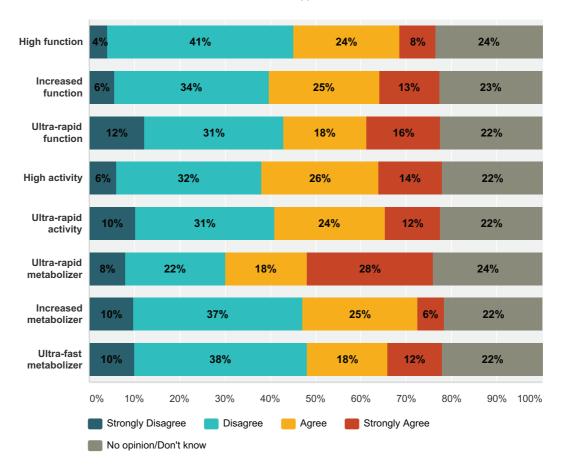


Answer Choices	Responses
Yes	64% 34.00
No	8% 4.00
No opinion/Don't know	28% 15.00
Total	53

#	If no, please indicate how many you think are needed and why:	Date
1	Need unknown	2/20/2015 5:16 PM
2	UGT1A1 genotyping assays also include 836 and *37	2/3/2015 3:49 PM
3	No evidence of clinical relevance of 4 phenotypes	2/2/2015 1:00 PM
4	need categories for genotypes with unknown alleles	2/2/2015 12:47 PM

Q36 Describe your degree of acceptance of the following terms to describe the presumed phenotype for UGT1A1 in an individual with high UGT1A1 function/activity (e.g., UGT1A1*36/*36):

Answered: 53 Skipped: 5



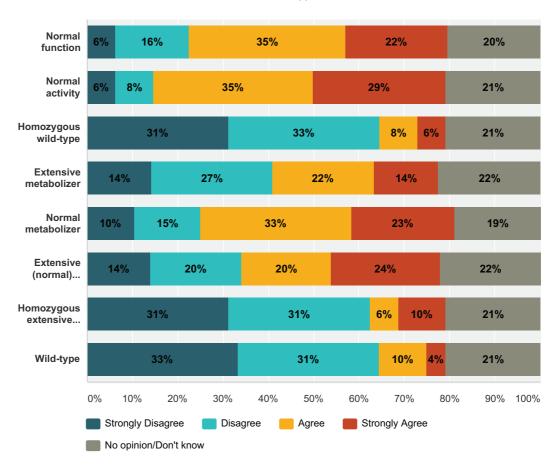
	Strongly Disagree	Disagree	Agree	Strongly Agree	No opinion/Don't know	Total	Weighted Average
High function	4%	41%	24%	8%	24%		
	2.00	21.00	12.00	4.00	12.00	51	2.46
Increased function	6%	34%	25%	13%	23%		
	3.00	18.00	13.00	7.00	12.00	53	2.59
Ultra-rapid function	12%	31%	18%	16%	22%		
	6.00	15.00	9.00	8.00	11.00	49	2.50
High activity	6%	32%	26%	14%	22%		
	3.00	16.00	13.00	7.00	11.00	50	2.62
Ultra-rapid activity	10%	31%	24%	12%	22%		
	5.00	15.00	12.00	6.00	11.00	49	2.50
Ultra-rapid metabolizer	8%	22%	18%	28%	24%		
	4.00	11.00	9.00	14.00	12.00	50	2.87
Increased metabolizer	10%	37%	25%	6%	22%		
	5.00	19.00	13.00	3.00	11.00	51	2.35

Ultra-fast metabolizer	10%	38%	18%	12%	22%		
	5.00	19.00	9.00	6.00	11.00	50	2.41

#	Other (please specify)	Date
1	Increased activity	2/21/2015 7:52 PM
2	Very increased function	2/20/2015 5:16 PM
3	Increased Activity	2/20/2015 4:13 PM
4	Homozygous increased metabolizer	2/18/2015 10:27 AM

Q37 Describe your degree of acceptance of the following terms to describe the presumed phenotype for UGT1A1 in an individual with normal UGT1A1 function/activity (e.g., UGT1A1*1/*1):

Answered: 52 Skipped: 6



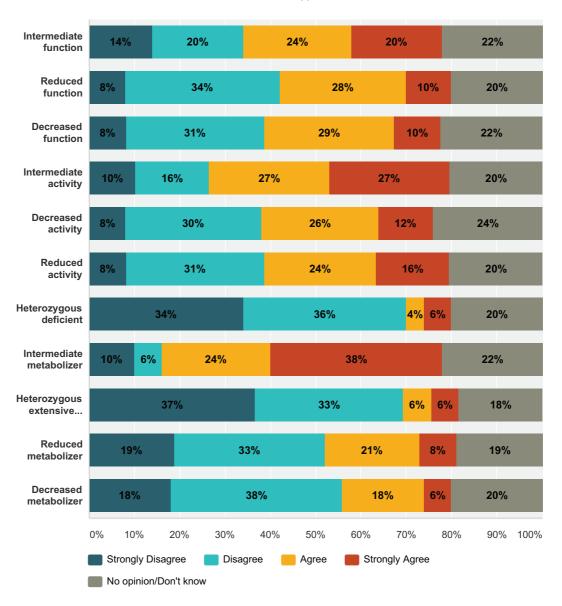
	Strongly Disagree	Disagree	Agree	Strongly Agree	No opinion/Don't know	Total	Weighted Average
Normal function	6%	16%	35%	22%	20%		
	3.00	8.00	17.00	11.00	10.00	49	2.92
Normal activity	6%	8%	35%	29%	21%		
	3.00	4.00	17.00	14.00	10.00	48	3.11
Homozygous wild-type	31%	33%	8%	6%	21%		
	15.00	16.00	4.00	3.00	10.00	48	1.87
Extensive metabolizer	14%	27%	22%	14%	22%		
	7.00	13.00	11.00	7.00	11.00	49	2.47
Normal metabolizer	10%	15%	33%	23%	19%		
	5.00	7.00	16.00	11.00	9.00	48	2.85
Extensive (normal) metabolizer	14%	20%	20%	24%	22%		
	7.00	10.00	10.00	12.00	11.00	50	2.69

Homozygous extensive metabolizer	31% 15.00	31% 15.00	6% 3.00	10% 5.00	21% 10.00	48	1.95
Wild-type	33%	31%	10%	4%	21%		
	16.00	15.00	5.00	2.00	10.00	48	1.82

#	Other (please specify)	Date
1	Reference function	2/20/2015 5:16 PM
2	Homozygous normal metabolizer	2/18/2015 10:27 AM

Q38 Describe your degree of acceptance of the following terms to describe the presumed phenotype for UGT1A1 in an individual with medium/some UGT1A1 function/activity (e.g., UGT1A1*1/*28):

Answered: 53 Skipped: 5



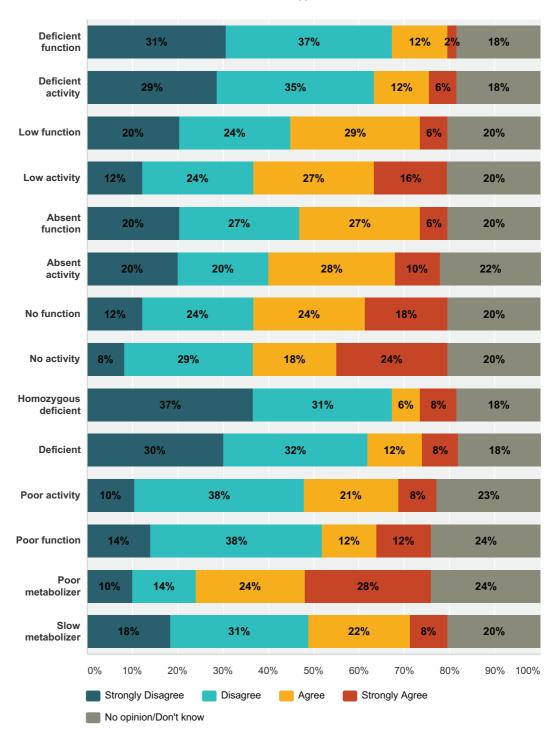
	Strongly Disagree	Disagree	Agree	Strongly Agree	No opinion/Don't know	Total	Weighted Average
Intermediate function	14%	20%	24%	20%	22%		
	7.00	10.00	12.00	10.00	11.00	50	2.64
Reduced function	8%	34%	28%	10%	20%		
	4.00	17.00	14.00	5.00	10.00	50	2.50
Decreased function	8%	31%	29%	10%	22%		
	4.00	15.00	14.00	5.00	11.00	49	2.53

