HEALTH TECHNOLOGY ASSESSMENT OF NEWBORN PULSE OXIMETRY FOR THE SCREENING OF CRITICAL CONGENITAL HEART DISEASE AMONG ASYMPTOMATIC, APPARENTLY HEALTHY NEWBORNS

Health Technology Assessment Philippines

BACKGROUND OF THE ASSESSMENT

Context

Nominator: DOH Disease Prevention and Control Bureau *(Nomination Form)*

Rationale for Nomination:

- Potential benefits of **early identification of Critical Congenital Heart Disease (CCHD)** through POS: immediate treatment (Thangaratinam et al., 2012).
- Newborn screening for CCHD through POS is:
  - **Not mandated by law**
  - **Not part of routine newborn care in the Philippines** (i.e., **not included in the National Comprehensive Newborn Screening Policy of the DOH and the Newborn Screening Package of PHIC)**
- Studies and international scientific groups recommend NPOS for CCHD to save lives through early diagnosis
- Positive recommendation from: **2023 Omnibus Health Guidelines for the Child** and the **2021 Philippine PHEx Guidelines**

Population	Intervention	Comparator	Outcomes
Asymptomatic, apparently healthy newborns	Screening for congenital heart disease with pulse oximeter (handheld or tabletop type)	2D Echocardiography	- Early detection of congenital heart disease - Mortality - Early intervention and referral

PICO of the assessment

Population	Asymptomatic, apparently healthy newborns
Intervention	Pulse oximetry screening in addition to physical examination
Comparator	Physical examination of the newborn ***Reference standard for diagnostic performance: 2D-Echo
Outcomes	Clinical: - Early detection of critical congenital heart disease at 1 week of age (represents timely diagnosis of CCHD) - Mortality at 1 year of age Economic: - Incremental cost-effectiveness ratio (ICER) - Budget impact - Household financial impact Ethical, legal, social, health systems impact

PICO of the assessment

Population	Asymptomatic, apparently healthy newborns
Intervention	Pulse oximetry screening in addition to physical examination
Comparator	Phys ***Re 2D-Echo
Outcomes	Clinic - ase at 1 week of age - Economic: - Incremental cost effectiveness ratio (ICER) - Budget impact - Household financial impact Ethical, legal, social, health systems impact

Proposed service delivery settings:
- General hospital: level 1, 2, 3
- Specialty hospital
- Primary care facility
- Diagnostic / Therapeutic Facility

Ref: Topic nomination form (2022)

Policy Question

- *Should newborn pulse oximetry screening (NPOS) for critical congenital heart disease (CCHD) among asymptomatic, apparently healthy newborns be included in the National Comprehensive Newborn Screening Policy of the DOH and the Newborn Screening Package of PHIC?*

Research Questions

C1: Responsiveness to Magnitude and Severity **(IAG)**

- What is the magnitude and severity of critical congenital heart disease among newborns as a public health problem?

C2: Clinical Efficacy, Effectiveness, Safety, and Accuracy **(IAG)**

- What is the effectiveness of pulse oximetry screening in addition to physical examination among asymptomatic or apparently healthy newborns compared to physical examination only in the early detection of critical congenital heart disease and reduction of mortality?
- What are the performance characteristics (sensitivity, specificity, PPV, NPV, LR) of pulse oximetry screening in addition to physical examination among asymptomatic or apparently healthy newborns compared to 2D echocardiography in the detection of critical congenital heart disease?
- What are the harms associated with pulse oximetry screening in addition to physical examination among asymptomatic or apparently healthy newborns compared to physical examination only in the early detection of critical congenital heart disease?
- What are the recommendations and guidelines of HTA agencies and ministries of health on the screening of newborns for critical congenital heart disease?

Research Questions

C3: Cost-effectiveness **(EAG)**

- What is the cost-effectiveness of pulse oximetry screening in addition to physical examination among asymptomatic or apparently healthy newborns compared to physical examination only in the early detection of critical congenital heart disease and reduction of mortality?

C4: Affordability and Viability **(EAG)**

- What is the budget impact of pulse oximetry screening in addition to physical examination among asymptomatic or apparently healthy newborns for the early detection of critical congenital heart disease?

C5: Household Financial Impact **(IAG)**

- What is the household financial impact of critical congenital heart disease?

C6: Ethical, Legal, Social and Health System Impact **(EAG)**

- What are the ethical, legal, social, and health systems implications of the use of pulse oximetry screening in addition to physical examination among asymptomatic or apparently healthy newborns for early detection of critical congenital heart disease?

HEALTH PROBLEM AND CLINICAL MANAGEMENT OPTIONS

CRITICAL CONGENITAL HEART DISEASE (CCHD)

(Jullien, 2021; Illinois Dept of Public Health, 2025)

- Congenital heart disease (CHD) is a defect or abnormality of the heart and not merely a disease. CCHD is a subset of CHD which requires newborn babies to undergo surgery or cardiac catheterization
- Exists at birth and can affect the structure and function of a baby's heart
- Incidence of 18 per 10,000 births per year

https://www.cdc.gov/ncbddd/heartdefects/data.html

CCHD: Causes, Signs and Symptoms

(CDC, 2023; Illinois Dept of Public Health, 2025)

- Most causes are unknown but a combination of attributable factors are linked to **genetics, mother's pre-existing conditions, diet, medication use during the entire pregnancy period, maternal and paternal age extremes (<21 and above 35 years old)**.

- Signs and symptoms are **dependent on the type and severity of the defect. Some defects may not have any manifestations at all**.

CURRENT MANAGEMENT OPTIONS

CCHD: Current management options *[1 of 4]*

Screening for CCHD using pulse oximetry: Local Situation

- Recommended by medical societies after the 24th hour of life, as part of newborn discharge procedure (Philippine Society of Pediatric Cardiology, 2020).
- Recommended by DOH as part of CCHD screening among asymptomatic and apparently healthy newborns through the 2021 Philippine Guidelines on Periodic Health Examination (PHEX)
- Performed in healthcare facilities within the Metro Manila area (NIH, 2018).

- **Not included** in the Enhanced Newborn Care Package of PhilHealth
  - No screening method for CCHD detection

CCHD: Current management options *[2 of 4]*

Current screening and diagnostic test for CCHD detection (AHA, 2023)

