UNITY BY BILLIONTOONE

Shifting the Paradigm of Non-Invasive Prenatal Screening

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UNITY Screen™ is the only non-invasive prenatal (cell-free DNA) test that assesses fetal risk for **recessive conditions** and **aneuploidies** and integrates a **carrier screen**.

Accurate screening of ***all genetic conditions recommended by ACOG*** *is enabled by BillionToOne's proprietary molecular counting technology.*

Unity Screen is not a diagnostic test. Any high-risk results should be followed up with diagnostic testing.

UNITY Screen is the only non-invasive prenatal screen providing this important information in a consolidated way.

	Recessive Condition Screening			Aneuploidy Screening			RhD	Integrated Test	Billing
	Carrier Screen for ACOG-Recommended Conditions	Fetal Risk Assessment	No Paternal Sample Needed	Aneuploidy NIPT for ACOG-Recommended Conditions	Twins	Fetal Sex	Fetal RhD Detection	Carrier Status + Fetal Risk for Recessive Conditions & Aneuploidies + RhD Status	Streamlined, single bill
UNITY Screen	✓	✓	✓	✓	✓	✓	✓	✓	✓
******	✓	-	-	✓	✓	✓	-	-	-
******	✓	-	-	✓	✓	✓	-	-	-
******	✓	-	-	✓	✓	✓	-	-	-
******	✓	-	-	✓	✓	✓	-	-	-
******	✓	-	-	✓	✓	✓	-	-	-
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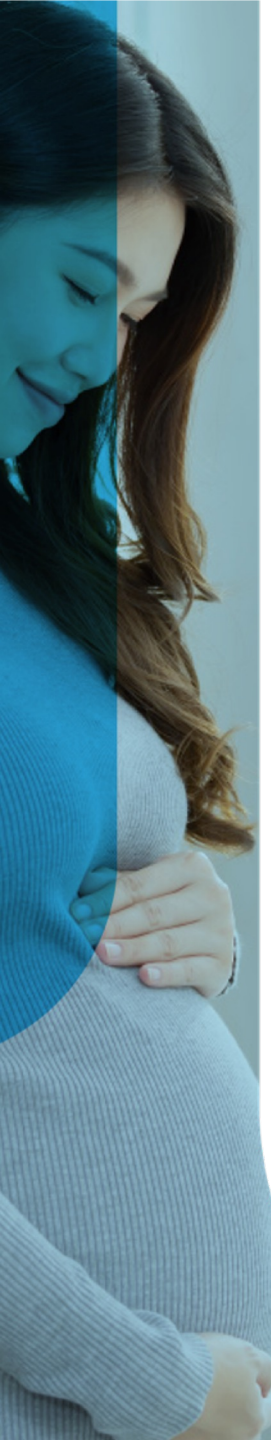


With traditional carrier screening, patients who are carriers experience additional costs, wait time, and emotional burden regardless of paternal sample availability

Pregnant patient is a carrier

Paternal sample - unavailable

Is the fetus at risk - unknown

Referral to maternal fetal medicine

While diagnostic testing may not be recommended, the patient will have more:

- Doctors appointments
- Scans
- Logistical burden
- Worry

Paternal sample available

- Possible additional cost
- Possible lack of insurance coverage
- Possible time away from work
- Unclear who manages paternal patient

Only calculate couple's reproductive risk

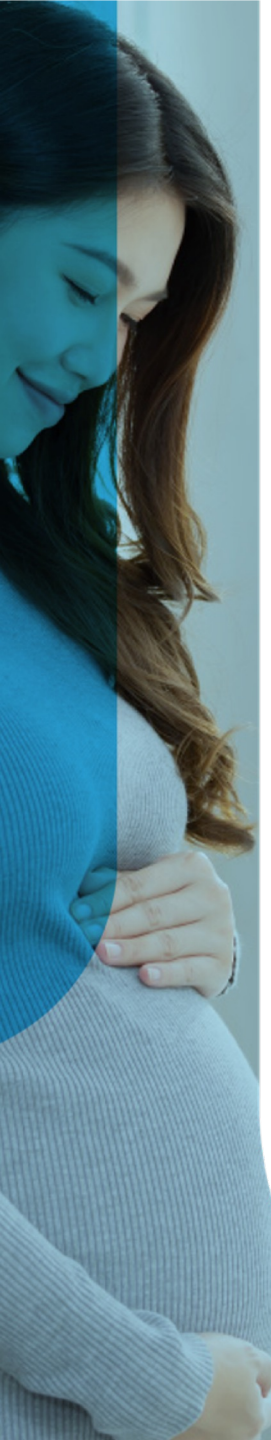
Amnio recommended for carrier couple

THE CHALLENGE

58% missed[1].