Intermediate activity	10%	16%	27%	27%	20%		
	5.00	8.00	13.00	13.00	10.00	49	2
Decreased activity	8%	30%	26%	12%	24%		
	4.00	15.00	13.00	6.00	12.00	50	2
Reduced activity	8%	31%	24%	16%	20%		
	4.00	15.00	12.00	8.00	10.00	49	2
Heterozygous deficient	34%	36%	4%	6%	20%		
	17.00	18.00	2.00	3.00	10.00	50	,
Intermediate metabolizer	10%	6%	24%	38%	22%		
	5.00	3.00	12.00	19.00	11.00	50	(
Heterozygous extensive	37%	33%	6%	6%	18%		
metabolizer	18.00	16.00	3.00	3.00	9.00	49	,
Reduced metabolizer	19%	33%	21%	8%	19%		
	9.00	16.00	10.00	4.00	9.00	48	2
Decreased metabolizer	18%	38%	18%	6%	20%		
	9.00	19.00	9.00	3.00	10.00	50	2

#	Other (please specify)	Date
1	Heterozygous decreased metabolizer	2/18/2015 10:27 AM

Q39 Describe your degree of acceptance of the following terms to describe the presumed phenotype for UGT1A1 in an individual with no or very little UGT1A1 function/activity (e.g., UGT1A1*28/*28):

Answered: 53 Skipped: 5

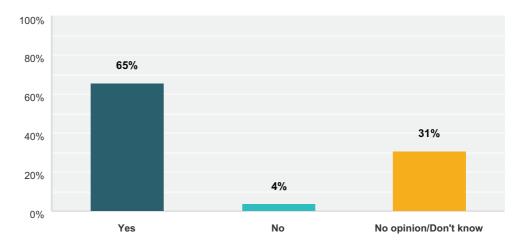


Deficient function	31%	37%	12%	2%	18%		
	15.00	18.00	6.00	1.00	9.00	49	1.8
Deficient activity	29%	35%	12%	6%	18%		
	14.00	17.00	6.00	3.00	9.00	49	1.9
Low function	20%	24%	29%	6%	20%		
	10.00	12.00	14.00	3.00	10.00	49	2.2
Low activity	12%	24%	27%	16%	20%		
	6.00	12.00	13.00	8.00	10.00	49	2.5
Absent function	20%	27%	27%	6%	20%		
	10.00	13.00	13.00	3.00	10.00	49	2.:
Absent activity	20%	20%	28%	10%	22%		
	10.00	10.00	14.00	5.00	11.00	50	2.3
No function	12%	24%	24%	18%	20%		
	6.00	12.00	12.00	9.00	10.00	49	2.
No activity	8%	29%	18%	24%	20%		
	4.00	14.00	9.00	12.00	10.00	49	2.
Homozygous deficient	37%	31%	6%	8%	18%		
	18.00	15.00	3.00	4.00	9.00	49	1.
Deficient	30%	32%	12%	8%	18%		
	15.00	16.00	6.00	4.00	9.00	50	1.
Poor activity	10%	38%	21%	8%	23%		
	5.00	18.00	10.00	4.00	11.00	48	2.
Poor function	14%	38%	12%	12%	24%		
	7.00	19.00	6.00	6.00	12.00	50	2.
Poor metabolizer	10%	14%	24%	28%	24%		
	5.00	7.00	12.00	14.00	12.00	50	2.
Slow metabolizer	18%	31%	22%	8%	20%		
	9.00	15.00	11.00	4.00	10.00	49	2.

#	Other (please specify)	Date
1	Don't lump "no activity" and "very little activity" together	2/20/2015 4:59 PM
2	homozygous low activity	2/6/2015 11:54 AM
3	"Little or no activity" would seem to be appropriate	2/3/2015 1:49 PM

Q40 We assume that 3 major categories of allele function are needed for SLCO1B1. Do you agree (yes or no)? If no, please indicate how many you think are needed and why:

Answered: 52 Skipped: 6

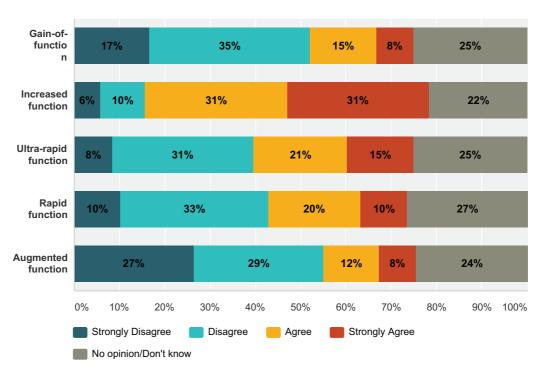


Answer Choices	Responses	
Yes	65%	34.00
No	4%	2.00
No opinion/Don't know	31%	16.00
Total		52

#	If No, please indicate how many you think are needed and why:	Date
1	consistency across genes (keep 4 categories)	2/3/2015 1:07 PM
2	need category for unknown function	2/2/2015 12:49 PM

Q41 Describe your degree of acceptance of the following terms to describe the allele function for a SLCO1B1 allele with high function (e.g., SLCO1B1*14):

Answered: 53 Skipped: 5

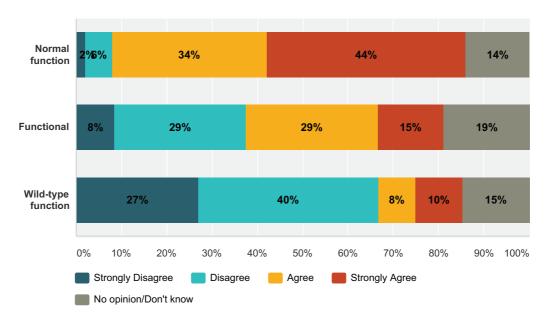


	Strongly Disagree	Disagree	Agree	Strongly Agree	No opinion/Don't know	Total	Weighted Average
Gain-of-function	17%	35%	15%	8%	25%		
	8.00	17.00	7.00	4.00	12.00	48	2.19
Increased function	6%	10%	31%	31%	22%		
	3.00	5.00	16.00	16.00	11.00	51	3.13
Ultra-rapid function	8%	31%	21%	15%	25%		
	4.00	15.00	10.00	7.00	12.00	48	2.50
Rapid function	10%	33%	20%	10%	27%		
	5.00	16.00	10.00	5.00	13.00	49	2.42
Augmented function	27%	29%	12%	8%	24%		
	13.00	14.00	6.00	4.00	12.00	49	2.03

#	Other (please specify)	Date
1	Increased activity	2/20/2015 5:18 PM
2	Increased Activity	2/20/2015 4:14 PM
3	Increased activity	2/20/2015 3:26 PM
4	higher than normal transport activity	2/16/2015 8:06 AM

Q42 Describe your degree of acceptance of the following terms to describe the allele function for a SLCO1B1 allele with normal function (e.g., SLCO1B1*1):