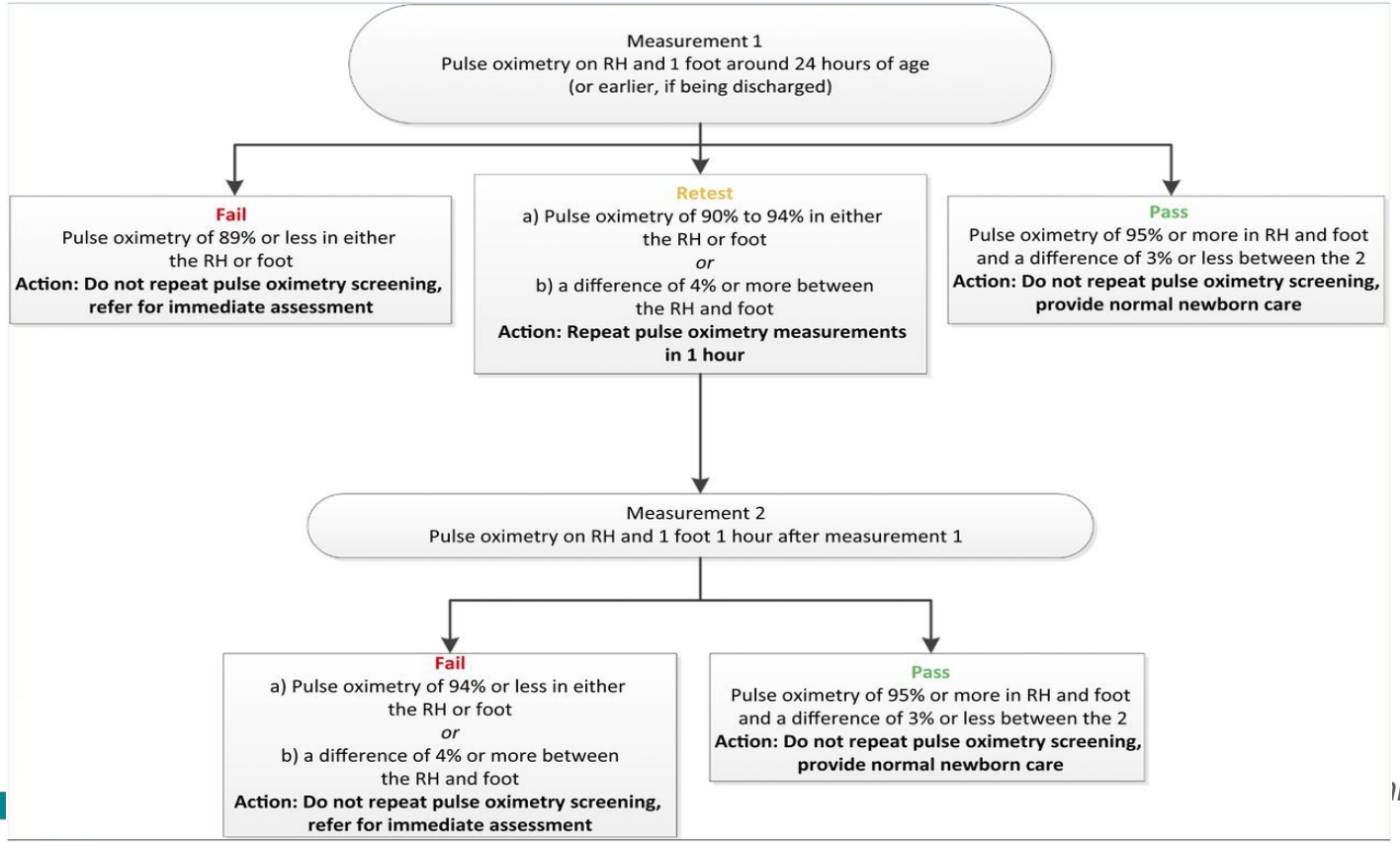
- **Prenatal**
  - Fetal echocardiogram (abdominal or endovaginal ultrasound)
- **Post-natal**
  - Pulse oximetry screening to detect early signs of CCHD
  - Echocardiogram as confirmatory test for CCHD

Adopted guideline of the Philippine Society of Pediatric Cardiology

Guideline	Population indicated	Screening site	Time period for screening
American Academy of Pediatrics (2020)	Newborns	Right hand and either foot	around 24 hours of life or earlier if being discharged

CCHD: Current management options *[3 of 4]*

NPOS Flowchart from the *American Academy of Pediatrics (2020)*



CCHD: Current management options *[4 of 4]*

Management after screening

- **Severe** cases: either **surgery** (such as the tetralogy of Fallot surgery) or **catheter intervention** together with a lifelong monitoring with a cardiologist (NHS, 2021).

Cost of NPOS vs 2D Echo in Public and Private Hospitals in the Philippines *(PHEX Guidelines, 2021)*

Parameter	NPOS	2D Echo
Unit Cost of procedure: Public (PGH)	Free	Php 600-750
Unit Cost of procedure: Private	Php 1,800 per single use of probe	Php 7,000 before professional fees

PhilHealth Coverage Related to Diagnosis

RVS Code	Description	First Case Rate	Applicable Healthcare Institutions
PMR06J	2D Echo	Php 3,200.00	• Level I-III HC Institutions • Ambulatory Surgical Clinic (ASC) • Primary Care Facility: Infirmary/Dispensary (PCF) • Maternity Care Package Provider (MCP • Free-Standing Dialysis Clinic (FSDC) • Animal Bite Center (ABTC) • Community Isolation Unit (CIU) • Drug Abuse Treatment and Rehabilitation Center (DATRC) • Diagnostic Service Provider (DSP) • HIV Treatment Hub (HIVTH) • Outpatient Malaria Center (OPMC) • PCB/EPCB Provider (PCB) • Rural Health Unit (RHU) • TB DOTS Center(TBDOTSC)

Philhealth Coverage related to Management of CCHD

For surgical procedures related to CCHD:

Package code	Management/ Procedure	Package Rate
Z031A	Closure of Ventricular Septal Defect (VSD) with or without Associated Special Conditions	**Php 498,000.00**
Z031B	Closure of VSD with Severe Pulmonary Stenosis	**Php 614,000.00**
Z032A	Total correction of Tetralogy of Fallot (ToF)	**Php 614,000.00**
The approved clinical pathways for both ToF and VSD shall reflect the mandatory and other services specified in the PhilHealth Circular 2025-0004		

For hospital confinement related to CHD:

ICD 10 Code	Diagnosis	First Case Rate
Q20.0-Q26.9	Congenital Heart Diseases	**Php 11,600.00 to 22,620.00**

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DESCRIPTION, CHARACTERISTICS, AND USE OF HT

Description, Characteristics and Use of HT *(1 of 4)*

(WHO, 2019, John Hopkins Medicine)

Pulse Oximetry

- A simple and **non-invasive** procedure that **utilizes a pulse oximeter** to:
  - **detect a pulsatile signal in an extremity** (i.e., finger, toe)
  - **calculates the level of oxygenated hemoglobin in arterial blood (SpO2*) and the pulse rate.**

**Peripheral Oxygen saturation*

Types of Pulse Oximeter
• Self-contained fingertip/Finger clip oximeter
• Handheld oximeter
• Tabletop/Stand-alone oximeter

Can be used for newborns; nominated by DPCB

Description, Characteristics and Use of HT (2 of 4)

(Kirk et al, 2022; Brookman et al, 2024)

- In newborns, the probes are usually placed on the right hand (pre-ductal) and either foot (post-ductal)
- Some factors (i.e., skin pigmentation, altitude) can affect pulse oximeter readings which can lead to inaccurate readings

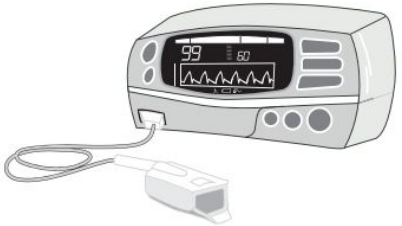
Photograph retrieved from Pulse Oximetry Provides Higher Screening Sensitivity for CCHD in Newborns | Respiratory Therapy

Photograph retrieved from Newborn pulse oximetry screening pilot under way – PHE Screening

Newborn Pulse Oxir

Description, Characteristics and Use of the HT *(3 of 4)*

(WHO, 2019)

	Handheld oximeter	Tabletop or stand-alone oximeter
Illustration		
Description	A **portable device** that estimates oxygen saturation and includes a display screen and attached probe. It is commonly applied to the fingertip or around the wrist.	A **stationary device** that measures oxygen saturation in real time using an external probe on the skin. It may also use physiological parameters as additional features (i.e., capnography, blood pressure and temperature monitoring).
Use	For **spot checks, or for continuous monitoring**	For **longer term/continuous monitoring**

Description, Characteristics and Use of HT *(WHO, 2019) (4 of 4)*

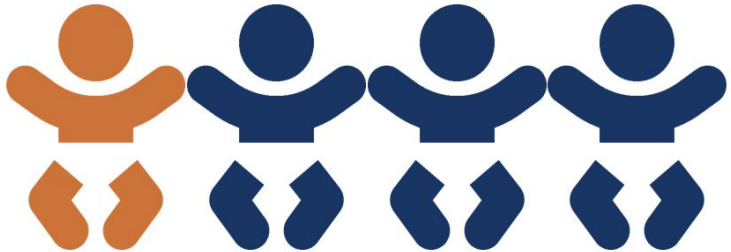
	Handheld oximeter	Tabletop or stand-alone oximeter
Parameters Monitored	• SpO2 • pulse rate (some may have additional features such as respiratory rate)	
Accessories Required	• Probes with patient-specific sizes to neonate, infant, child, and adult (reusable probes, replaceable for at least once per year) • Charging/power cable	
	• Replacement batteries	
Advantages	• Portable • More alarms and internal memory than fingertip devices • ≥ 12 hours' operational capacity on rechargeable built-in battery and take ≤ 4 hours to charge	• May be pole-mounted • Large internal memory to store patient IDs and records • **Most accurate** (in general)
	• With port (or Wi-Fi) for downloading and/or printing data	