The complexities of screening a fetus for recessive conditions result in **more than half** of at risk pregnancies to be missed.

[1]Giles Choates, Meagan et al. “It takes two: uptake of carrier screening among male reproductive partners.” Prenatal diagnosis vol. 40,3 (2020): 311-316. doi:10.1002/pd.5588.



In addition to the timeline differences, UNITY provides a fetal risk instead of a couple's reproductive risk calculation as provided with carrier screening alone

Traditional carrier screen

if **maternal** carrier

~16 %

16%[1] maternal carrier rate

if **paternal** carrier

~42%

ONLY 42%[1] complete paternal testing

receive the **couple's reproductive risk** only

Couple's risk identified if both the maternal and paternal samples are collected.

1/4

Calculated 1 in 4 risk

UNITY Screen™

if **maternal** carrier

reflex **single-gene** NIPT

receive **individualized fetal risk assessment**

Fetal risk assessment using only maternal sample to inform diagnostic testing early in pregnancy

9/10

Tailored risk up to 9/10

1 Unity data on file

2 Choates G. et al. Prenat Diagn. 2020 Feb; 40(3): 311-316

UNITY Screen™ is a screening test and not a diagnostic test. Follow-up diagnostic testing is recommended for all high risk results.

THE SOLUTION

The UNITY Screen™ Power of One

An integrated carrier and fetal cfDNA screen that detects both recessive conditions and aneuploidies + fetal RhD status.

No paternal sample needed.

Aneuploidy NIPT and maternal carrier screening are performed from one maternal blood sample. If mom is a carrier, single-gene NIPT (sgNIPT) is automatically performed to assess fetal risk using the same sample. Unity Screen is not a diagnostic test. Any high-risk results should be followed up with diagnostic testing.

ACOG guidelines recommend **all pregnant women** be offered carrier screening and aneuploidy screening.

screening for **recessive conditions**

> *All patients who are considering pregnancy or are already pregnant…should be offered* ***carrier screening*** *for cystic fibrosis and spinal muscular atrophy… thalassemias… hemoglobinopathies.*

ACOG Committee Opinions 690 & 691

fetal risk for **aneuploidies**

> *Screening (serum screening with or without NT ultrasound or* ***cell-free DNA screening****)… for chromosomal abnormalities should be… offered to all patients early in pregnancy…*

ACOG Practice Bulletin 226

With **a maternal blood draw at 10+ weeks:**

maternal carrier status for

- cystic fibrosis
- spinal muscular atrophy
- sickle cell disease
- alpha thalassemia
- beta thalassemia

fetal risk for

recessive conditions + **aneuploidies** + **RhD status***

- cystic fibrosis
- spinal muscular atrophy
- sickle cell disease
- alpha thalassemia
- beta thalassemia
- trisomy 21**
- trisomy 18**
- trisomy 13**
- sex chromosome aneuploidy

opt in* * also available for twins*

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THE SOLUTION

UNITY's tailored fetal risk score offers clarity **without needing a paternal sample,** supporting equitable care.

WEEK 10

single maternal blood draw

WEEK 11

aneuploidy **NIPT** results + **RhD** status

CONDITIONS SCREENED	FETAL RISK by NIPT	Risk *Before NPT*	Risk *After* NPT
Trisomy 21	HIGH	1 in 86	9 in 10

CONDITIONS SCREENED	FETAL RISK by NIPT	Risk *Before NPT*	Risk *After* NPT
Trisomy 21	LOW	1 in 86	<1 in 10,000