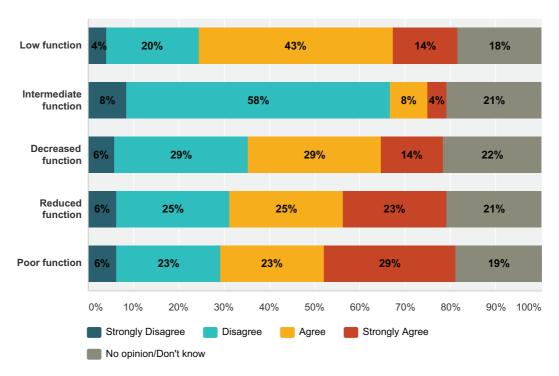
Answered: 52 Skipped: 6



	Strongly Disagree	Disagree	Agree	Strongly Agree	No opinion/Don't know	Total	Weighted Average
Normal function	2%	6%	34%	44%	14%		
	1.00	3.00	17.00	22.00	7.00	50	3.40
Functional	8%	29%	29%	15%	19%		
	4.00	14.00	14.00	7.00	9.00	48	2.62
Wild-type function	27%	40%	8%	10%	15%		
	13.00	19.00	4.00	5.00	7.00	48	2.02

#	Other please specifiy	Date
1	Reference activity	2/20/2015 5:18 PM
2	Normal Activity or Wild-type activity	2/20/2015 4:14 PM
3	normal transport activity	2/16/2015 8:06 AM

Q43 Describe your degree of acceptance of the following terms to describe the allele function for a SLCO1B1 allele very little function (e.g., SLCO1B1*5):

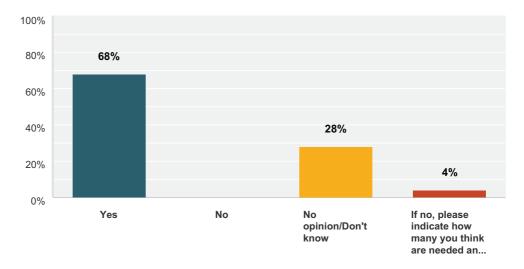


	Strongly Disagree	Disagree	Agree	Strongly Agree	No opinion/Don't know	Total	Weighted Average
Low function	4%	20%	43%	14%	18%		
	2.00	10.00	21.00	7.00	9.00	49	2.83
Intermediate function	8%	58%	8%	4%	21%		
	4.00	28.00	4.00	2.00	10.00	48	2.11
Decreased function	6%	29%	29%	14%	22%		
	3.00	15.00	15.00	7.00	11.00	51	2.65
Reduced function	6%	25%	25%	23%	21%		
	3.00	12.00	12.00	11.00	10.00	48	2.82
Poor function	6%	23%	23%	29%	19%		
	3.00	11.00	11.00	14.00	9.00	48	2.92

#	Other (please specify)	Date
1	Low activity	2/20/2015 5:18 PM
2	Reduced Activity or Decreased Activity	2/20/2015 4:14 PM
3	poor transport activity	2/16/2015 8:06 AM
4	Loss-of-function	2/11/2015 1:02 PM

Q44 We assume that 4 major categories of allele function are needed for SLCO1B1. Do you agree (yes or no)? If no, please indicate how many you think are needed and why:

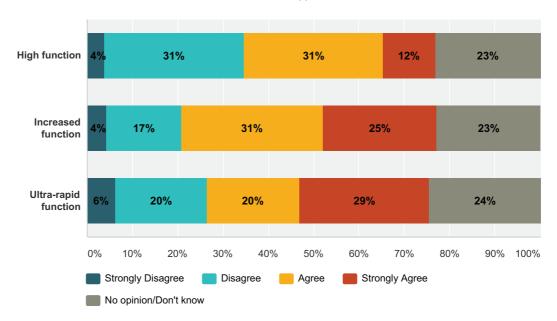
Answered: 50 Skipped: 8



Answer Choices	Responses	Responses	
Yes	68%	34.00	
No	0%	0.00	
No opinion/Don't know	28%	14.00	
If no, please indicate how many you think are needed and why:	4%	2.00	
Total		50	

#	If no, please indicate how many you think are needed and why:	Date	
1	I have no knowledge on this gene	2/11/2015 12:42 PM	
2	need categories for unknown	2/2/2015 12:50 PM	

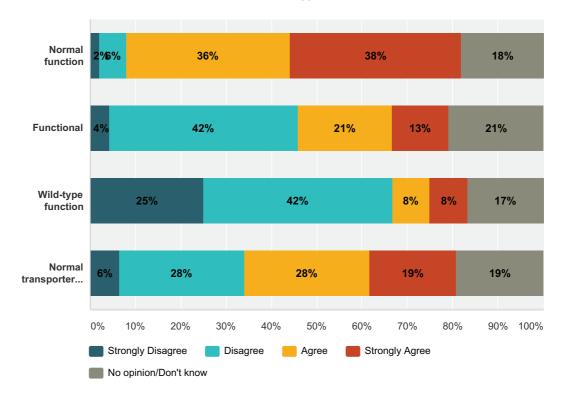
Q45 Describe your degree of acceptance of the following terms to describe the presumed phenotype for SLCO1B1 in an individual with very high SLCO1B1 function (e.g., SLCO1B1*14/*14):



	Strongly Disagree	Disagree	Agree	Strongly Agree	No opinion/Don't know	Total	Weighted Average
High function	4%	31%	31%	12%	23%		
	2.00	16.00	16.00	6.00	12.00	52	2.65
Increased function	4%	17%	31%	25%	23%		
	2.00	8.00	15.00	12.00	11.00	48	3.00
Ultra-rapid function	6%	20%	20%	29%	24%		
	3.00	10.00	10.00	14.00	12.00	49	2.95

#	Other (please specify)	Date
1	Very increased function	2/20/2015 5:18 PM
2	High Activity	2/20/2015 4:16 PM
3	higher than normal transport activity	2/16/2015 8:06 AM
4	High transporter function	2/11/2015 1:04 PM

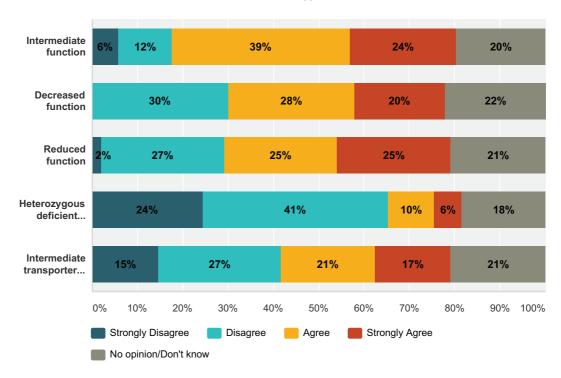
Q46 Describe your degree of acceptance of the following terms to describe the presumed phenotype for SLCO1B1 in an individual with normal SLCO1B1 function (e.g., SLCO1B1*1/*1):



	Strongly Disagree	Disagree	Agree	Strongly Agree	No opinion/Don't know	Total	Weighted Average
Normal function	2%	6%	36%	38%	18%		
	1.00	3.00	18.00	19.00	9.00	50	3.34
Functional	4%	42%	21%	13%	21%		
	2.00	20.00	10.00	6.00	10.00	48	2.53
Wild-type function	25%	42%	8%	8%	17%		
	12.00	20.00	4.00	4.00	8.00	48	2.00
Normal transporter	6%	28%	28%	19%	19%		
function	3.00	13.00	13.00	9.00	9.00	47	2.74

#	Other (please specify)	Date
1	Reference function	2/20/2015 5:18 PM
2	Normal Activity or Wild-type activity	2/20/2015 4:16 PM
3	normal transport activity	2/16/2015 8:06 AM

