Supplementary material

LAC SURVEY

Link: https://forms.gle/wnERH13ncFrD7yHj8

ENCUESTA: IMPLEMENTACIÓN FARMACOGENÓMICA EN AMERICA LATINA

Esta encuesta tiene por objeto evaluar los impedimentos, políticos, administrativos, sociales o clínicos existentes en la región Latinoamericana para la implementación de pruebas y protocolos farmacogenómicos, así mismo analizar que pares gen/fármaco consideran de relevancia para ser implementado en sus respectivos países.

edfarmaciaucr@gmail.com (no se comparten) Cambiar cuenta

*Obligatorio

Nombre *

Tu respuesta

País: *

Tu respuesta

Profesión: *

Tu respuesta

Correo electrónico: *

Tu respuesta

A. Considerando la relevancia la implementación de guías y ensayos farmacogenéticos/farmacogenómicos en Latinoamérica categorice en escala de 1 (baja relevancia) a 10 (alta relevancia), la relevancia de las siguientes barreras como impedimentos para implementación de la farmacogenómica en el ejercicio clínico.

1. Reticencia de los clínicos a usar marcadores farmacogenéticos *

	1	2	3	4	5	6	7	8	9	10	
Baja relevancia	○	○	○	○	○	○	○	○	○	○	Alta relevancia

2. Falta de clara información acerca de variantes genéticas que tengan relevancia * funcional en la farmacoterapia

	1	2	3	4	5	6	7	8	9	10	
Baja relevancia	○	○	○	○	○	○	○	○	○	○	Alta relevancia

3. Ausencia de instituciones o normas regulatorias que faciliten el uso de pruebas farmacogenéticas/farmacogenómicas *

	1	2	3	4	5	6	7	8	9	10	
Baja relevancia	○	○	○	○	○	○	○	○	○	○	Alta relevancia

4. Insuficiente caracterización de la variabilidad farmacogenética en Latinoamérica *

	1	2	3	4	5	6	7	8	9	10	
Baja relevancia	○	○	○	○	○	○	○	○	○	○	Alta relevancia

5. Insuficiente uso de medios electrónicos para obtener información de pacientes *

	1	2	3	4	5	6	7	8	9	10	
Baja relevancia	○	○	○	○	○	○	○	○	○	○	Alta relevancia

6. Falta de promoción de la farmacogenómica en los sistemas de salud *

	1	2	3	4	5	6	7	8	9	10	
Baja relevancia	○	○	○	○	○	○	○	○	○	○	Alta relevancia

7. Insuficiente preocupación de los clínicos en la farmacogenómica *

	1	2	3	4	5	6	7	8	9	10	
Baja relevancia	○	○	○	○	○	○	○	○	○	○	Alta relevancia

8. Necesidad de guías, procesos y protocolos de aplicación clínica de la * farmacogenética/farmacogenómica.

	1	2	3	4	5	6	7	8	9	10	
Baja relevancia	○	○	○	○	○	○	○	○	○	○	Alta relevancia

9. Necesidad de demostración de la validez clínica y utilidad de los test * farmacogenéticos/farmacogenómicos

	1	2	3	4	5	6	7	8	9	10	
Baja relevancia	○	○	○	○	○	○	○	○	○	○	Alta relevancia

10. Necesidad de implementación de ensayos gene/fármaco *

	1	2	3	4	5	6	7	8	9	10	
Baja relevancia	○	○	○	○	○	○	○	○	○	○	Alta relevancia

11. Preocupación acerca de los costos *

	1	2	3	4	5	6	7	8	9	10	
Baja relevancia	○	○	○	○	○	○	○	○	○	○	Alta relevancia

12. Falta de estudios farmacogenómicos de costo-efectividad en la región *

	1	2	3	4	5	6	7	8	9	10	
Baja relevancia	○	○	○	○	○	○	○	○	○	○	Alta relevancia

13. Fragmentación de los sistemas de salud *

	1	2	3	4	5	6	7	8	9	10	
Baja relevancia	○	○	○	○	○	○	○	○	○	○	Alta relevancia

14. Implicancias éticas, legales y sociales para la implementación de la farmacogenómica *

	1	2	3	4	5	6	7	8	9	10	
Baja relevancia	○	○	○	○	○	○	○	○	○	○	Alta relevancia

B. Considerando la relevancia del uso de los siguientes fármacos y la evidencia existente que usted conozca, categorice en escala de 1 a 5 la importancia de la implementación de determinaciones farmacogenómicas (variantes) de los genes involucrados. Considere que el listado se encuentra en el orden GEN-Fármaco(s). Para su apoyo se le adjunta links de acceso a CPIC y PharmGKB.
(https://cpicpgx.org/guidelines/ ; https://www.pharmgkb.org)