FETAL RhD	NEGATIVE

FETAL RhD	LIKELY POSITiVE

WEEK 12/13

maternal carrier status + **sgNIPT** results

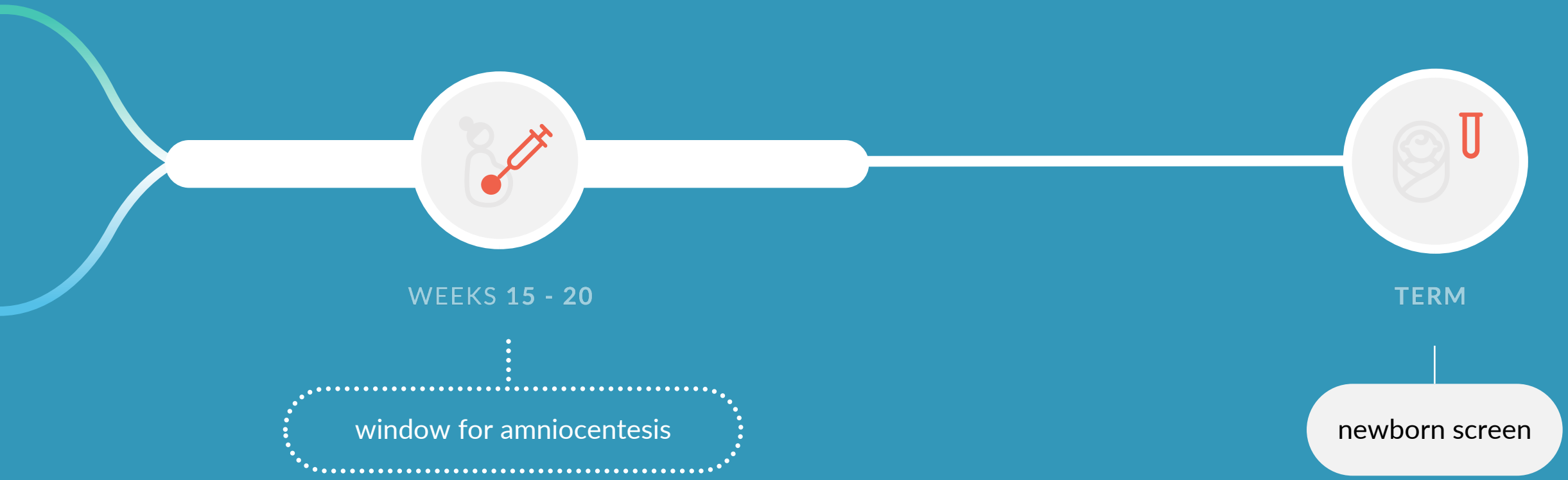
CONDITIONS SCREENED	FETAL RISK	Risk *Before NPT*	Risk *After* NPT
Cystic Fibrosis	LOW	1 in 96 – 1 in 376	1 in 2000

CONDITIONS SCREENED	FETAL RISK	Risk *Before NPT*	Risk *After* NPT
Cystic Fibrosis	HIGH	1 in 96 – 1 in 376	9 in 10

Unity Screen is not a diagnostic test. Any high-risk results should be followed up with diagnostic testing.

THE SOLUTION

Critical information early in pregnancy can then **inform more invasive testing** and neonatal treatment.



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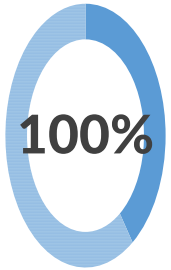
Fortunately, more therapies for single-gene, recessive conditions have emerged in the **past few years**:

condition	2016	2017	2018	2019	2020	2021 +
spinal muscular atrophy	SPINRAZA			zolgensma	Evrysdi	
beta thalassemia				EU zynteglo	US zynteglo	
sickle cell disease				Oxbryta, ADAKVEO		pending FDA approval bluebirdbio gene therapy
cystic fibrosis			symdeko	trikafta		

UNITY's optional fetal RhD detection is helpful information for pregnant patients who are Rh negative.