CI: BURDEN OF THE DISEASE
(MAGNITUDE AND SEVERITY)

CCHD: Burden of the Disease (Magnitude and Severity)

Global evidence

- In 2021, the global prevalent cases of CHD in infants younger than 1 year was 1,241,054.32 (a 2.9% decrease from 1990 to 2021) (*Deng et al., 2025*)
- It is estimated that 25% of CHDs are life-threatening CCHDs which require surgery or cardiac catheterization (*Jullien, 2021*)
- **Southeast Asia**: remains as one of the regions with the **highest infant mortality and rates** of CHD (including CCHD) at birth (*Ward et al., 2024*)
- In 2021, congenital birth defects (which includes CCHD) was one of the leading 25 Level 3 causes of global disability adjusted life years (DALYs) for both sexes combined, in all ages. (*CDC, 2024*)



1 in every 4 babies born with a heart defect has CCHD, of which *timely screening is significant in preventing disability or death in early life.*

CHD: Burden of the Disease (Magnitude and Severity)

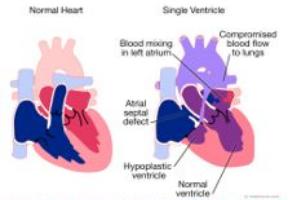
(IHME Data, 2021; Del Rosario et al., 2024)

Philippines

- **According to global burden of disease estimates 2021 (modeled data)**
  - **0.55% of all deaths** locally is CHD-associated
    - **4.27 deaths in 100,000** across all age groups
    - **130.29 deaths in 100,000** children < 1 y.o.
  - Prevalence data:
    - **208,586** cases of CHD among all ages and in both sexes (0.19%)
    - **20,013** cases of CHD among < 1 y.o. and in both sexes (1.16%)
- **Pilot study** in the Philippines involving multiple centers in the country → **14 cases of CCHD in 32,349 screened newborns (4.33 in 10,000)**

CCHD: Burden of the Disease (Magnitude and Severity)

(US Health Resources & Services Administration, 2025; Mahle et al., 2009; Huisenga et al., 2021)



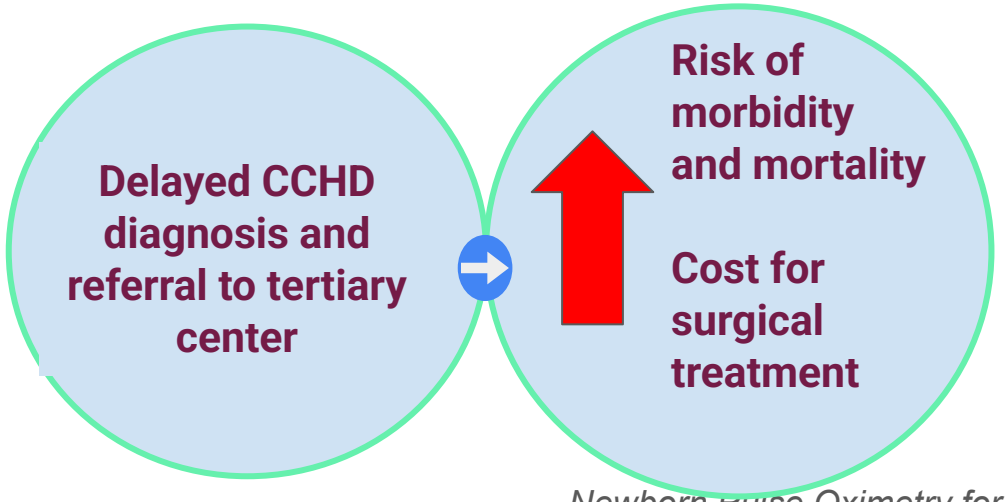
- Infants are usually asymptomatic and may appear healthy during the first few days of life before the heart defect is detected.
- Babies with CCHD can clinically deteriorate within the first 48 hours of life
  - signs of hemodynamic and circulatory collapse (hypoxemia, shock, acidosis, mortality)
- Increased risk of impaired developmental outcomes, especially for single ventricle pathologies.

https://www.bangkokhearthospital.com/en/content/congenital-heart-disease;
https://medmovie.com/library_id/5855/topic/cvml_0053a;
https://www.docplexus.com/posts/pulse-oximetry-for-screening-of-critical-congenital-heart-disease-in-newborn
https://clipart-library.com/clipart/1071912.htm

CCHD: Burden of the Disease (Magnitude and Severity)

(*Harold, J.G, 2014*)

- **Unmanaged and delayed CCHD detection** lead to some children being **severely compromised** due to ischemic brain injury at presentation that **they die even before surgical intervention.**
- **Early detection** with non-invasive, cost-effective screening → **reduced chance of late stage CCHD** requiring surgery or catheter intervention.



C2: CLINICAL EFFICACY/ EFFECTIVENESS, SAFETY

Description of the Available Systematic Review
(PHEX Guidelines, 2021)

P	Apparently healthy, asymptomatic newborns
I	NPOS
C	No screening - Reference standard test: 2D Echocardiography
O	• Mortality • Early intervention for CHD for the prevention of complications • Impact on family

Description of the Available Systematic Review
(PHEX Guidelines, 2021)

- Reviews were conducted as evidence for development of guidelines
- **Only a rapid review, not a full systematic review**
- ***General methodology:***
  - Searched for existing international CPGs; if **good quality and within 5 years → adopt evidence summary**
  - Conducted separate systematic search, de novo SR-MA, if needed (based on the results of the appraisal of existing CPGs and ES)
  - Also searched relevant local databases and medical society websites
  - Authors of relevant articles were also contacted
  - Studies were appraised for directness, methodological validity, results, and applicability
  - RevMan, STATA, and GRADEPro were used for quantitative synthesis

Description of the Available Systematic Review
(PHEX Guidelines, 2021)

- AMSTAR Appraisal: **Critically Low**
  - Did not include list of excluded studies
  - Did not assess the potential impact of RoB in individual studies on the results of the meta-analysis
  - Did not investigate for publication bias

The jSC recognizes and takes note of the limitations of the review, but it is still the best available evidence that can be used

Description of the Available Systematic Review
(PHEX Guidelines, 2021)

STUDIES INCLUDED

- **Evidence on the risk of mortality (NPOS vs no screening) (k=2):**
  - Abouk et al. 2017 (Observational study)
  - Banait et al. 2018 (Retrospective cohort study)

- **Evidence on the performance characteristics of NPOS (k=17):**
  - Plana et al. 2018 (Cochrane systematic review)
    - Note: 6/21 studies from the Cochrane SR were included in this review
  - Additional search of 11 diagnostic accuracy studies

- **Evidence on the harms of NPOS (k=3)**
  - UK National Screening Committee Pilot Study (2016)
  - Public Health England recommendation to UK NSC (2019)
  - Banait et al, 2018 (Retrospective cohort study)

Description of the Available Systematic Review
(PHEX Guidelines, 2021)

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  - Banait et al, 2018

Evidence on the risk of mortality (NPOS vs no screening)

Study Characteristics

Author, Year (Setting)	Study Design	Population	Intervention	Comparator	Outcomes
Abouk et al. 2017 (US)	Observational study with group-level analyses of pooled cross-sectional time-series data	• Infants (<1 year of age) who died in a particular year • (Live) infants born in the same year	Mandatory CCHD screening policies in 8 states *(n=2,827,528 live births)*	No mandatory screening policy in 5 states *(n=15,469,617 live births)* Mandatory POS policy but not yet implemented by June 1, 2013 in 9 states *(n=2,721,897 live births)*	Number of early infant (from 24 hours to <6mos of age) deaths due to CCHD or other unspecified defects, with sensitivity analysis for birth to <12 months

Risk of mortality between NPOS vs No Screening

- **Results of Abouk et al. 2017**
  - Found that states with mandatory pulse oximetry screening had **33.4% lower rates (95% CI, 10.6%-50.3%) in CCHD deaths**, with an absolute **decrease of 3.9 deaths (95% CI: 3.6-4.1) per 100,000 births** compared to those without the mandated policy.

