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A Comparative Effectiveness Study of Newborn Screening Methods for Four Lysosomal Storage Disorders †

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Table S1. Comparison of screening results for Fabry disease using different assay platforms and molecular genetic testing as employed in this study. Relevant results from other newborn screening programs are also included for additional comparison.

Country/State	***This study***	***This study***	**MO [1]**	***This study***	**Taiwan [2]**	**NY [3]**	**IL [4]**
Test Platform	*Immunocapture + GLA sequencing*	*DMF + GLA sequencing*	DMF	*FIA-MS/MS + GLA sequencing*	FIA-MS/MS	FIA-MS/MS	LC-MS/MS
# of newborns	*89,508*	*89,508*	308,000	*89,508*	191,767	65,605	219,793
TP (excl. p.A143T)	*50 (27)*	*41 (22)*	94	*44 (23)*	64	7	26
FP[1] (excl. p.A143T)	*53 (76)*	*53 (76)*	85	*53 (76)*	315	24	65
FPR[2] (excl. p.A143T)	*0.059% (0.085%)*	*0.059% (0.085%)*	0.030%	*0.059% (0.085%)*	0.16%	0.037%	0.03%
PPV[3] (excl. p.A143T)	*48.5% (26.2%)*	*43.6% (22.4%)*	53%	*45.4% (23.2%)*	17%	22.6%	28.6%
FN (excl. p.A143T)	*0 (0)*	*9 (5)*	-	*6 (4)*	-	-	-
Incidence (excl. p.A143T): 1 in	*1,790 (3,315)*	*1,790 (3,315)*	3,277	*1,790 (3,315)*	2,996	9,372	8,454

[1]FP, false positive cases of either sex based on the first DBS sample. [2]FPR, false positive rate calculated as FP/(FP + true negative cases). [3]PPV, positive predictive value calculated as TP/(TP + FP). FIA-MS/MS, flow injection analysis tandem mass spectrometry. LC-MS/MS, liquid chromatography MS/MS.

Table S2. Comparison of screening results for Gaucher disease using different assay platforms and 2nd tier testing as employed in this study. Relevant results from other newborn screening programs are also included for additional comparison.

Country/State	***This study***	***This study***	**MO [1]**	***This study***	**Taiwan [2]**	**NY [3]**	**IL [4]**
Test Platform	*Immunocapture + 2TT*	*DMF + 2TT*	DMF	*FIA-MS/MS + 2TT*	FIA-MS/MS	FIA-MS/MS	LC-MS/MS
# of newborns	*89,508*	*89,508*	308,000	*89,508*	101,134	65,605	219,793
TP	*1*	*2*	5	*2*	1	15	5
FP[1]	*111*	*111*	32	*111*	140	2	91
FPR[2]	*0.124%*	*0.124%*	0.010%	*0.124%*	0.138%	0.003%	0.041%
PPV[3]	*0.9%*	*1.77%*	13.5%	*1.77%*	0.7%	88.2%	5.2%
FN	*1*	*0*	-	*0*	-	-	-
Incidence: 1 in	*44,754*	*44,754*	61,600	*44,754*	101,134	4,374	43,959

[1]FP, false positive cases based on the first DBS sample, includes non-carriers, carriers, and cases with genotypes leading to pseudodeficient enzyme activity. [2]FPR, false positive rate calculated as FP/(FP + true negative cases). [3]PPV, positive predictive value calculated as TP/(TP + FP). 2TT, 2nd tier test; FIA-MS/MS, flow injection analysis tandem mass spectrometry. LC-MS/MS, liquid chromatography MS/MS.

Table S3. Comparison of screening results for Mucopolysaccharidosis type I using different assay platforms and 2nd tier testing as employed in this study. Relevant results from other newborn screening programs are also included for additional comparison.

Country/State	***This study***	***This study***	**MO [1]**	***This study***	**Taiwan [5]**	**NY [3]**	**IL [4]**
Test Platform	*Immunocapture + 2TT*	*DMF + 2TT*	DMF	*FIA-MS/MS + 2TT*	FIA-MS/MS	FIA-MS/MS	LC-MS/MS
# of newborns	*89,508*	*89,508*	308,000	*89,508*	130,237	35,816	219,793
TP	*1*	*1*	2	*1*	5[4]	0	1
FP[1]	*160*	*160*	126	*160*	115	13	126
FPR[2]	*0.178%*	*0.178%*	0.041%	*0.178%*	0.088%	0.036%	0.057%
PPV[3]	*0.6%*	*0.6%*	1.6%	*0.6%*	3.4%	-%	0.8%
FN	*0*	*0*	-	*0*	-	-	-
Incidence: 1 in	*89,508*	*89,508*	154,000	*89,508*	43,412[5]	>35,000	219,793

[1]FP, false positive cases based on the first DBS sample, includes non-carriers, carriers, and cases with genotypes leading to pseudodeficient enzyme activity. [2]FPR, false positive rate calculated as FP/(FP + true negative cases). [3]PPV, positive predictive value calculated as TP/(TP + FP). [4]TP cases include two pairs of siblings; [5]calculated based on three affected families. 2TT, 2nd tier test; FIA-MS/MS, flow injection analysis tandem mass spectrometry. LC-MS/MS, liquid chromatography MS/MS.

Table S4. Comparison of screening results for Pompe disease using different assay platforms and 2nd tier testing as employed in this study. Relevant results from other newborn screening programs are also included for additional comparison.

Country/State	***This study***	***This study***	**MO [6]**	***This study***	**Taiwan [2]**	**CA [7]**	**NY [3]**	**IL [8]**
Test Platform	*Immunocapture + 2TT*	*DMF + 2TT*	DMF	*FIA-MS/MS*[4] *+ 2TT*	FIA-MS/MS	FIA-MS/MS + 2TT[5]	FIA-MS/MS	LC-MS/MS
# of newborns	*89,508*	*89,508*	467,000	*89,508*	191,786	453,152	38,816	684,290
TP	*6*	*5*	46	*6*	16	18	1	29
FP[1]	*99*	*99*	223	*99*	858	70	5	368
FPR[2]	*0.111%*	*0.111%*	0.048%	*0.111%*	0.447%	0.015%	0.028%	0.054%
PPV[3]	*5.7%*	*4.8%*	17.1%	*5.7%*	1.83%	20.45%	16.7%	7.3%
FN	*0*	*1*	-	*0*	-	-	-	-
Incidence: 1 in	*14,918*	*14,918*	10,152	*14,918*	11,987	25,175	38,816	23,596

[1]FP, false positive cases based on the first DBS sample, includes non-carriers, carriers, and cases with genotypes leading to pseudodeficient enzyme activity. [2]FPR, false positive rate calculated as FP/(FP + true negative cases). [3]PPV, positive predictive value calculated as TP/(TP + FP). [5]Molecular genetic analysis of *GAA*; 2TT, 2nd tier test; FIA-MS/MS, flow injection analysis tandem mass spectrometry. LC-MS/MS, liquid chromatography MS/MS.

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