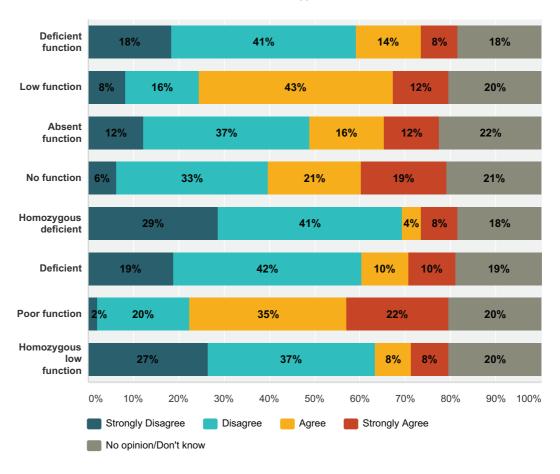
Q47 Describe your degree of acceptance of the following terms to describe the presumed phenotype for SLCO1B1 in an individual with medium/some SLCO1B1 function (e.g., SLCO1B1*1/*5):



	Strongly Disagree	Disagree	Agree	Strongly Agree	No opinion/Don't know	Total	Weighted Average
Intermediate function	6%	12%	39%	24%	20%		
	3.00	6.00	20.00	12.00	10.00	51	3.0
Decreased function	0%	30%	28%	20%	22%		
	0.00	15.00	14.00	10.00	11.00	50	2.8
Reduced function	2%	27%	25%	25%	21%		
	1.00	13.00	12.00	12.00	10.00	48	2.9
Heterozygous deficient	24%	41%	10%	6%	18%		
function	12.00	20.00	5.00	3.00	9.00	49	1.9
Intermediate transporter	15%	27%	21%	17%	21%		
function	7.00	13.00	10.00	8.00	10.00	48	2.5

#	Other (please specify)	Date
1	Reduced Activity or Decreased Activity	2/20/2015 4:16 PM
2	Heterozygous decreased function	2/18/2015 10:50 AM
3	decreased transport activity	2/16/2015 8:06 AM

Q48 Describe your degree of acceptance of the following terms to describe the presumed phenotype for SLCO1B1 in an individual with very little SLCO1B1 function (e.g., SLCO1B1*5/*5):



	Strongly Disagree	Disagree	Agree	Strongly Agree	No opinion/Don't know	Total	Weighted Average
Deficient function	18% 9.00	41% 20.00	14% 7.00	8% 4.00	18% 9.00	49	2.15
Low function	8% 4.00	16% 8.00	43% 21.00	12% 6.00	20% 10.00	49	2.74
Absent function	12% 6.00	37% 18.00	16% 8.00	12% 6.00	22% 11.00	49	2.37
No function	6% 3.00	33% 16.00	21% 10.00	19% 9.00	21% 10.00	48	2.66
Homozygous deficient	29% 14.00	41% 20.00	4% 2.00	8% 4.00	18% 9.00	49	1.90
Deficient	19% 9.00	42% 20.00	10% 5.00	10% 5.00	19% 9.00	48	2.15
Poor function	2% 1.00	20% 10.00	35% 17.00	22% 11.00	20% 10.00	49	2.97

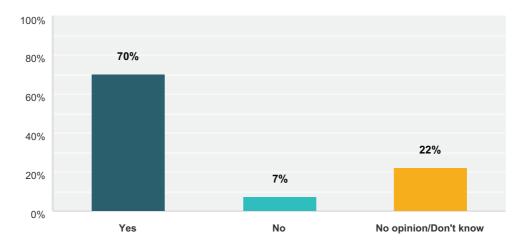
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Homozygous low function	27%	37%	8%	8%	20%		
	13.00	18.00	4.00	4.00	10.00	49	1.97

#	Other (please specify)	Date
1	No activity	2/20/2015 4:16 PM
2	poor transport activity	2/16/2015 8:06 AM
3	Low transporter function	2/11/2015 1:04 PM

Q49 We assume that 4 major categories of allele function are needed for VKORC1. Do you agree (yes or no)? If no, please indicate how many you think are needed and why:

Answered: 54 Skipped: 4

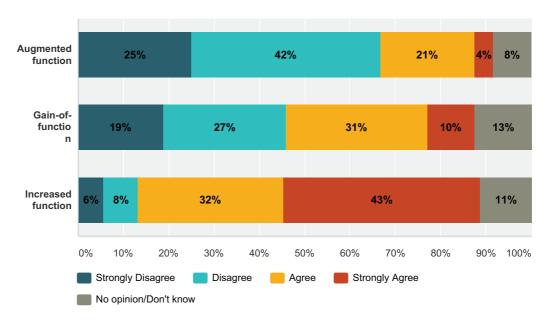


Answer Choices	Responses	
Yes	70%	38.00
No	7%	4.00
No opinion/Don't know	22%	12.00
Total		54

#	If No, please indicate how many you think are needed and why:	Date
1	I am not sure if VKORC1 variants can be classified according to functional activities, I am not sure there is sufficient biochemical studies to classify the activity of the VKORC1 variants.	2/13/2015 10:34 PM
2	I think that I would describe this as a target: resistant to inhibitors, normal activity, and sensitive based on EC50s to warfarin.	2/4/2015 1:35 PM
3	Such a categorization strategy would be nice for consistency, but clinical use of VKORC1 genotyping only requires results at a few SNPs. We don't need to summarize allele function at the moment, although starting the project would be nice to support future research.	2/3/2015 1:54 PM
4	NO convincing evidence for 4 phenotypes	2/2/2015 1:04 PM
5	need categories for unknown alleles	2/2/2015 12:52 PM

Q50 Describe your degree of acceptance of the following terms to describe the allele function for a VKORC1 allele with high function (e.g., VKORC1 D36Y):

Answered: 53 Skipped: 5

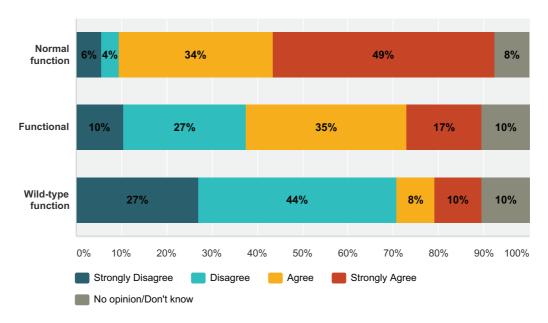


	Strongly Disagree	Disagree	Agree	Strongly Agree	No opinion/Don't know	Total	Weighted Average
Augmented function	25%	42%	21%	4%	8%		
	12.00	20.00	10.00	2.00	4.00	48	2.05
Gain-of-function	19%	27%	31%	10%	13%		
	9.00	13.00	15.00	5.00	6.00	48	2.38
Increased function	6%	8%	32%	43%	11%		
	3.00	4.00	17.00	23.00	6.00	53	3.28

#	Other (please specify)	Date
1	rather than function, might be more logical to categorize as degree of sensitivity to warfarin (or to inhibition)	2/21/2015 8:09 PM
2	Increased activity	2/20/2015 5:19 PM
3	Increased Activity	2/20/2015 4:17 PM
4	This allele is associated with higher doses. I wouldn't ascribe functional status to it.	2/20/2015 3:34 PM
5	higher than normal enzyme activity	2/16/2015 8:06 AM
6	Low warfarin sensitivity	2/4/2015 2:28 PM

Q51 Describe your degree of acceptance of the following terms to describe the allele function for a VKORC1 allele with normal function:

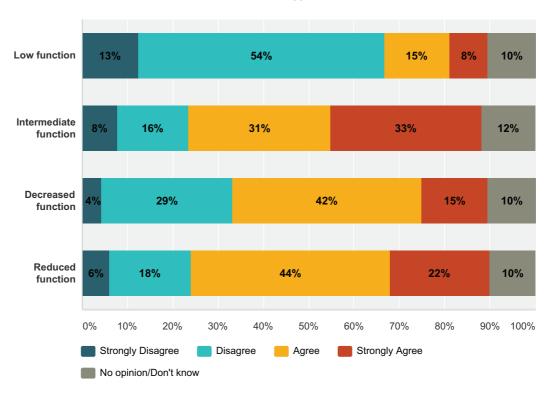
Answered: 53 Skipped: 5



	Strongly Disagree	Disagree	Agree	Strongly Agree	No opinion/Don't know	Total	Weighted Average
Normal function	6%	4%	34%	49%	8%		
	3.00	2.00	18.00	26.00	4.00	53	3.37
Functional	10%	27%	35%	17%	10%		
	5.00	13.00	17.00	8.00	5.00	48	2.65
Wild-type function	27%	44%	8%	10%	10%		
	13.00	21.00	4.00	5.00	5.00	48	2.02

#	Other please specifiy	Date
1	rather than function, might be more logical to categorize as degree of sensitivity to warfarin (or to inhibition)	2/21/2015 8:09 PM
2	Reference activity	2/20/2015 5:19 PM
3	Normal Activity or Wild-type activity	2/20/2015 4:17 PM
4	normal enzyme activity	2/16/2015 8:06 AM
5	Normal warfarin sensitivity	2/4/2015 2:28 PM
6	Active	2/2/2015 1:04 PM

Q52 Describe your degree of acceptance of the following terms to describe the allele function for a VKORC1 allele with medium/some function (e.g., VKORC1-1639G>A (rs9923231):

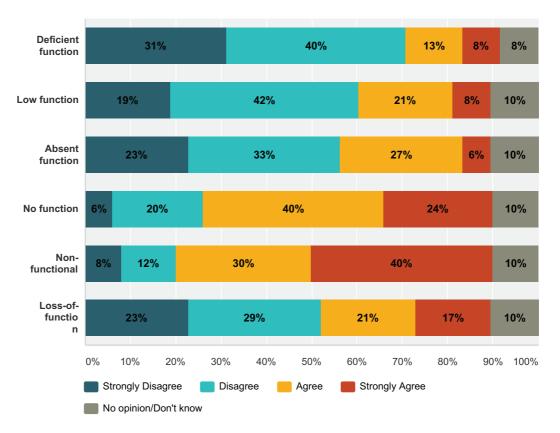


	Strongly Disagree	Disagree	Agree	Strongly Agree	No opinion/Don't know	Total	Weighted Average
Low function	13%	54%	15%	8%	10%		
	6.00	26.00	7.00	4.00	5.00	48	2.21
Intermediate function	8%	16%	31%	33%	12%		
	4.00	8.00	16.00	17.00	6.00	51	3.02
Decreased function	4%	29%	42%	15%	10%		
	2.00	14.00	20.00	7.00	5.00	48	2.74
Reduced function	6%	18%	44%	22%	10%		
	3.00	9.00	22.00	11.00	5.00	50	2.91

#	Other (please specify)	Date
1	rather than function, might be more logical to categorize as degree of sensitivity to warfarin (or to inhibition)	2/21/2015 8:09 PM
2	Decreased activity	2/20/2015 5:19 PM
3	Reduced activity or decreased activity	2/20/2015 4:17 PM
4	Reduced activity	2/20/2015 3:34 PM
5	lower than normal enzyme activity	2/16/2015 8:06 AM
6	Decreased activity or reduced activity	2/2/2015 1:04 PM

Q53 Describe your degree of acceptance of the following terms to describe the allele function for a VKORC1 allele with no function (e.g., VKORC1 L128R):

Answered: 53 Skipped: 5



	Strongly Disagree	Disagree	Agree	Strongly Agree	No opinion/Don't know	Total	Weighted Average
Deficient function	31%	40%	13%	8%	8%		
	15.00	19.00	6.00	4.00	4.00	48	1.9
Low function	19%	42%	21%	8%	10%		
	9.00	20.00	10.00	4.00	5.00	48	2.2
Absent function	23%	33%	27%	6%	10%		
	11.00	16.00	13.00	3.00	5.00	48	2.1
No function	6%	20%	40%	24%	10%		
	3.00	10.00	20.00	12.00	5.00	50	2.9
Non-functional	8%	12%	30%	40%	10%		
	4.00	6.00	15.00	20.00	5.00	50	3.1
Loss-of-function	23%	29%	21%	17%	10%		
	11.00	14.00	10.00	8.00	5.00	48	2.

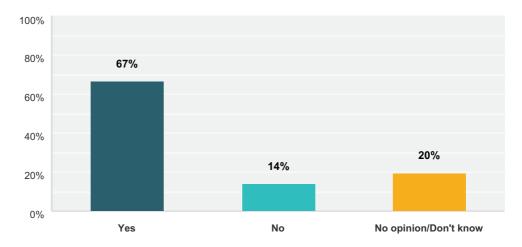
#	Other (please specify)	Date
1	rather than function, might be more logical to categorize as degree of sensitivity to warfarin (or to inhibition)	2/21/2015 8:09 PM
2	No activity	2/20/2015 5:19 PM

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3	No Activity	2/20/2015 4:17 PM
4	absent enzyme activity	2/16/2015 8:06 AM
5	High warfarin sensitivity	2/4/2015 2:28 PM
6	No activity	2/2/2015 1:04 PM

Q54 We assume that 4 major categories of phenotypes are needed for VKORC1. Do you agree (yes or no)? If no, please indicate how many you think are needed and why:

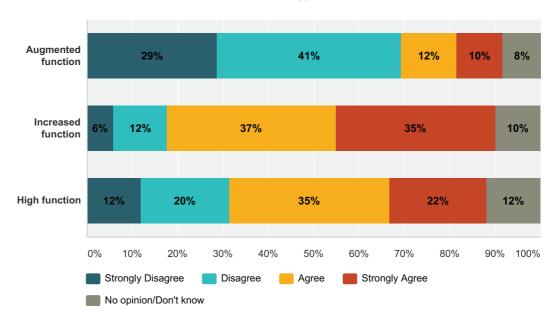
Answered: 51 Skipped: 7



Answer Choices	Responses	
Yes	67%	34.00
No	14%	7.00
No opinion/Don't know	20%	10.00
Total		51

#	If no, please indicate how many you think are needed and why:	Date
1	I am not sure if VKORC1 variants can be classified according to functional activities, I am not sure there is sufficient biochemical studies to classify the activity of the VKORC1 variants.	2/13/2015 10:35 PM
2	VKORC1 is reported with CYP2C9 for warfarin sensitivity. I don't know of any clinical scenario where VKORC1 would be needed separately from CYP2C9. Having a separate phenotype for VKORC1 seems unnecessarily complicated.	2/9/2015 4:19 PM
3	3. Low, Normal, High warfarin sensitivity	2/4/2015 2:29 PM
4	See my prior comment. The issue is whether VKOR resists inhibition or is more sensitive.	2/4/2015 1:37 PM
5	Again, summarization of VKORC1 results is not necessary in the current clinical landscape, but may be in the future. If it is, 4 categories would seem appropriate.	2/3/2015 2:28 PM
6	we need three 1. Low Warfarin Sensitivity 2. Intermediate Warfarin Sensitivity 3. High Warfarin Sensitivity	2/3/2015 11:29 AM
7	No clinical relevance of 4 phenotypes	2/2/2015 1:06 PM
8	need categories for genotypes with unknown alleles	2/2/2015 12:53 PM

Q55 Describe your degree of acceptance of the following terms to describe the presumed phenotype for VKORC1 in an individual with high function (e.g., individual carrying VKORC1 D36Y):