Evidence on the risk of mortality (NPOS vs no screening)

Study Characteristics

Author, Year (Setting)	Study Design	Population	Intervention	Comparator	Outcomes
Banait et al. 2018 (UK)	Retrospective cohort study	Babies born at more than 34-week gestation with CCHD from three tertiary hospitals (N= 138,176)	Routine POS in two hospitals; done after 4 hours of age and before discharge n=76,232	No POS policy in one hospital n= 61,944	• Post-discharge diagnosis rate • Mortality at one year between cohorts

Risk of mortality between NPOS vs No Screening

- **Results of Banait et al. 2018**
  - The study noted **5 deaths (one neonatal and four post-neonatal) within the first year of life in the screened cohort (n=76,232) vs 1 death in the unscreened cohort (n=61,944).**

Overall risk of mortality between NPOS vs No Screening

Overall, the pooled analysis of the two observational studies, with 18,435,321 person-years of follow-up, found that there is a **1 in 10,000 risk of mortality from CCHD until 1 year of age among newborns who are not screened** *(moderate certainty of evidence).*

(See GRADE Evidence Profile in next slide)

GRADE Evidence Profile: POS on Mortality

(*Abouk et al., 2017* and *Banait et al., 2018*)

Pulse Oximetry Screening compared to No Screening for CCHD in Asymptomatic Newborns
Bibliography: Abouk 2017, Banait 2018

Certainty assessment							Summary of findings				
							Study event rates (%)			Anticipated absolute effects	
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	With No Screening	With Pulse Oximetry Screening	Relative effect (95% CI)	Risk with No Screening	Risk difference with Pulse Oximetry Screening
Mortality (follow-up: 12 months)											
18435321 (2 observational studies)	serious[a]	not serious	not serious	not serious	none	⨁⨁⨁◯ Moderate	1911/15531561 (0.0%)	281/2903760 (0.0%)	not estimable	1 per 10,000	

HTAD computed RR: 0.79 (95% CI 0.69 to 0.89)
HTAD computed risk
Screened: 0.97 in 10,000
Unscreened: 1.23 in 10,000

GRADE Evidence Profile: POS on Mortality

(*Abouk et al., 2017* and *Banait et al., 2018*)

Pulse Oximetry Screening compared to No Screening for CCHD in Asymptomatic Newborns

Bibliography: Abouk 2017, Banait 2018

Serious risk of bias:

- Abouk and Banait: Limited information on the baseline characteristics of the populations studied (Abouk: only age was provided)
- Abouk and Banait: With risk for selection bias in allocation between screened and unscreened cohorts
- Abouk: CCHD prevalence may vary between states

Participants (studies) Follow-up	Risk of bias	Inc					of findings		Relative effect (95% CI)	Anticipated absolute effects	
										Risk with No Screening	Risk difference with Pulse Oximetry Screening
Mortality (follow-up: 12 months)											
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Description of the Adopted Systematic Review
(PHEX Guidelines, 2021)

STUDIES INCLUDED

- **Evidence on the risk of mortality (NPOS vs no screening):**
  - Abouk et al. 2017
  - Banait et al. 2018

- **Evidence on the performance characteristics of NPOS (k=17):**
  - Plana et al. 2018 (Cochrane systematic review)
    - Note: 6/21 studies from the Cochrane SR were included in this review
  - Additional search of 11 diagnostic accuracy studies

- **Evidence on the harms of NPOS (k=3)**
  - UK National Screening Committee Pilot Study (2016)
  - Public Health England recommendation to UK NSC (2019)
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- Evidence on the harms of NPOS (k=3)
  - UK National Screening Committee
  - Public Health England recommend
  - Banait et al, 2018

Only 6 of 21 studies from the Cochrane review were included in the repooling:

- Only studies published in 2015 onwards
  - Pulse oximeters improved through time and adding studies before 2015 would undermine the sensitivity and specificity of POS if old pulse oximeters were used

DOST PHILIPPINES

Description of the Adopted Systematic Review
(PHEX Guidelines, 2021)

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- Evidence on the harms of NPOS (k=3)
  - UK National Screening Committee Pilot Study (2
  - Public Health England recommendation to UK N
  - Banait et al, 2018

6 studies from the Cochrane review:

1. Klausner et al, 2017
2. Jones et al., 2016
3. Van Niekerk et al., 2016
4. Ozalkaya et al., 2015
5. Gomez-Rogriguez at al., 2015
6. Zuppa, 2015

Description of the Adopted Systematic Review
(PHEX Guidelines, 2021)

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  - UK National Screening Committee Pilot Study (201
  - Public Health England recommendation to UK NSC
  - Banait et al, 2018

11 studies from additional search:

1. Almawizini et al. 2017
2. Cloete et al. 2019
3. Diller et al. 2018
4. Gopalakrishnan et al. 2021
5. Hamilcikan et al. 2018
6. Hu et al. 2017
7. Narayen et al. 2018
8. Nuntnarumit et al. 2017
9. Paranka et al. 2018
10. Schwartz et al. 2021
11. Slitine et al. 2020

APPENDIX F. GRADE Evidence Profile: Pulse Oximetry Screening for Critical Congenital Heart Disease in Asymptomatic Newborns

Question: Should Pulse Oximetry Screening be used to screen for Critical Congenital Heart Disease in Asymptomatic Newborns?

Sensitivity	0.71 (95% CI: 0.53 to 0.85)
Specificity	1.00 (95% CI: 1.00 to 1.00)

Prevalences	0.044%[7]

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 10,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of0.044%	
True positives (patients with Critical Congenital Heart Disease)	17 studies 418219 patients	cross-sectional (cohort type accuracy study)	serious[a]	not serious	not serious[b]	serious[c]	none[d]	3 (2 to 4)	⊕⊕◯◯ Low
False negatives (patients incorrectly classified as not having Critical Congenital Heart Disease)								1 (0 to 2)	
True negatives (patients without Critical Congenital Heart Disease)	17 studies 418219 patients	cross-sectional (cohort type accuracy study)	serious[a]	not serious	not serious[b]	not serious	none[d]	9996 (9996 to 9996)	⊕⊕⊕◯ Moderate
False positives (patients incorrectly classified as having Critical Congenital Heart Disease)								0 (0 to 0)	

APPENDIX F. GRADE Evidence Profile: Pulse Oximetry Screening for Critical Congenital Heart Disease in Asymptomatic Newborns

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classified as having Critical Congenital Heart Disease)			erious[a]	not serious	not serious[b]	not serious	none[d]	9996 (9996 to 9996)	⊕⊕⊕◯ Moderate
								0 (0 to 0)	

a. Serious ROB because of unclear issues on conduct of reference standard (issues on partial verification and differential verification bias) and flow, timing.

10 out of 17 studies had High RoB

APPENDIX F. GRADE Evidence Profile: Pulse Oximetry Screening for Critical Congenital Heart Disease in Asymptomatic Newborns

Question: Should Pulse Oximetry Screening be used to screen for Critical Congenital Heart Disease in Asymptomatic Newborns?