vs

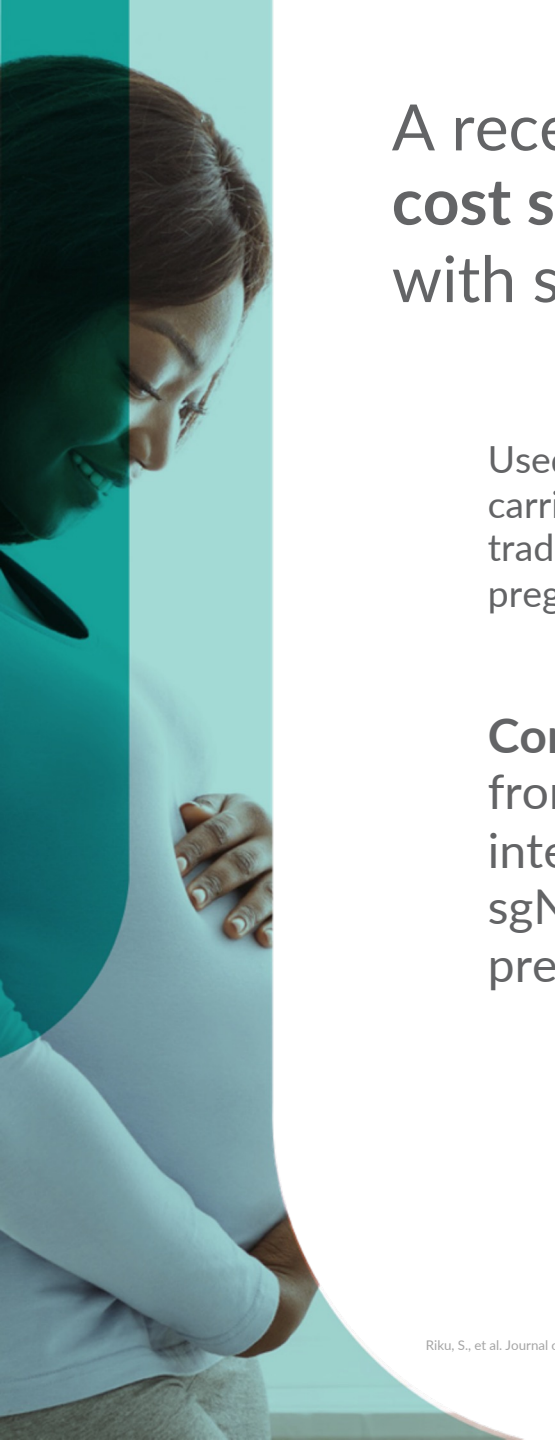
in US	Fetal RhD Status	Challenges
All Rh-neg mothers receive anti-D regardless of their fetuses' RhD status	**Unknown**	− Some women prefer not to receive blood products − Access to anti-D immune globulin can be challenging − Slight risk of sensitization

in EU	Fetal RhD Status	Benefits
Only Rh-neg mothers carrying Rh-pos fetuses receive anti-D (~60%)	**Known** RhD NIPT is offered to Rh-neg mothers	+ Anti-D immune globulin is used for women who need it + Reassurance for the 40% of Rh-neg fetuses

UNITY BY BILLION TO ONE

UNITY Screen™: Reducing the Cost, Logistical, and Emotional Burden of Traditional Carrier Screening

UNITY Screen: Carrier Screen PLUS Fetal Risk for Recessive Conditions & Aneuploidies



A recent study evaluated the **clinical benefits** and **achievable cost savings** associated with the adoption of a carrier screen with single-gene non-invasive prenatal testing (sgNIPT)

Used a decision-analytical model to compare carrier screen with sgNIPT (UNITY Screen) vs traditional carrier screening alone in singleton pregnancies.

Conclusion: The total cost savings from testing and earlier clinical intervention made possible by reflex sgNIPT is $37.6 million per 100,000 pregnancies.

Study published in *Journal of Medical Economics* in April 2022

Riku, S., et al. Journal of Medical Economics, (2022) 25:1, 403-411, DOI: 10.1080/13696998.2022.2053384

Study Goals

Clinical Outcomes

Comparison of traditional carrier screening to carrier screening with reflex to sgNIPT in identifying affected fetuses

Healthcare Costs

Comparison of costs associated with traditional carrier screening and required follow-up to carrier screening with reflex to sgNIPT

Evaluate clinical benefit (number of affected fetuses detected and workflow)

Evaluate cost savings using two different unit costs:

- Cost per pregnancy (or 100,000 pregnancies) screened
- Cost per affected pregnancy