Categorice según las siguientes opciones: 1 (Muy poca importancia), 2 (Poca importancia), 3 (Moderada importancia), 4 (Importante) y 5 (Muy importante) *

	1	2	3	4	5
1. CFTR-Ivacaftor	○	○	○	○	○
2. CYP2B6-Efavirenz	○	○	○	○	○
3. CYP2C19-Clopidogrel	○	○	○	○	○
4. CYP2C19-Inhibidores de bomba de protones (prazoles)	○	○	○	○	○
5. CYP2C19-voriconazol	○	○	○	○	○
6. CYP2C9-Anti-inflamatorios no esteroidales (NSAIDs)	○	○	○	○	○
7. CYP2C9-fenitoína/fosfenitoína	○	○	○	○	○
8. HLA-B-fenitoína/fosfenitoína	○	○	○	○	○

9. CYP2C9-Cumarinas (warfarina, acenocumarol, fenprocumon)	○	○	○	○	○
10. VKORC1-Cumarinas (warfarina, acenocumarol, fenprocumon)	○	○	○	○	○
11. CYP4F2-Cumarinas (warfarina, acenocumarol, fenprocumon)	○	○	○	○	○
12. CYP2D6-Atomoxetina	○	○	○	○	○
13. CYP2D6-Ondasentrón/topisentrón	○	○	○	○	○
14. CYP2D6-tamoxifeno	○	○	○	○	○
15. CYP2D6- Inhibidores de la recaptación de Serotonina (citalopram, escitalopram)	○	○	○	○	○
16. CYP2C19- Inhibidores de la recaptación de Serotonina (fluvoxamina, paroxetina, sertralina)	○	○	○	○	○
17. CYP2D6- Antidepresivos tricíclicos (amitriptilina, clomipramina, desipramina)	○	○	○	○	○
18. CYP2C19- Antidepresivos tricíclicos (doxepina, imipramina, nortriptilina, trimipramina).	○	○	○	○	○
19. CYP2D6-Opioides	○	○	○	○	○

20. OPRM1-Opioides	○	○	○	○	○
21. COMT-Opioides	○	○	○	○	○
22. CYP3A5-Tacrolimus	○	○	○	○	○
23. DPYD-Fluoropirimidinas (5-Fluorouracilo, capecitabina, tegafur)	○	○	○	○	○
24. G6PD-rasburicasa	○	○	○	○	○
25. HLA-Carbamazepina/oxcarbazepina	○	○	○	○	○
26. HLA-B-Abacavir	○	○	○	○	○
27. HLA-B-Alopurinol	○	○	○	○	○
28. IFNL3-peginterferón	○	○	○	○	○
29. MT-RNR1-aminoglicósidos	○	○	○	○	○
30. RYR1-Enflurano o derivados	○	○	○	○	○
31. CACNA1S- Enflurano o derivados	○	○	○	○	○
32. SLCO1B1-Estatinas	○	○	○	○	○
33. ABCG2-Estatinas	○	○	○	○	○

34. CYP2C9-Estatinas	○	○	○	○	○
35. TPMT-Tiopurinas (azatioprina, mercaptopurinas, tioguanina)	○	○	○	○	○
36. NUDT15- Tiopurinas (azatioprina, mercaptopurinas, tioguanina)	○	○	○	○	○
37. UGT1A1-Atazanavir	○	○	○	○	○

PARES NO-CPIC *

	1	2	3	4	5
1. CYP2C19-Drospirenona	○	○	○	○	○
2. CYP2C19-Etinilestradiol	○	○	○	○	○
3. CYP3A4-Benzodiazepinas	○	○	○	○	○
4. CYP2D6-Benzodiazepinas	○	○	○	○	○
5. CYP2D6-aripiprazol	○	○	○	○	○
6. CYP2D6-carvedilol	○	○	○	○	○

7. CYP2D6-venlafaxina	○	○	○	○	○
8. CYP2D6-risperidona	○	○	○	○	○
9. CYP1A2-clozapina/olanzapina	○	○	○	○	○
10. CYP3A4-Haloperidol	○	○	○	○	○
11. GSTs-cisplatino	○	○	○	○	○

Mencione algún otro par gen-droga que usted considere relevante, donde exista evidencia científica.