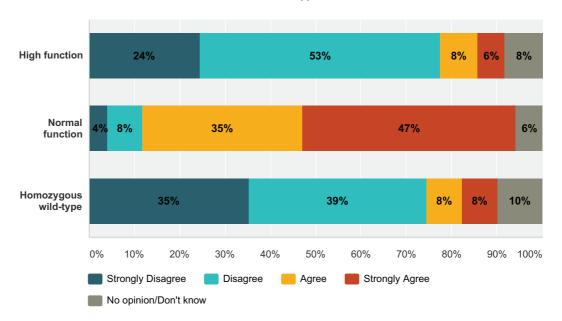


	Strongly Disagree	Disagree	Agree	Strongly Agree	No opinion/Don't know	Total	Weighted Average
Augmented function	29%	41%	12%	10%	8%		
	14.00	20.00	6.00	5.00	4.00	49	2.04
Increased function	6%	12%	37%	35%	10%		
	3.00	6.00	19.00	18.00	5.00	51	3.13
High function	12%	20%	35%	22%	12%		
	6.00	10.00	18.00	11.00	6.00	51	2.76

#	Other (please specify)	Date
1	Very increased function	2/20/2015 5:20 PM
2	Increased Activity	2/20/2015 4:18 PM
3	rapid metabolizer	2/16/2015 8:07 AM
4	Low warfarin sensitivity	2/4/2015 2:29 PM
5	see comment above	2/4/2015 1:37 PM

Q56 Describe your degree of acceptance of the following terms to describe the presumed phenotype for VKORC1 in an individual with normal VKORC1 function:

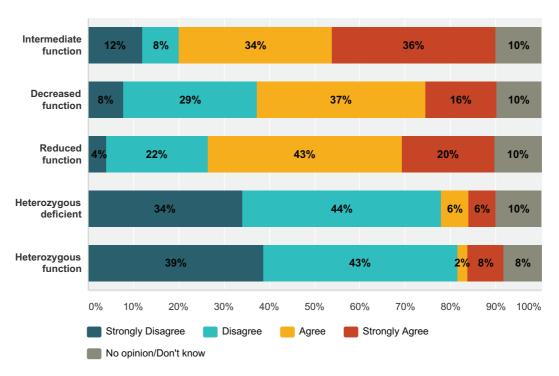
Answered: 53 Skipped: 5



	Strongly Disagree	Disagree	Agree	Strongly Agree	No opinion/Don't know	Total	Weighted Average
High function	24%	53%	8%	6%	8%		
	12.00	26.00	4.00	3.00	4.00	49	1.96
Normal function	4%	8%	35%	47%	6%		
	2.00	4.00	18.00	24.00	3.00	51	3.33
Homozygous wild-type	35%	39%	8%	8%	10%		
	18.00	20.00	4.00	4.00	5.00	51	1.87

#	Other (please specify)	Date
1	Reference function	2/20/2015 5:20 PM
2	Normal activity or wild-type activity	2/20/2015 4:18 PM
3	normal metabolizer	2/16/2015 8:07 AM
4	Normal warfarin sensitivity	2/4/2015 2:29 PM
5	see comment above	2/4/2015 1:37 PM
6	"Full function" seems more appropriate for proteins with highly polymorphic function	2/3/2015 2:28 PM
7	Normal activity	2/2/2015 1:06 PM

Q57 Describe your degree of acceptance of the following terms to describe the presumed phenotype for VKORC1 in an individual with medium/some function (e.g.,VKORC1-1639G>A (rs9923231) heterozygous individual):

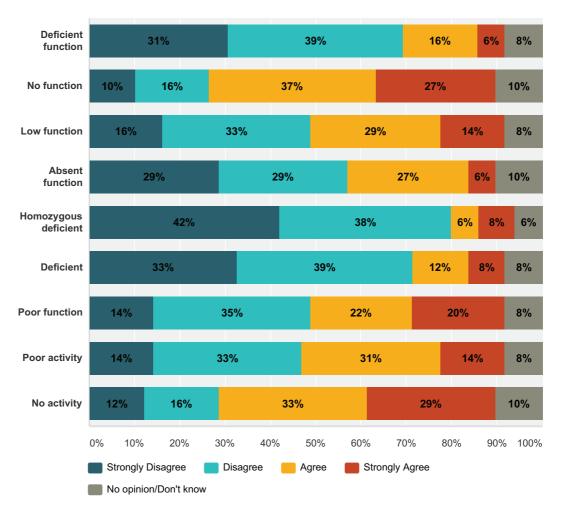


	Strongly Disagree	Disagree	Agree	Strongly Agree	No opinion/Don't know	Total	Weighted Average
Intermediate function	12%	8%	34%	36%	10%		
	6.00	4.00	17.00	18.00	5.00	50	3.04
Decreased function	8%	29%	37%	16%	10%		
	4.00	15.00	19.00	8.00	5.00	51	2.67
Reduced function	4%	22%	43%	20%	10%		
	2.00	11.00	21.00	10.00	5.00	49	2.89
Heterozygous deficient	34%	44%	6%	6%	10%		
	17.00	22.00	3.00	3.00	5.00	50	1.82
Heterozygous function	39%	43%	2%	8%	8%		
	19.00	21.00	1.00	4.00	4.00	49	1.78

#	Other (please specify)	Date
1	Decreased Activity or Reduced Activity	2/20/2015 4:18 PM
2	Heterozygous decreased function	2/18/2015 10:51 AM
3	intermediate metabolizer	2/16/2015 8:07 AM
4	see comment above	2/4/2015 1:37 PM

5 REduced activity 2/2/2015 1:06 PM

Q58 Describe your degree of acceptance of the following terms to describe the presumed phenotype for VKORC1 in an individual with no/very little function (e.g., VKORC1-1639G>A (rs9923231) homozygous individual):



	Strongly Disagree	Disagree	Agree	Strongly Agree	No opinion/Don't know	Total	Weighted Average
Deficient function	31%	39%	16%	6%	8%		
	15.00	19.00	8.00	3.00	4.00	49	1.98
No function	10%	16%	37%	27%	10%		
	5.00	8.00	18.00	13.00	5.00	49	2.89
Low function	16%	33%	29%	14%	8%		
	8.00	16.00	14.00	7.00	4.00	49	2.44
Absent function	29%	29%	27%	6%	10%		
	14.00	14.00	13.00	3.00	5.00	49	2.11
Homozygous deficient	42%	38%	6%	8%	6%		
	21.00	19.00	3.00	4.00	3.00	50	1.79

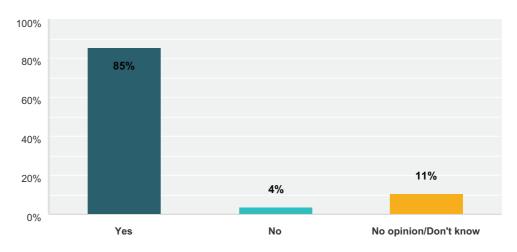
CPIC Term Standardization for Clinical Pharmacogenetic Test Results: alleles and phenotypes

Deficient	33%	39%	12%	8%	8%		
	16.00	19.00	6.00	4.00	4.00	49	1.9
Poor function	14%	35%	22%	20%	8%		
	7.00	17.00	11.00	10.00	4.00	49	2.5
Poor activity	14%	33%	31%	14%	8%		
	7.00	16.00	15.00	7.00	4.00	49	2.4
No activity	12%	16%	33%	29%	10%		
	6.00	8.00	16.00	14.00	5.00	49	2.8

#	Other (please specify)	Date
1	Separate terms for "no function" and "very little function"	2/20/2015 5:04 PM
2	Homozygous no function	2/18/2015 10:51 AM
3	poor metabolizer	2/16/2015 8:07 AM
4	High warfarin sensitivity	2/4/2015 2:29 PM
5	see comment above	2/4/2015 1:37 PM
6	"Little or no activity" or "Little or no function"	2/3/2015 2:28 PM

Q59 Currently, there are 3 HLA-B alleles that are subject to CPIC guidelines and strongly associated with specific adverse effects to drugs (HLA-B*57:01 for abacavir hypersensitivity; HLA-B*58:01 for allopurinol cutaneous reactions, and HLA-B*15:02 for carbamazepine and phenytoin cutaneous reactions). We assume that the PRESENCE and ABSENCE of each high risk allele should be documented. Do you agree? Yes or No. If no, what do you recommend?