Model Inputs

1. ACOG recommended disorders: cystic fibrosis, spinal muscular atrophy, sickle cell disease/hemoglobinopathies, and alpha thalassemia in the analysis.
2. Assumed 100% carrier detection rate for Unity and traditional carrier screening.
3. Maternal carrier screening costs $694 for both Unity and traditional carrier screen
4. Paternal testing cost: $944
5. Maternal Fetal Medicine (MFM) costs: $1236

Model Inputs, con’t

Screening Costs for both traditional and Unity Screen @ CMS rate	$694
Paternal Testing Cost	$944
MFM Cost	$1,236
Diagnostic Testing Costs	$730
sgNIPT price not established at this time	

Clinical Outcomes are impacted by low paternal participation

Critical ~8 week window for paternal result

what's needed:

- paternal sample collection
- receiving results
- patient counseling

why it's complicated:

- test cost/billing
- appointment logistics
- relationship with maternal carrier

Results in a failure to identify nearly 60% of affected pregnancies

1. Choates G. et al. Prenat Diagn. 2020 Feb; 40(3): 311-316

Traditional carrier screen

if maternal carrier

~16 %

16%[1] maternal carrier rate

if paternal carrier

~42 %

ONLY 42%[1] complete paternal testing

receive the couple's reproductive risk only

58% of high risk pregnancies are missed with traditional carrier screening and only 36% are referred to MFM for additional testing.

UNITY Screen™

if maternal carrier

~16 %

16%[1] maternal carrier rate

reflex single-gene NIPT

receive individualized fetal risk assessment

16% of pregnancies identified as carriers and 80% are referred to MFM for additional testing.