Sensitivity	0.71 (95% CI: 0.53 to 0.85)
Specificity	1.00 (95% CI: 1.00 to 1.00)

Prevalences	0.044%[7]

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 10,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of0.044%	
True positives (patients with Critical Congenital Heart Disease)	17 studies 418219 patients	cross-sectional (cohort type accuracy study)	serious[a]	not serious	not serious[b]	serious[c]	none[d]	3 (2 to 4)	⊕⊕◯◯ Low
False negatives (patients incorrectly classified as not having Critical Congenital Heart Disease)								1 (0 to 2)	
True negatives (patients without Critical Congenital Heart Disease)	17 s 418 pati					not serious	none[d]	9996 (9996 to 9996)	⊕⊕⊕◯ Moderate
False positives (patients incorrectly classified as having Critical Congenital Heart Disease)								0 (0 to 0)	

b. Not serious inconsistency = high heterogeneity between all studies but noted improved sensitivity with subgroup analyses

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True negatives (patients without Critical Congenital Heart Disease)	17 studies 418219 patients	cross-sectional (cohort type accuracy study)	serious[a]	not serious					⊕⊕⊕◯ Moderate
False positives (patients incorrectly classified as having Critical Congenital Heart Disease)								0 (0 to 0)	

c. Serious imprecision for sensitivity= high confidence interval noted across studies.

APPENDIX F. GRADE Evidence Profile: Pulse Oximetry Screening for Critical Congenital Heart Disease in Asymptomatic Newborns

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False positives (patients incorrectly classified as having Critical Congenital Heart Disease)								0 (0 to 0)	

d. No issues on publication bias = Publication bias cannot be excluded but deemed by reviewers to not be sufficient to downgrade evidence quality

Summary of effectiveness and mortality data

	Range	Pooled Estimate	Certainty of Evidence	Source
Mortality		1 in 10,000 risk of mortality from CCHD until 1 year of age among newborns who are not screened **HTAD-computed RR: 0.79 (95% CI 0.69 to 0.89)** **HTAD-computed risk** **Screened:** 0.97 in 10,000 **Unscreened:** 1.23 in 10,000	*moderate*	pooled analysis of *Abouk et al., 2017* and *Banait et al., 2018* (observational studies)
Sensitivity	0 to 100%	71% (95% CI: 53.0 to 85.0) (I^2 = 59.45%)	*low*	PHEX review (2021)pooled analysis of 17 studies N=418,219 newborns
Specificity	96 to 100%	100% (95% CI: 100.0 to 100.0) (I^2 not reported)	*moderate*	

Description of the Adopted Systematic Review
(PHEX Guidelines, 2021)

STUDIES INCLUDED

- **Evidence on the risk of mortality (NPOS vs no screening):**
  - Abouk et al. 2017
  - Banait et al. 2018

- **Evidence on the performance characteristics of NPOS (k=17):**
  - Plana et al. 2018 (Cochrane systematic review)
    - Note: 6/21 studies from the Cochrane SR were included in this review
  - Additional search of 11 diagnostic accuracy studies

- **Evidence on the harms of NPOS (k=3)**
  - UK National Screening Committee Pilot Study (Evans et al. 2016)
  - Public Health England recommendation to UK NSC (2019)
  - Banait et al, 2018

Harms of NPOS

- Studies with concern on the harms of NPOS:

1. **UK National Screening Committee Pilot Study (Evans et al. 2016)**
2. **Public Health England recommendation to UK NSC (2019)**
   - Did not recommend NPOS due to: a) delayed discharge, and b) parental anxiety
3. **UK 2018 cohort (Banait et al, 2018)**
   - No statistically significant difference in the post-discharge diagnosis rate between screened (7/100, 000) and unscreened cohorts (13/100, 000) [RR = 0.52 (95% CI 0.2-1.42)]

Study Characteristics of studies on Harms of NPOS, *PHEX, 2021 [1 of 2]*

Evans et al., 2016 (retrospective and prospective, pilot study) [UK National Screening Committee Pilot Study (2016)]	
P	• Asymptomatic newborns not admitted in a neonatal unit (including homebirths); gestational age of ≥34 weeks • N = 32,836 screened
I	• Newborn pulse oximetry screening using Masimo devices, Nellcor devices, Datascope and Nellcor via the GE Dash monitor • Site of testing: pre and post-ductal sites • Test timing: optimal time agreed was between 4-8 h but flexibility in timing were noted within 12 and after 24 h • Threshold for positive screen: either <90%-94% or difference of >2%
C (Reference std)	• If positive screen, admitted to NNU for urgent pediatric assessment of a senior clinician - -> blood tests and chest x-ray or echocardiography • If negative screen - -> continue with Healthy Child Programme
O	Delayed discharge

Study Characteristics of studies on Harms of NPOS, *PHEX, 2021 [2 of 2]*

Evans et al., 2016 (retrospective and prospective, pilot study) [UK National Screening Committee Pilot Study (2016)]	
Results and Conclusion	• ***Delayed discharge was reported in 68 (28%)*** *out of 239 screened positive, but of these,* ***53% had a significant clinical diagnosis*** *which is highly likely to have delayed discharge.* • *Discharge was reported as* ***inappropriately delayed* in 32 babies (13% of all screen positives)*** • ***There was little evidence of additional significant harm to the majority of babies who had a screen positive outcome.*** *It is possible however, that* ***some babies underwent unnecessary admission and investigation as a result of testing screen positive*** *Length of discharge delay ranged from 4 to 24 hours

Public Health England Recommendation to UK NSC 2019 on Pulse Oximetry as an Additional Test in the Newborn and Infant Physical Exam, *PHEX, 2021*

Key points of PHE review as basis for recommendation to the UK NSC	• Positive result will generate some harms (i.e., parental anxiety, a longer stay in hospital, possible transfer to the neonatal unit, further tests to assess for non-symptomatic conditions) • False positive results lead to unnecessary investigations on babies, only to be declared as healthy. • The review could not report with any certainty that the use of pulse oximetry would do more good than harm to all those offered screening due to lacking comparator data.
Conclusion	• *The review was unable to assess the benefits and harms of pulse oximetry compared to routine screening alone,* ***the review recommended against the introduction of pulse oximetry as an additional test in routine screening.***

Study Characteristics of studies on Harms of NPOS (*PHEX, 2021*)

Banait et al, 2018 (Retrospective, cohort study) UK	
P	Babies born at >34 weeks gestation with CCHD from three tertiary hospitals. (N=138,176)
I	• Routine POS in two hospitals, done after 4 hours of age and before discharge (test timing); n=76,232 • **Testing Site**: post-ductal • **Threshold for positive screen**: <95% • Positive screen→ echocardiography
C	No POS policy in one hospital n=61,944
Outcome	Post-discharge diagnosis rate, mortality at one year between cohorts

Results and Conclusion	• The rate of post-discharge diagnosis in the screened population was 7/100,000 and 13/100,000 in the unscreened population with a relative risk of 0.52 (CI 0.2 to 1.42).
	• Mortality at one year in postnatally diagnosed cases
	  ○ Screened cohort: 5
	  ○ Unscreened cohort: 1
	• **POS did not have a statistically significant impact in identifying cases of CCHD, when added to the present screening process of antenatal ultrasound and postnatal examination**.
	• Pulse oximetry may be more appropriate as a **screening tool for hypoxemia of any cause,** instead of being purely for CCHD

C2. REVIEW OF GUIDELINES

Review of Guidelines (N=29)

Agency	Recommended	No recommendation	Not Recommended
World Health Organization	WHO		
Ministry of Health *(N=15)*	n = 6 US, Australia, New Zealand, China, Thailand, Philippines	n = 8 Europe, Canada, South Korea, Japan, Malaysia, Singapore, Indonesia, Vietnam	n = 1 UK
HTA Agency *(N=10)*	n = 1 Canada (INESS)	n = 9 EUnetHTA, UK NICE, MSAC (AUS), CADTH, NHEI (CHN), NECA (SK) InaHTAC (IND), ACE (SG), MAHTAS	
Medical Society *(N=3)*	n = 3 European Pulse Oximetry Screening Workgroup, Canada, Philippines		

LEGEND
High income Countries
Upper-Middle income countries
Low income countries

Review of Guidelines (N=29)

Agency	Recommended	No recommendation	Not Recommended
World Health Organization	WHO		
Ministry of Health *(N=15)*			n = 1 UK
HTA Agency *(N=10)*		MAHTAS	
Medical Society *(N=3)*	n = 3 European Pulse Oximetry Screening Workgroup, Canada, Philippines		

Reasons for non-recommendation:

- Insufficient evidence to suggest that there is a greater benefit to babies than that afforded by the current screening program
- Harms associated with screening and further investigations following a positive screen result

LEGEND
High income Countries
Upper-Middle income countries
Low income countries

World Health Organization 2020

Quality statement 1.10 NEW: All newborns are assessed for congenital abnormalities, managed appropriately and referred in a timely manner.