Tu respuesta

Enviar

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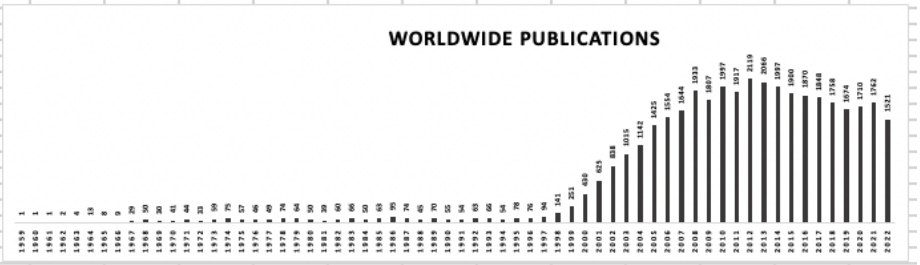
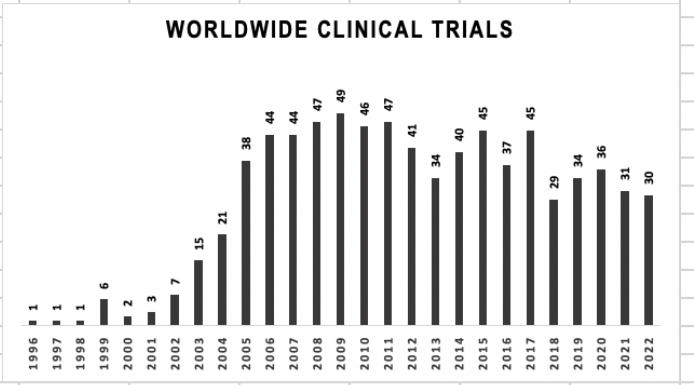
PGX WORLDWIDE PUBLICATIONS (1959-2022)

Year	Number of Publicacions
2022	1521
2021	1762
2020	1710
2019	1674
2018	1758
2017	1848
2016	1870
2015	1900
2014	1997
2013	2066
2012	2119
2011	1917
2010	1997
2009	1807
2008	1933
2007	1644
2006	1554
2005	1425
2004	1142
2003	1015
2002	838
2001	625
2000	430
1999	251
1998	141
1997	94
1996	76
1995	78
1994	54
1993	66
1992	63
1991	54
1990	55
1989	70
1988	45
1987	74
1986	95
1985	63
1984	50
1983	66
1982	60
1981	39
1980	50
1979	64
1978	74
1977	49
1976	46
1975	57
1974	75
1973	59
1972	33
1971	44
1970	41
1969	30
1968	50
1967	29
1966	9
1965	8
1964	13
1963	4
1962	2
1961	1
1960	1
1959	1
	38786 38786



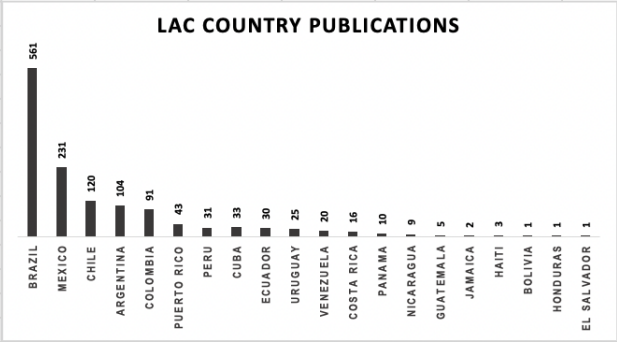
PGX-RELATED CLINICAL TRIALS WORLDWIDE (1996-2022)

Year	Trials
2022	30
2021	31
2020	36
2019	34
2018	29
2017	45
2016	37
2015	45
2014	40
2013	34
2012	41
2011	47
2010	46
2009	49
2008	47
2007	44
2006	44
2005	38
2004	21
2003	15
2002	7
2001	3
2000	2
1999	6
1998	1
1997	1
1996	1