2 Choates G. et al. Prenat Diagn. 2020 Feb; 40(3): 311-316

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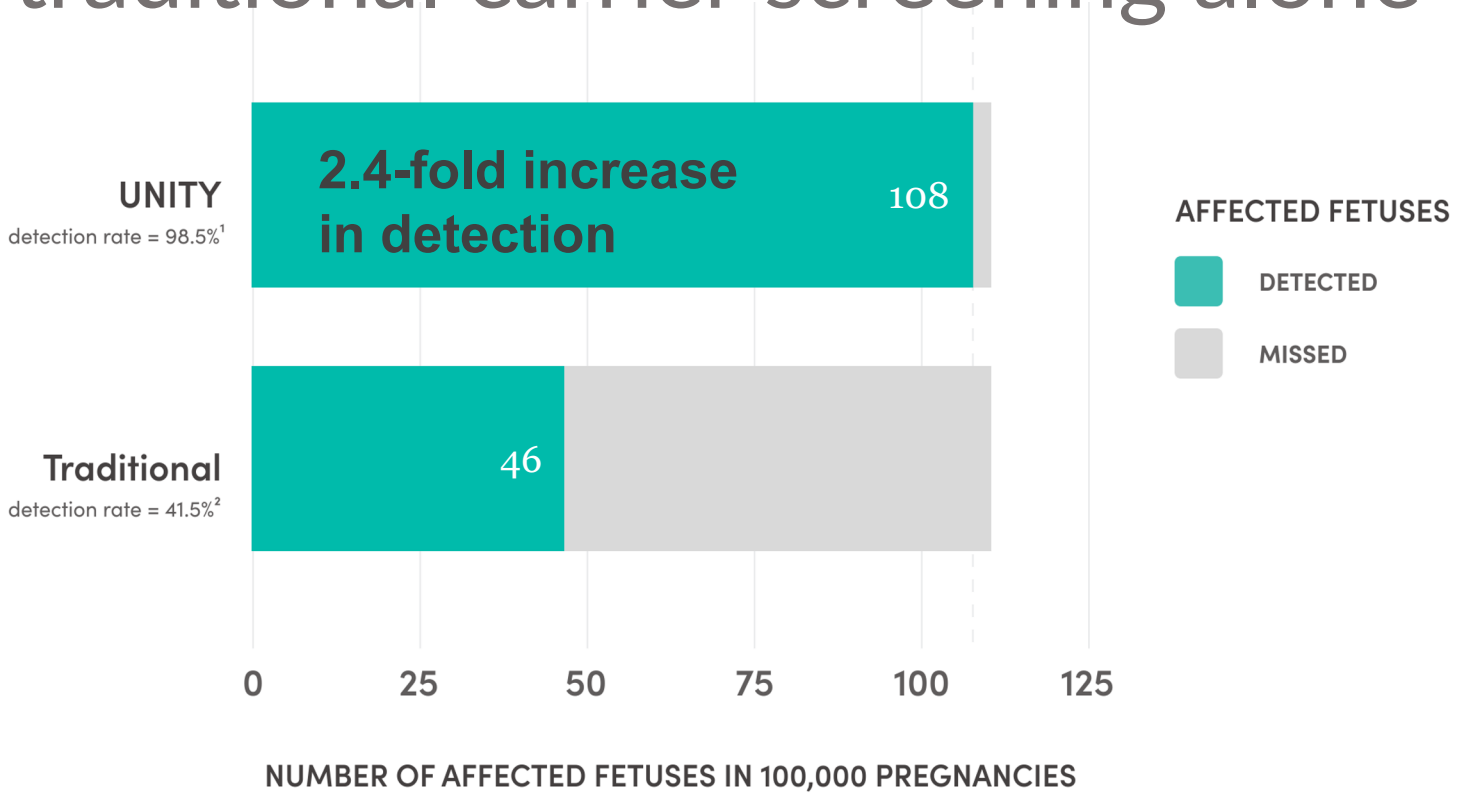
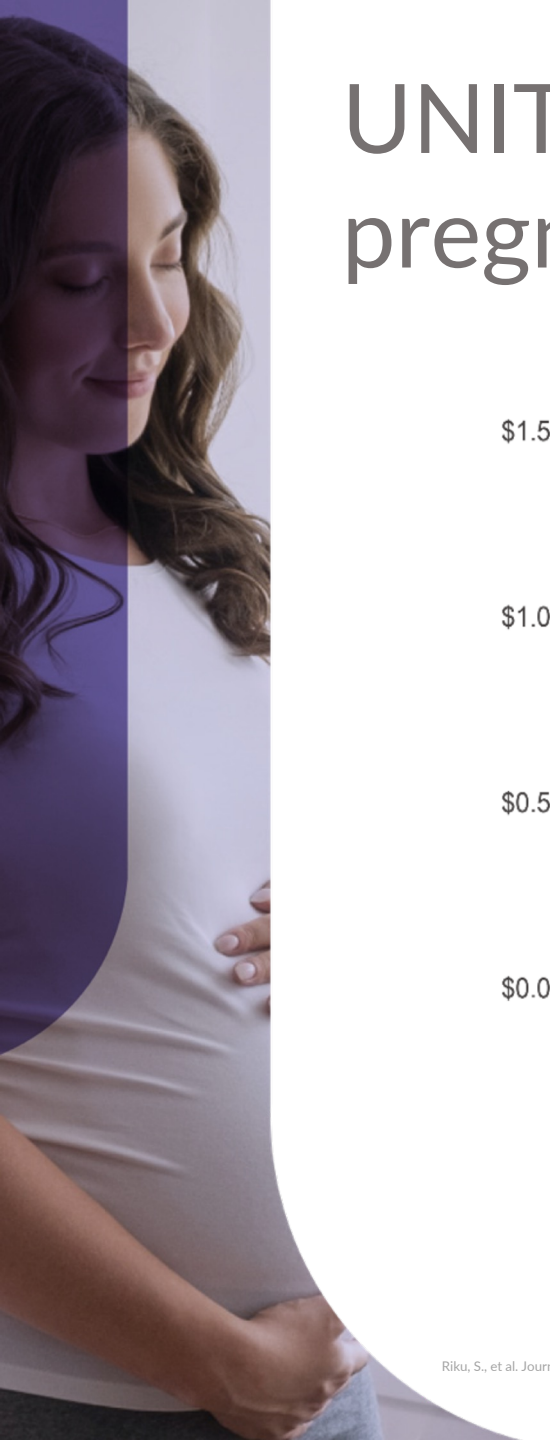
UNITY identifies more affected fetuses than traditional carrier screening alone