"Pulse oximetry is a highly specific, moderately sensitive test for detecting critical congenital heart defects, with very low false positive rates. Current evidence supports the introduction of routine screening for such defects in asymptomatic newborns before discharge from the well-baby nursery."

C3: COST-EFFECTIVENESS

Cost-effectiveness analysis

Objective: *To determine the cost effectiveness of newborn pulse oximetry in screening critical congenital heart disease (CCHD) among asymptomatic, apparently healthy newborns*

PICO of the assessment

Population	Asymptomatic, apparently healthy newborns
Intervention	Pulse oximetry screening in addition to physical examination
Comparator	Physical examination of the newborn
Outcomes	Clinical: - Early detection of critical congenital heart disease at 1 week of age (represents timely diagnosis of CCHD) - Mortality at 1 year of age Economic: - Incremental cost effectiveness ratio (ICER) - Budget impact - HFI ELSHI

Cost-effectiveness analysis

Economic model

- Decision-tree model by *Trujillo et al., 2019*
- **Population:** asymptomatic, apparently healthy newborns
- **Intervention:** pulse oximetry screening in addition to physical examination (SOC)
- **Comparator**: physical examination only (SOC)
- **Time horizon:** 1 week of life and 1 year of life
- No discount rate applied because of the short time horizons
- **Government or payor perspective**
- **Health outcomes:**
  - Correct diagnosis at 1 week of age (timely diagnosis)
  - Survival at one year of age
- **CE threshold**: 75% of GDP per capita of the Philippines (2023) ➞ Php 155,441 (USD 2,794.19)
- ICERs computed at 1 week and 1 year time horizon

Cost-effectiveness analysis

Economic model

- ***ICER formula:***

$$\frac{\textit{Cost of POS+PE} - \textit{Cost of PE alone}}{\textit{Effectiveness of POS+PE} - \textit{Effectiveness of PE alone}}$$

- At 1 week and at 1 year timepoints
  - **Outcome at 1 week:** number of correctly diagnosed newborns with CCHD
  - **Outcome at 1 year**: number of CCHD who are alive

Cost-effectiveness analysis

Model Assumptions

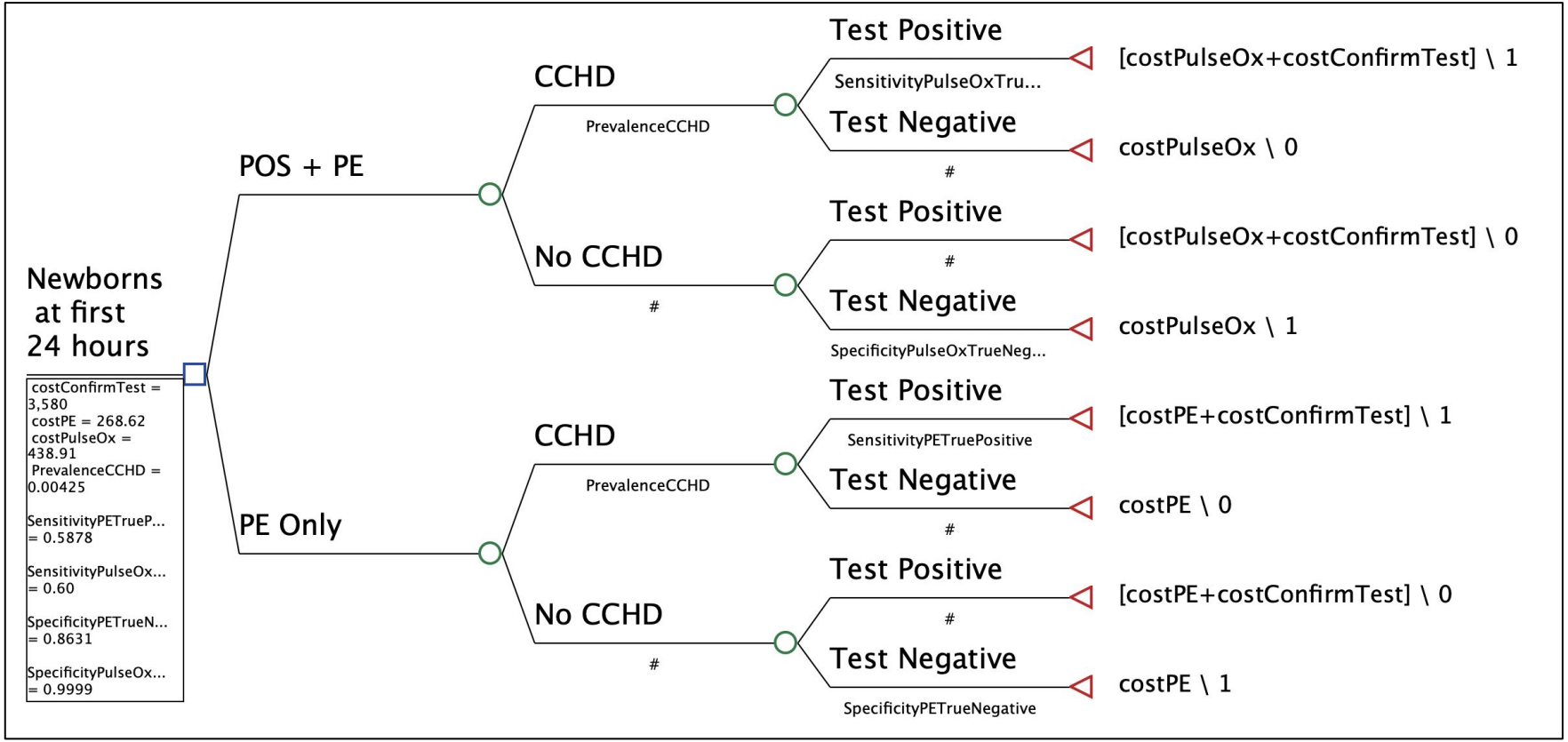
- The decision tree model focuses only on direct medical costs, using cost estimates derived from PhilHealth, and excludes indirect costs and productivity loss.
- The model assumes that all infants with positive POS or PE screens will get confirmatory 2D echocardiography; hence the timeliness or availability of the confirmatory test was not considered.
- In the model, 77% of all infants confirmed to have CCHD will undergo intervention (through cardiac catheterization and/or surgical procedures) while 23% of CCHD infants who will have comorbidities will preclude the performance of interventional procedures *(Del Rosario et al., 2024)*
- Assumes that all newborns who are medically indicated to undergo surgery after diagnosis of CCHD will undergo surgery. Hence, it does not take into account the following that could further lower down the proportion of those who will undergo surgery:
    - Acceptability issues regarding parents to allow their newborns to undergo surgery
    - Accessibility issues
- Handheld type pulse oximeter with a lifespan of five (5) years will be used