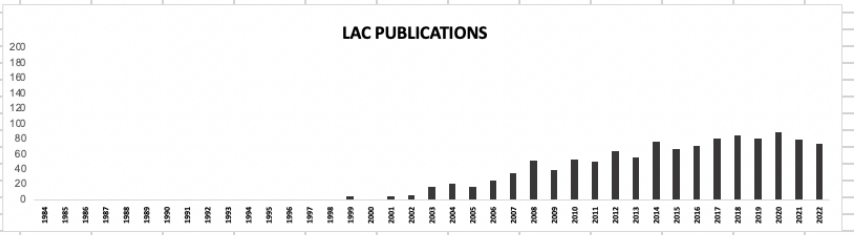
PGX LAC PUBLICATIONS BY COUNTRY

Países	Número de Publicaciones	Responden la encuesta	%
BRAZIL	561	SI	41,95961107
MEXICO	231	SI	17,27748691
CHILE	120	SI	8,975317876
ARGENTINA	104	SI	7,778608826
COLOMBIA	91	SI	6,806282723
PUERTO RICO	43	NO	3,216155572
PERU	31	SI	2,318623785
CUBA	33	SI	2,468212416
ECUADOR	30	SI	2,243829469
URUGUAY	25	SI	1,869857891
VENEZUELA	20	SI	1,495886313
COSTA RICA	16	SI	1,19670905
PANAMA	10	NO	0,747943156
NICARAGUA	9	SI	0,673148841
GUATEMALA	5	SI	0,373971578
JAMAICA	2	NO	0,149588631
HAITI	3	NO	0,224382947
BOLIVIA	1	SI	0,074794316
HONDURAS	1	SI	0,074794316
EL SALVADOR	1	SI	0,074794316
BÉLICE	0	SI	
	1337		



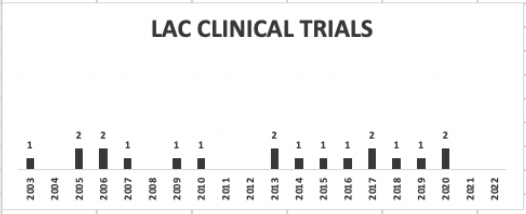
PGX LAC PUBLICATIONS BY YEAR (1984-2022)

Año	Número de Publicaciones
2022	74
2021	80
2020	90
2019	81
2018	86
2017	81
2016	72
2015	68
2014	77
2013	56
2012	65
2011	51
2010	54
2009	39
2008	52
2007	36
2006	26
2005	18
2004	22
2003	17
2002	6
2001	5
2000	1
1999	5
1998	1
1997	0
1996	0
1995	1
1994	1
1993	1
1992	0
1991	0
1990	0
1989	0
1988	1
1987	0
1986	0
1985	0
1984	1



LAC CLINICAL TRIALS (2003-2022)

Clinical trials LAC					
2022	0				
2021	0				
2020	2		CHILE, MÉXICO, PERÚ	MÉXICO	
2019	1		BRASIL		
2018	1		MÉXICO, PERÚ		
2017	2	COLOMBIA	CHILE, MÉXICO, PERÚ		
2016	1		MÉXICO		
2015	1		URUGUAY		
2014	1	PUERTO RICO			
2013	2		BRASIL	PUERTO RICO	
2012	0				
2011	0				
2010	1		BRAZIL		
2009	1	CHILE			
2008	0				
2007	1		ARGENTINA		
2006	2	PUERTO RICO	ARGENTINA		
2005	2	MÉXICO	PUERTO RICO		
2004	0				
2003	1		MÉXICO		
2002	0				
2001	0				
2000	0				
1999	0				
1998	0				
1997	0				
1996	0				
	19				



LAC PGx Courses: Links:

1. https://www.fq.edu.uy/?q=es/node/1269
2. https://www.favaloro.edu.ar/informacion/bioFARG_curso-de-farmacogenomica/
3. https://www.fcq.unc.edu.ar/node/128
4. https://www.infobioquimica.com/new/2020/08/12/entrevista-con-el-dr-german-perez-argentina-curso-virtual-de-farmacogenomica-en-oncologia/
5. https://www.portaleducacao.com.br/curso-online-farmacia-farmacogenetica/p?utm_term=&utm_campaign=2022_abr_mai_conv-purch_vds_portal-educacao_play-estudante-ongoing&utm_source=adwords&utm_medium=ppc&hsa_acc=2284317825&hsa_cam=17076386131&hsa_grp=&hsa_ad=&hsa_src=x&hsa_tgt=&hsa_kw=&hsa_mt=&hsa_net=adwords&hsa_ver=3&gclid=CjwKCAjwiOCgBhAgEiwAjv5whNfjrf-_qXQghcc1TrIJ-Np3mJVFMiumgpd8gO4YiHOAABSGQfVgnhoC53MQAvD_BwE
6. https://www.galileo.edu/fabiq/carrera/maestria-biologia-molecular/pensum/
7. https://cursalud.cl/producto/curso-de-farmacogenetica-y-farmacogenomica-e-learning/
8. https://www.uv.mx/mlcat/files/2019/06/Farmacogenomica.pdf
9. https://www.inmegen.gob.mx/media/filer_public/d6/82/d68282c4-28f7-4fe1-aa70-e38e5c45077d/33_edc_farma_facebook.jpg

STATISTICS

		Average (2014)	Standard deviation +- (2014)		Average (2022)	Standard deviation +- (2022)	*p- value **
Reluctance of clinicians to use pharmacogenetic markers	20	6,748466258	1,355828221	106	5,575471698	2,522085732	***0,0042***
Lack of clear information about genetic variants that will have functional relevance in pharmacotherapy	20	7,141104294	1,116564417	106	7,056603774	2,731928287	*0,8173*
Absence of institutions or regulatory norms that facilitate the use of pharmacogenetic/pharmacogenomic tests	20	8,45398773	1,18404908	106	8,849056604	1,845418795	*0,2240*
Insufficient characterization of pharmacogenetic variability in Latin American populations	20	8,141104294	1,153374233	106	8,075471698	1,993790901	*0,8397*
Insufficient use of electronic records information on patient	20	7,797546012	1,030674847	106	7,311320755	2,485628052	*0,1497*
Healthcare systems do not promote pharmacogenomics use	20	7,748466258	1,90797546	106	8,858490566	2,063001416	***0,0257***
Insufficient concern about pharmacogenomics among clinicians	20	8,496932515	0,932515337	106	7,301886792	2,403052865	***0,0003***
Need for clear guidelines, processes and protocols for the clinical application of pharmacogenetics/pharmacogenomics in LAC	20	8,748466258	0,914110429	106	9,056603774	1,73934957	*0,2508*
Need for demonstration of clinical validity and utility of pharmacogenetic/pharmacogenomic tests	20	6,889570552	1,122699387	106	8,556603774	1,867415778	***<0,0001***
Need for implementation of gene/drug trials	20	7,423312883	0,993865031	106	8,745283019	1,621647139	***<0,0001***
Concerns about test costs	20	7,484662577	1,104294479	106	8,481132075	1,837343486	***0,0021***
Lack of cost-effectiveness pharmacogenomics studies in the region	20	**	**	106	8,962264151	1,5487293	
Fragmentation of healthcare systems	20	8,325153374	1,073619632	106	8,103773585	2,284228515	*0,5010*
Ethical, legal and social implications for the implementation of pharmacogenomics	20	6,049079755	1,214723926	106	7,58490566	2,49138678	***0,0001***
		N (year 2014) = 20			N (year 2022) = 106		

* Two-sample student test with unequal variances

* Empty data: No requested in 2014

Reluctance of clinicians to use pharmacogenetic markers

```
Two-sample t test with unequal variances

   |        Obs        Mean    Std. err.   Std. dev.   [95% conf. interval]
---+--------------------------------------------------------------------
   x |         20     6,04908    ,2716205    1,214724    5,480571    6,617588
   y |        106    7,584906    ,2419849    2,491387    7,105094    8,064717
---+--------------------------------------------------------------------
Combined |        126    7,341124    ,2137286    2,399097    6,918128    7,764119
---+--------------------------------------------------------------------
    diff |           -1,535826    ,3637779               -2,264891   -,806761
------------------------------------------------------------------------------
    diff = mean(x) - mean(y)                                      t =  -4,2219
H0: diff = 0                     Satterthwaite's degrees of freedom =  54,8741

    Ha: diff < 0                 Ha: diff != 0                 Ha: diff > 0
 Pr(T < t) = 0,0000         Pr(|T| > |t|) = 0,0001          Pr(T > t) = 1,0000

. ttesti 20 6.748466258 1.355828221 106 5.575471698 2.522085732, une
```