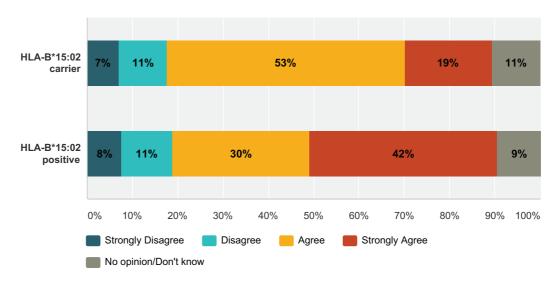
Answered: 55 Skipped: 3



Answer Choices	Responses	
Yes	85%	47.00
No	4%	2.00
No opinion/Don't know	11%	6.00
Total		55

#	If No, what do you recommend:	Date
1	I have experienced the issues with a reference lab reporting the strands of DNA code and no interpretation - the physicians have NO idea what to do with that information. I completely agree with the presence or absence approach.	2/19/2015 3:00 PM
2	For *57:01, *58:01, *15:02 I agree. Just wanted to note that there have been case(s) in which HLA alleles show a gene-dose effect, see Zhang et al. NEJM 2013: http://www.nejm.org/doi/full/10.1056/NEJMoa1213096, in case this becomes relevant in future CPIC guidelines.	2/3/2015 12:28 PM

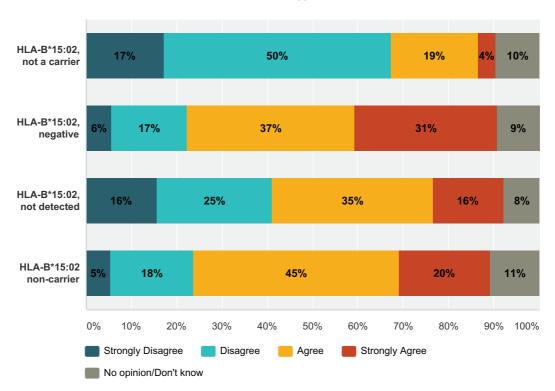
Q60 Describe your degree of acceptance of the following terms to describe the allele status for each high risk HLA-B allele tested (e.g., HLA-B*15:02):



	Strongly Disagree	Disagree	Agree	Strongly Agree	No opinion/Don't know	Total	Weighted Average
HLA-B*15:02 carrier	7%	11%	53%	19%	11%		
	4.00	6.00	30.00	11.00	6.00	57	2.94
HLA-B*15:02 positive	8%	11%	30%	42%	9%		
	4.00	6.00	16.00	22.00	5.00	53	3.17

#	Other (please specify)	Date
1	HLA-B*15:02 heterozygote and HLA-B*15:02 homozygote	2/20/2015 4:19 PM
2	HLA-B*15:02 present	2/16/2015 8:07 AM
3	the terms need to make sense genetically	2/3/2015 1:38 AM

Q61 Describe your degree of acceptance of the following terms to describe the allele status for each high risk HLA-B allele tested for (e.g., HLA-B*15:02) but found to be negative:

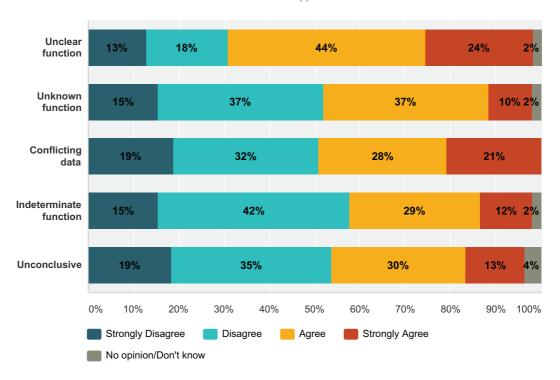


	Strongly Disagree	Disagree	Agree	Strongly Agree	No opinion/Don't know	Total	Weighted Average
HLA-B*15:02, not a carrier	17%	50%	19%	4%	10%		
	9.00	26.00	10.00	2.00	5.00	52	2.11
HLA-B*15:02, negative	6%	17%	37%	31%	9%		
	3.00	9.00	20.00	17.00	5.00	54	3.04
HLA-B*15:02, not detected	16%	25%	35%	16%	8%		
	8.00	13.00	18.00	8.00	4.00	51	2.55
HLA-B*15:02 non-carrier	5%	18%	45%	20%	11%		
	3.00	10.00	25.00	11.00	6.00	55	2.90

#	Other please specifiy	Date
1	HLA-B*15:02 absent	2/16/2015 8:07 AM

Q62 For variants with unclear function (i.e. literature supporting function is conflicting), describe your degree of acceptance of the following terms to describe the allele functions:

Answered: 57 Skipped: 1



	Strongly Disagree	Disagree	Agree	Strongly Agree	No opinion/Don't know	Total	Weighted Average
Unclear function	13%	18%	44%	24%	2%		
	7.00	10.00	24.00	13.00	1.00	55	2.80
Unknown function	15%	37%	37%	10%	2%		
	8.00	19.00	19.00	5.00	1.00	52	2.41
Conflicting data	19%	32%	28%	21%	0%		
	10.00	17.00	15.00	11.00	0.00	53	2.51
Indeterminate function	15%	42%	29%	12%	2%		
	8.00	22.00	15.00	6.00	1.00	52	2.37
Unconclusive	19%	35%	30%	13%	4%		
	10.00	19.00	16.00	7.00	2.00	54	2.38

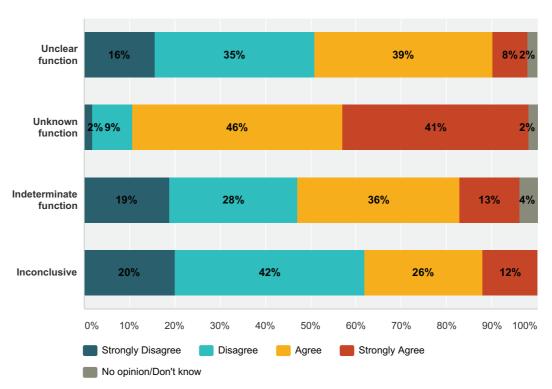
#	Other (please specify)	Date
1	Inconclusive	2/22/2015 2:49 PM
2	Uncertain function	2/21/2015 8:19 PM
3	Indeterminate activity	2/20/2015 5:22 PM
4	Prefer "inconclusive" to "unconclusive"	2/20/2015 5:08 PM
5	Uncertain significance	2/20/2015 4:24 PM

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6	Uncertain	2/20/2015 3:39 PM
7	A better terms would be "Uncertain function" which encompasses both Unknown (no data) and conflicting data and is also consistent with ACMG guidelines for Mendelian variants where we use "Uncertain significance" . Inconclusiev should be reserved for the overall result, not the individual variant.	2/19/2015 3:06 PM
8	I think you meant "Inconclusive"	2/19/2015 3:02 PM
9	unclear enzyme activity	2/16/2015 8:08 AM
10	Inconclusive	2/11/2015 12:51 PM
11	not known or not well understood	2/3/2015 3:54 PM
12	"Inconclusive" would be okay. "Unconclusive" is not standard English.	2/3/2015 2:33 PM
13	Inconclusive	2/3/2015 10:58 AM
14	Should use the term variant of uncertain significance to be compatible with ACMG terminology	2/3/2015 1:39 AM
15	Unclear activity	2/2/2015 1:08 PM