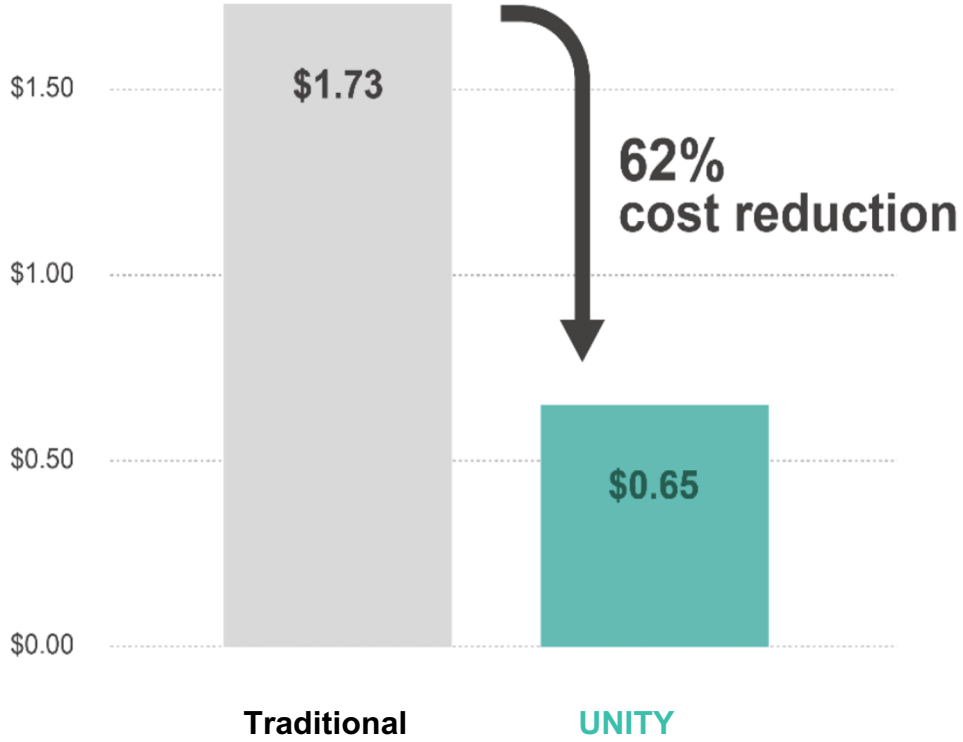
Due to low paternal carrier screening follow-up, traditional carrier screening fails to identify nearly 60% of affected pregnancies.

1. Analytical sensitivity; Tsao D, et al. Scientific Reports, (2019), 9, 14382, DOI: 10.1038/s41598-019-50378-8
2. Paternal follow-up rate; Choates M, et al. Prenatal Diagnosis (2020), 40(3), 311-6, DOI: 10.1002/PD.5588
3. Riku, S., et al. Journal of Medical Economics, (2022) 25:1, 403-411, DOI: 10.1080/13696998.2022.2053384

110 affected fetuses expected (0.11% disease incidence)[3]



UNITY can decrease screening costs per affected pregnancy detected



Reducing the need for paternal testing decreases the cost per affected pregnancy.

Traditional Costs/per 100K pregnancies: $78.7M / 46 detected = $1.73M
UNITY Costs per 100K pregnancies: $70.3M / 108 detected = $0.65M

Riku, S., et al. Journal of Medical Economics, (2022) 25:1, 403-411, DOI: 10.1080/13696998.2022.2053384