Lack of clear information about genetic variants that will have functional relevance in pharmacotherapy

```
Two-sample t test with unequal variances

   |        Obs        Mean    Std. err.   Std. dev.   [95% conf. interval]
---+--------------------------------------------------------------------
   x |         20    6,748466    ,3031724    1,355828    6,113919    7,383013
   y |        106    5,575472    ,2449666    2,522086    5,089748    6,061195
---+--------------------------------------------------------------------
Combined |        126    5,761661    ,2146941    2,409936    5,336755    6,186568
---+--------------------------------------------------------------------
    diff |            1,172995    ,3897719                ,3893859    1,956603
------------------------------------------------------------------------------
    diff = mean(x) - mean(y)                                      t =   3,0094
H0: diff = 0                     Satterthwaite's degrees of freedom =  48,1913

    Ha: diff < 0                 Ha: diff != 0                 Ha: diff > 0
 Pr(T < t) = 0,9979         Pr(|T| > |t|) = 0,0042          Pr(T > t) = 0,0021

.  ttesti 20 7.141104294 1.116564417106 106 7.056603774 2.731928287, une
```

Absence of institutions or regulatory norms that facilitate the use of pharmacogenetic/pharmacogenomic tests

```
Two-sample t test with unequal variances

   |        Obs        Mean    Std. err.   Std. dev.   [95% conf. interval]
---+--------------------------------------------------------------------
   x |         20    7,141104    ,2496714    1,116564    6,618536    7,663673
   y |        106    7,056604    ,2653483    2,731928    6,530467     7,58274
---+--------------------------------------------------------------------
Combined |        126    7,070017     ,226424    2,541603    6,621895    7,518138
---+--------------------------------------------------------------------
    diff |           ,0845005    ,3643426               -,6421576    ,8111586
------------------------------------------------------------------------------
    diff = mean(x) - mean(y)                                      t =   0,2319
H0: diff = 0                     Satterthwaite's degrees of freedom =  70,0017

    Ha: diff < 0                 Ha: diff != 0                 Ha: diff > 0
 Pr(T < t) = 0,5914         Pr(|T| > |t|) = 0,8173          Pr(T > t) = 0,4086

. ttesti 20 8.45398773 1.18404908 106 8.849056604 1.845418795, une
```

Insufficient characterization of pharmacogenetic variability in Latin American populations

```
Two-sample t test with unequal variances

   |     Obs        Mean    Std. err.   Std. dev.   [95% conf. interval]
---+--------------------------------------------------------------------
   x |      20    8,453988   ,2647614   1,184049    7,899836    9,00814
   y |     106    8,849057   ,1792429   1,845419    8,493651    9,204462
---+--------------------------------------------------------------------
Combined |     126    8,786347   ,1567221   1,759201    8,476175    9,09652
---+--------------------------------------------------------------------
    diff |           -,3950689    ,319729               -1,04182    ,2516824
------------------------------------------------------------------------------
    diff = mean(x) - mean(y)                                      t =  -1,2356
H0: diff = 0                     Satterthwaite's degrees of freedom =  38,9279

    Ha: diff < 0                 Ha: diff != 0                 Ha: diff > 0
 Pr(T < t) = 0,1120         Pr(|T| > |t|) = 0,2240          Pr(T > t) = 0,8880

. ttesti 20 8.141104294 1.153374233 106 8.075471698 1.993790901, une
```

Insufficient use of electronic records information on patient

```
Two-sample t test with unequal variances

   |     Obs        Mean    Std. err.   Std. dev.   [95% conf. interval]
---+--------------------------------------------------------------------
   x |      20    8,141104   ,2579023   1,153374    7,601309      8,6809
   y |     106    8,075472   ,1936541   1,993791    7,691491    8,459452
---+--------------------------------------------------------------------
Combined |     126     8,08589   ,1676625   1,882007    7,754065    8,417715
---+--------------------------------------------------------------------
    diff |            ,0656326   ,3225144               -,5843784    ,7156436
------------------------------------------------------------------------------
    diff = mean(x) - mean(y)                                      t =   0,2035
H0: diff = 0                     Satterthwaite's degrees of freedom =  43,9378

    Ha: diff < 0                 Ha: diff != 0                 Ha: diff > 0
 Pr(T < t) = 0,5802         Pr(|T| > |t|) = 0,8397          Pr(T > t) = 0,4198

. ttesti 20 7.797546012 1.030674847 106 7.311320755 2.485628052, une
```