Cost-effectiveness analysis

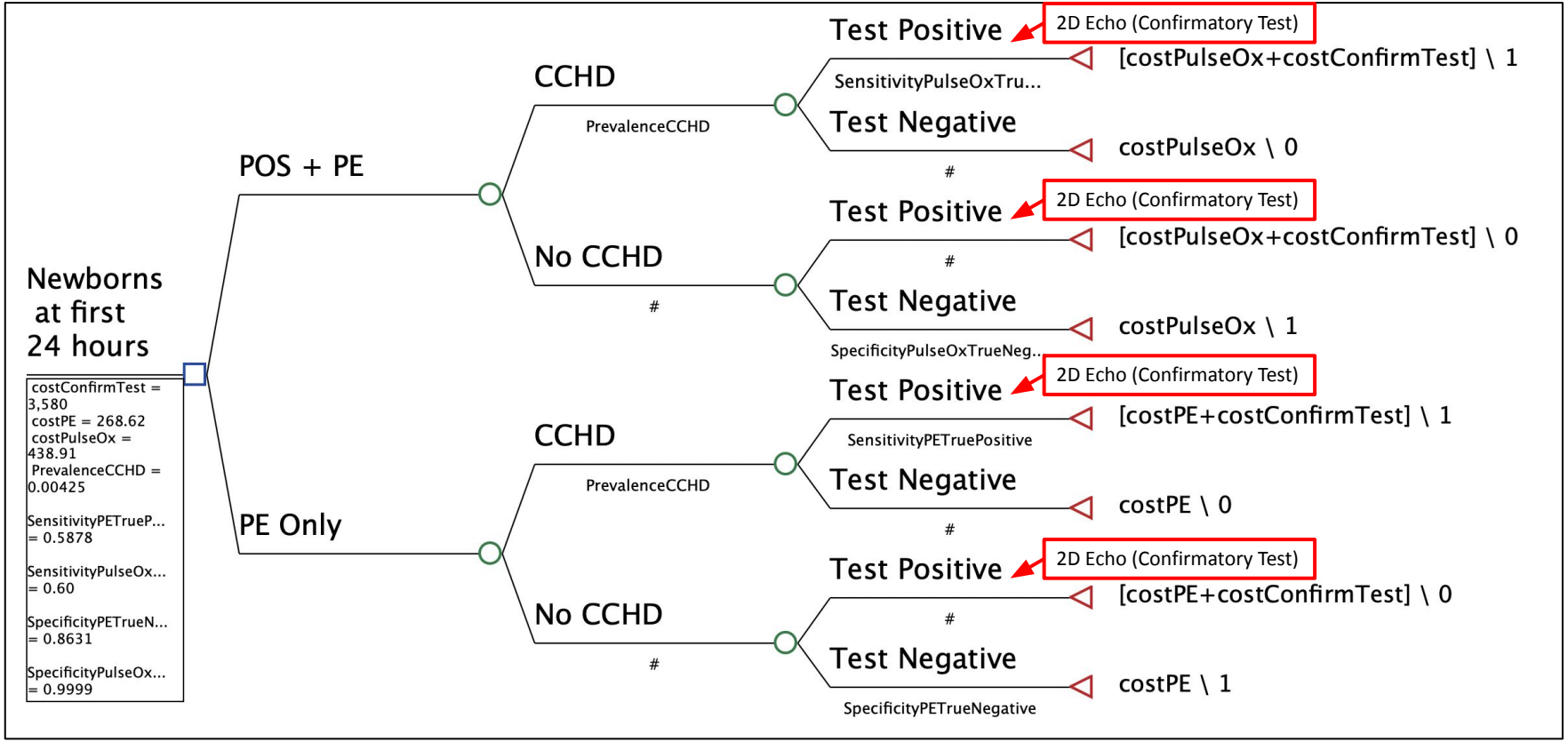
Model Assumptions

- A 1-week time frame for detecting CCHD and a 1-year time frame for estimating lives saved were utilized from the adopted model of Trujillo et al.
- For parameters without predefined ranges, the model applies a 20% adjustment, consistent with health economic evaluation practices recommended by the International Society for Pharmacoeconomics and Outcomes Research (ISPOR). *(This approach follows examples like the "Guideline for Health Technology Assessment in Thailand," which advises adjusting parameters by ±10–25% when specific data is unavailable)*
- Costs were no longer discounted due to the short time horizon of 1 year.

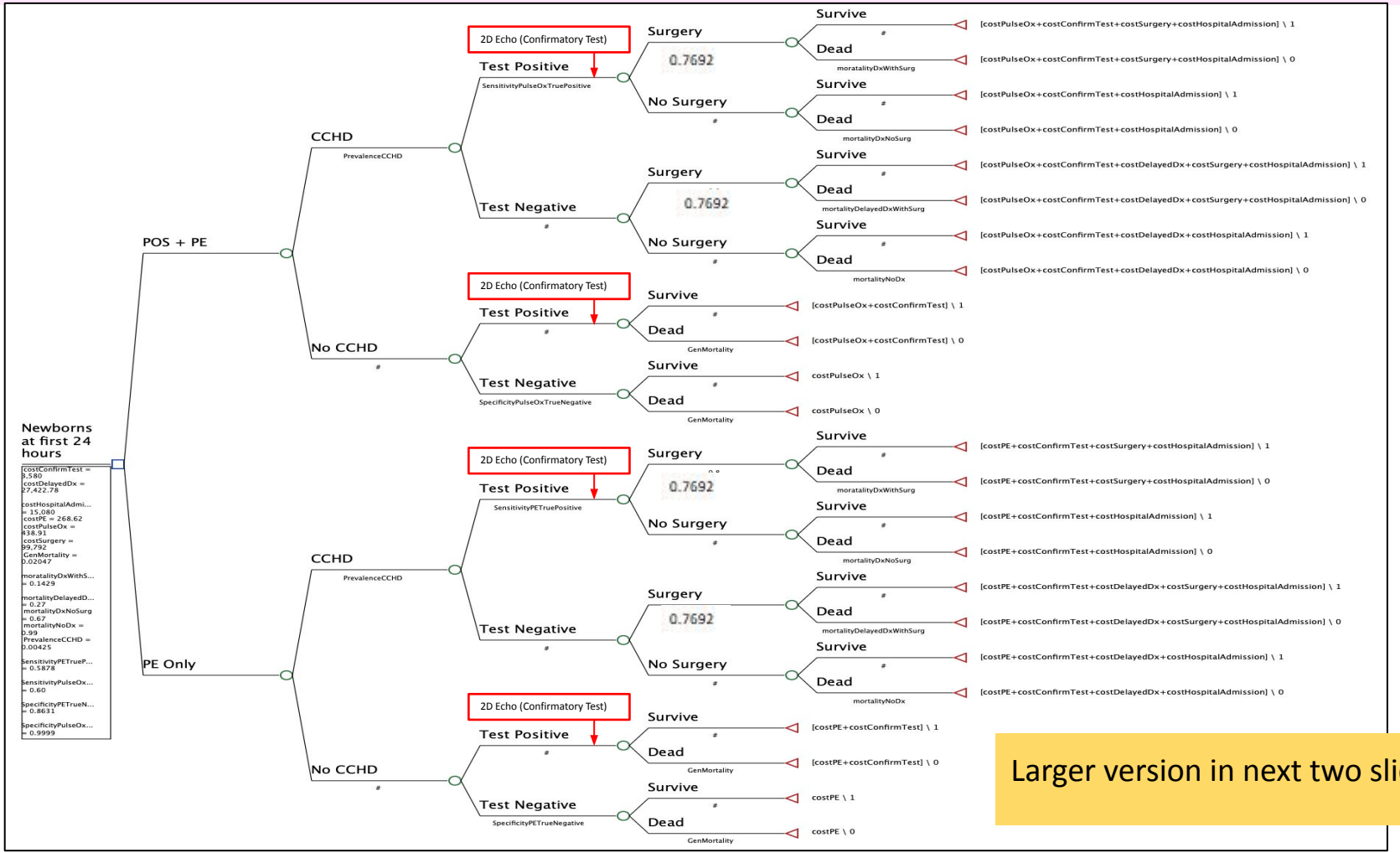
Decision tree model for cost-effectiveness: Pulse Oximetry + PE versus PE Alone after 1 week of birth



Decision tree model for cost-effectiveness: Pulse Oximetry + PE versus PE Alone after 1 week of birth