Q63 For variants with unknown function (i.e. no literature describing function), describe your degree of acceptance of the following terms to describe allele functions:

Answered: 57 Skipped: 1

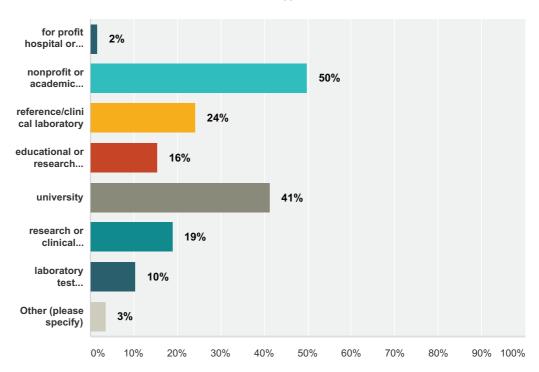


	Strongly Disagree	Disagree	Agree	Strongly Agree	No opinion/Don't know	Total	Weighted Average
Unclear function	16%	35%	39%	8%	2%		
	8.00	18.00	20.00	4.00	1.00	51	2.40
Unknown function	2%	9%	46%	41%	2%		
	1.00	5.00	26.00	23.00	1.00	56	3.29
Indeterminate function	19%	28%	36%	13%	4%		
	10.00	15.00	19.00	7.00	2.00	53	2.45
Inconclusive	20%	42%	26%	12%	0%		
	10.00	21.00	13.00	6.00	0.00	50	2.30

#	Other (please specify)	Date
1	Uncertain function	2/21/2015 8:19 PM
2	Unknown activity	2/20/2015 5:22 PM
3	Uncertain significance	2/20/2015 4:24 PM
4	Uncertain	2/20/2015 3:39 PM
5	see above	2/19/2015 3:06 PM
6	evidence unknown	2/18/2015 10:57 AM
7	unclear enzyme activity, unclear transport activity	2/16/2015 8:08 AM

8 Unknown activity 2/2/2015 1:08 PM

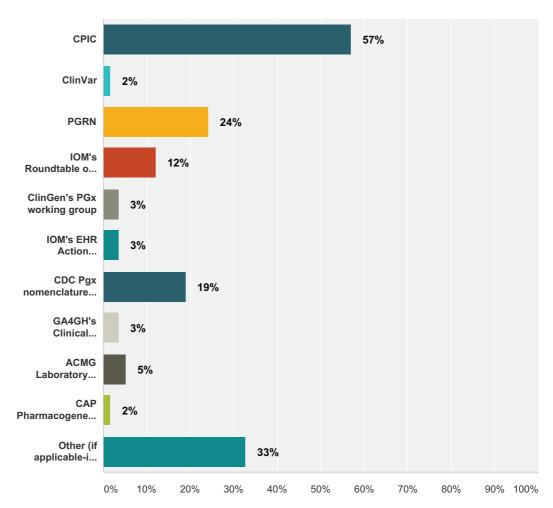
Q64 Which of the following describes your workplace setting (choose all that apply)?



Answer Choices	Responses	
for profit hospital or clinic	2%	1.00
nonprofit or academic hospital or clinic	50%	29.00
reference/clinical laboratory	24%	14.00
educational or research resource	16%	9.00
university	41%	24.00
research or clinical institute	19%	11.00
laboratory test interpretation sevice	10%	6.00
Other (please specify)	3%	2.00
otal Respondents: 58		

#	Other (please specify)	Date
1	Pharma	2/6/2015 12:00 PM
2	Manufacturer of genotyping and detection assays	2/3/2015 3:56 PM

Q65 Which of the following groups are you associated/a member (choose all that apply)?



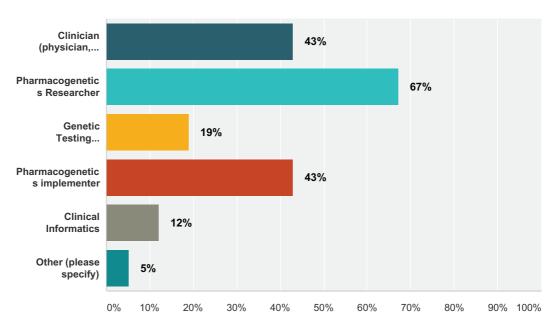
wer Choices	Responses	
CPIC	57%	33.00
ClinVar	2%	1.00
PGRN	24%	14.00
IOM's Roundtable on Translating Genomic-Based Research for Health	12%	7.00
ClinGen's PGx working group	3%	2.00
IOM's EHR Action Collaborative	3%	2.00
CDC Pgx nomenclature working group	19%	11.00
GA4GH's Clinical Working Group	3%	2.00
ACMG Laboratory Standards and Guidelines Committee	5%	3.00

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CAP Pharmacogenetics Working Group	2%	1.00
Other (if applicable-i.e. pharmacogenetics related):	33%	19.00
Total Respondents: 58		

#	Other (if applicable-i.e. pharmacogenetics related):	Date
1	Pharmacogenetics testing laboratory	2/22/2015 2:52 PM
2	none of the above	2/21/2015 8:21 PM
3	ClinGen Data Modeling working group, AMIA Genomics and Translational Bioinformatics working group, HL7 Clinical Genomics working group	2/20/2015 5:12 PM
4	N/A	2/19/2015 3:30 PM
5	eMERGE	2/19/2015 3:03 PM
6	DPWG	2/18/2015 3:59 PM
7	OBO foundry	2/18/2015 10:58 AM
8	PharmGKB	2/13/2015 10:37 PM
9	psychiatrists, other physicians	2/11/2015 12:46 PM
10	Children's Mercy Hospital Clinical Pharmacology	2/11/2015 12:44 PM
11	IPWG, ASCPT	2/6/2015 12:00 PM
12	TPMT nomenclature committee	2/6/2015 7:56 AM
13	PGRN TPP	2/5/2015 7:24 AM
14	AMP	2/4/2015 2:32 PM
15	AMP Member	2/3/2015 11:31 AM
16	IGNITE	2/3/2015 10:57 AM
17	European Medicines Agency, CHMP Pharmacogenomics Working Party; G2MC Pharmacogenomics Woking Group leader	2/3/2015 10:46 AM
18	n/a	2/3/2015 10:15 AM
19	IUPHAR Pharmacogenomics and genetics section	2/2/2015 1:10 PM

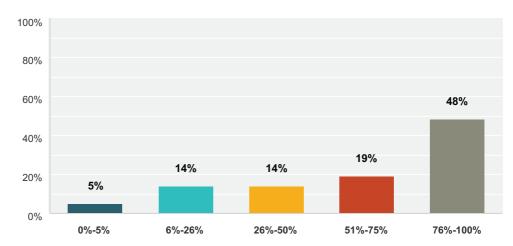
Q66 What capacity are you involved in clinical pharmacogenetics (choose all that apply)?



swer Choices	Responses	
Clinician (physician, pharmacist, nurse, etc.)	43%	25.0
Pharmacogenetics Researcher	67%	39.0
Genetic Testing Laboratory Staff	19%	11.0
Pharmacogenetics implementer	43%	25.0
Clinical Informatics	12%	7.0
Other (please specify)	5%	3.0
tal Respondents: 58		

#	Other (please specify)	Date
1	Developer of pg. educational materials for physicians	2/11/2015 1:28 PM
2	Scientific Curator	2/5/2015 1:19 PM
3	PGX Lab Director	2/4/2015 2:32 PM

Q67 What percentage of time do you devote to pharmacogenetics (i.e. research time, clinic time, etc.)?



Answer Choices	Responses	
0%-5%	5%	3.00
6%-26%	14%	8.00
26%-50%	14%	8.00
51%-75%	19%	11.00
76%-100%	48%	28.00
Total		58