UNITY can lower downstream SMA healthcare costs

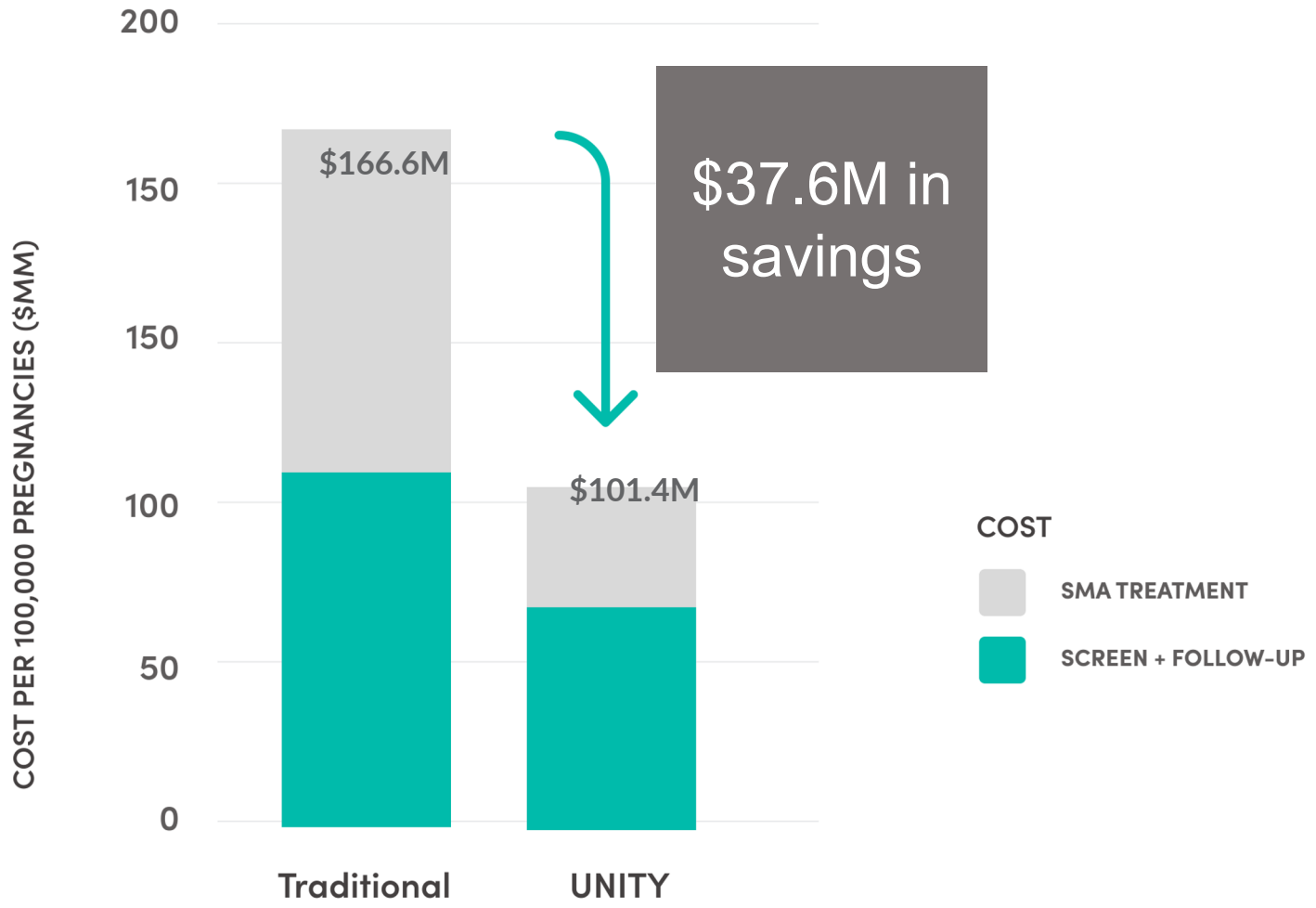
$29.3M saved per 100,000 pregnancies from improved SMA treatment selection

zolgensma®

Item (per 100,000 pregnancies)	Traditional	UNITY
SMA treatment cost ($MM)[1]	$60.3	$31.1
Number of SMA-affected pregnancies	9	9
% Eligible patients (diagnosed < 2 years old)	70%	99%
% Eligible patients choosing Zolgensma	90%	90%
Lifetime SMA treatment cost ($MM)	$6.8	$3.5

1. Most cost-efficient SMA treatment ($2.1M/patient)
Early administration more effective; must be administered to patients when < 2 years old

UNITY can save $37.6M per 100,000 pregnancies in total healthcare costs



In Conclusion

- A recent study evaluated the clinical benefits and achievable cost savings associated with the adoption of a carrier screen with single-gene non-invasive prenatal testing (sgNIPT)
- UNITY sgNIPT can offer meaningful fetal risk results that may also improve workflow and turnaround time compared to traditional carrier screening
- Based on the analytical model, UNITY can identify more affected pregnancies than traditional carrier screening and save the healthcare system per pregnancy and across 100K pregnancies