Healthcare systems do not promote pharmacogenomics use

```
Two-sample t test with unequal variances

   |     Obs        Mean    Std. err.   Std. dev.   [95% conf. interval]
---+--------------------------------------------------------------------
   x |      20    7,797546   ,2304659   1,030675    7,315175    8,279917
   y |     106    7,311321   ,2414255   2,485628    6,832619    7,790023
---+--------------------------------------------------------------------
Combined |     126    7,388499   ,2066955   2,320151    6,979423    7,797575
---+--------------------------------------------------------------------
    diff |            ,4862253   ,3337676               -,1796876    1,152138
------------------------------------------------------------------------------
    diff = mean(x) - mean(y)                                      t =   1,4568
H0: diff = 0                     Satterthwaite's degrees of freedom =  68,6262

    Ha: diff < 0                 Ha: diff != 0                 Ha: diff > 0
 Pr(T < t) = 0,9251         Pr(|T| > |t|) = 0,1497          Pr(T > t) = 0,0749

. ttesti 20 7.748466258 1.90797546 106 8.858490566 2.063001416, une
```

Insufficient concern about pharmacogenomics among clinicians

Two-sample t test with unequal variances

	Obs	Mean	Std. err.	Std. dev.	[95% conf.	interval]
x	20	7,748466	,4266363	1,907975	6,855506	8,641426
y	106	8,858491	,2003764	2,063001	8,461181	9,2558
Combined	126	8,682296	,1846104	2,072247	8,316929	9,047663
diff		-1,110024	,4713483		-2,075445	-,1446036

diff = mean(x) - mean(y) t = -2,3550
H0: diff = 0 Satterthwaite's degrees of freedom = 28,0597

Ha: diff < 0 Ha: diff != 0 Ha: diff > 0
Pr(T < t) = 0,0129 Pr(|T| > |t|) = 0,0257 Pr(T > t) = 0,9871

```
. ttesti 20 8.496932515 0.932515337 106 7.301886792 2.403052865, une
```

Need for clear guidelines, processes and protocols for the clinical application of pharmacogenetics/pharmacogenomics in LAC

Two-sample t test with unequal variances

	Obs	Mean	Std. err.	Std. dev.	[95% conf.	interval]
x	20	8,496933	,2085168	,9325153	8,060502	8,933363
y	106	7,301887	,2334051	2,403053	6,839088	7,764686
Combined	126	7,491577	,2026633	2,27489	7,090481	7,892672
diff		1,195046	,3129811		,5715696	1,818522

diff = mean(x) - mean(y) t = 3,8183
H0: diff = 0 Satterthwaite's degrees of freedom = 75,1052

Ha: diff < 0 Ha: diff != 0 Ha: diff > 0
Pr(T < t) = 0,9999 Pr(|T| > |t|) = 0,0003 Pr(T > t) = 0,0001

```
. ttesti 20 8.748466258 0.914110429 106 9.056603774 1.73934957, une
```

Need for demonstration of clinical validity and utility of pharmacogenetic/pharmacogenomic tests

Two-sample t test with unequal variances

	Obs	Mean	Std. err.	Std. dev.	[95% conf.	interval]
x	20	8,748466	,2044013	,9141104	8,320649	9,176283
y	106	9,056604	,1689406	1,73935	8,721626	9,391582
Combined	126	9,007693	,1458711	1,637399	8,718996	9,29639
diff		-,3081375	,2651807		-,840866	,2245909

diff = mean(x) - mean(y) t = -1,1620
H0: diff = 0 Satterthwaite's degrees of freedom = 49,6341

Ha: diff < 0 Ha: diff != 0 Ha: diff > 0
Pr(T < t) = 0,1254 Pr(|T| > |t|) = 0,2508 Pr(T > t) = 0,8746

```
. ttesti 20 6.889570552 1.122699387 106 8.556603774 1.867415778, une
```

Need for implementation of gene/drug trials

```
Two-sample t test with unequal variances

   |        Obs        Mean    Std. err.   Std. dev.   [95% conf. interval]
---+--------------------------------------------------------------------
   x |         20    6,889571    ,2510432    1,122699    6,364131    7,41501
   y |        106    8,556604    ,1813795    1,867416    8,196962    8,916246
---+--------------------------------------------------------------------
Combined |        126    8,291995     ,166546    1,869474     7,96238    8,621611
---+--------------------------------------------------------------------
    diff |           -1,667033    ,3097115               -2,29208   -1,041986
------------------------------------------------------------------------------
    diff = mean(x) - mean(y)                                      t =  -5,3825
H0: diff = 0                     Satterthwaite's degrees of freedom =  41,9455

    Ha: diff < 0                 Ha: diff != 0                 Ha: diff > 0
 Pr(T < t) = 0,0000         Pr(|T| > |t|) = 0,0000          Pr(T > t) = 1,0000

.  ttesti 20 7.423312883 0.993865031 106 8.745283019 1.621647139, une
```

Concerns about test costs

```
Two-sample t test with unequal variances

   |        Obs        Mean    Std. err.   Std. dev.   [95% conf. interval]
---+--------------------------------------------------------------------
   x |         20    7,423313    ,222235    ,993865    6,95817    7,888456
   y |        106    8,745283    ,1575083    1,621647    8,432973    9,057593
---+--------------------------------------------------------------------
Combined |        126    8,535446    ,1434926      1,6107    8,251457    8,819436
---+--------------------------------------------------------------------
    diff |           -1,32197    ,2723917              -1,872072   -,771868
------------------------------------------------------------------------------
    diff = mean(x) - mean(y)                                      t =  -4,8532
H0: diff = 0                     Satterthwaite's degrees of freedom =    41,01

    Ha: diff < 0                 Ha: diff != 0                 Ha: diff > 0
 Pr(T < t) = 0,0000         Pr(|T| > |t|) = 0,0000          Pr(T > t) = 1,0000

. ttesti 20 7.484662577 1.104294479 106 8.481132075 1.837343486, une
```

Fragmentation of healthcare systems

```
Two-sample t test with unequal variances

   |        Obs        Mean    Std. err.   Std. dev.   [95% conf. interval]
---+--------------------------------------------------------------------
   x |         20    7,484663    ,2469278    1,104294    6,967837    8,001488
   y |        106    8,481132    ,1784586    1,837343    8,127282    8,834982
---+--------------------------------------------------------------------
Combined |        126    8,322962    ,1582321    1,776151    8,009801    8,636123
---+--------------------------------------------------------------------
    diff |          -,9964695     ,304665              -1,611326   -,3816133
------------------------------------------------------------------------------
    diff = mean(x) - mean(y)                                      t =  -3,2707
H0: diff = 0                     Satterthwaite's degrees of freedom =  41,9602

    Ha: diff < 0                 Ha: diff != 0                 Ha: diff > 0
 Pr(T < t) = 0,0011         Pr(|T| > |t|) = 0,0021          Pr(T > t) = 0,9989

.  ttesti 20 8.325153374 1.073619632 106 8.103773585 2.284228515, une
```

```
Two-sample t test with unequal variances

   |        Obs        Mean    Std. err.   Std. dev.   [95% conf. interval]
---+--------------------------------------------------------------------
   x |         20    8,325153    ,2400686     1,07362    7,822684    8,827623
   y |        106    8,103774    ,2218639    2,284229    7,663858    8,543689
---+--------------------------------------------------------------------
Combined |        126    8,138913    ,1903353    2,136509    7,762216     8,51561
---+--------------------------------------------------------------------
    diff |            ,2213798    ,3268892               -,4330327    ,8757923
------------------------------------------------------------------------------
    diff = mean(x) - mean(y)                                      t =   0,6772
H0: diff = 0                     Satterthwaite's degrees of freedom =   57,699

    Ha: diff < 0                 Ha: diff != 0                 Ha: diff > 0
 Pr(T < t) = 0,7495         Pr(|T| > |t|) = 0,5010          Pr(T > t) = 0,2505

. ttesti 20 6.049079755 1.214723926 106 7.58490566 2.49138678, une
```