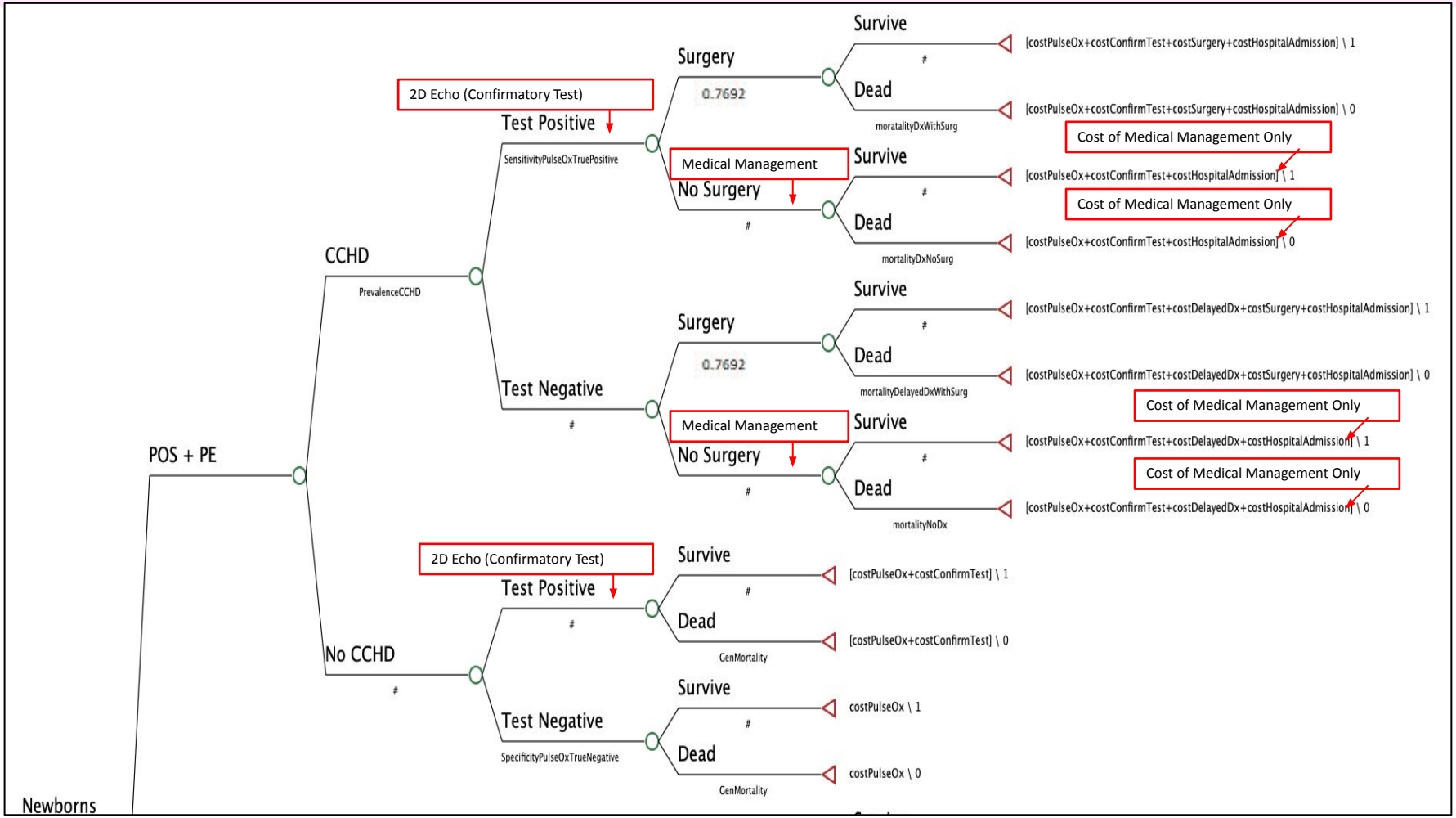


Decision tree model for cost-effectiveness Pulse Oximetry + PE versus PE Alone after 1 year of birth

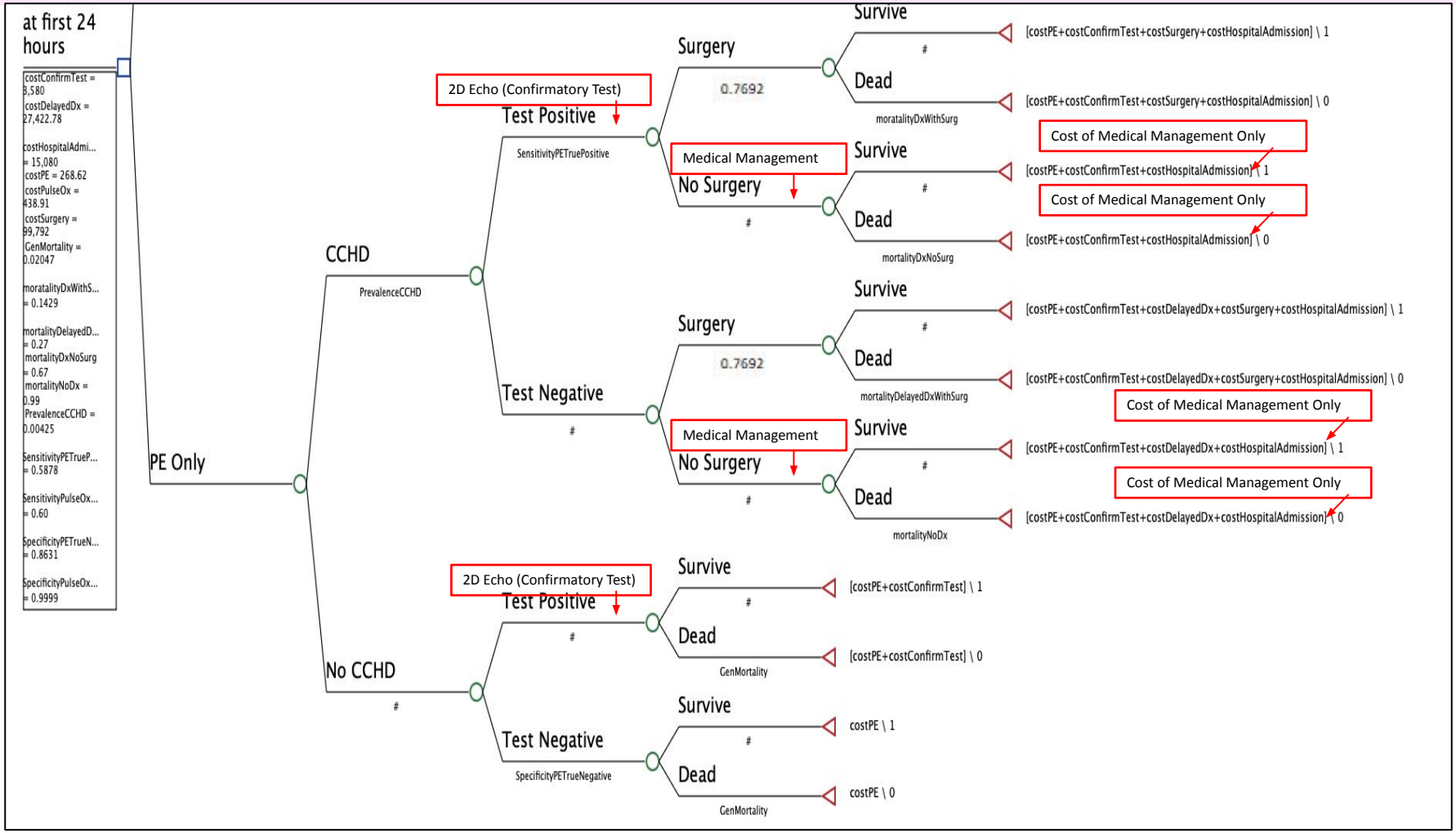


Larger version in next two slides

Decision tree model for cost-effectiveness Pulse Oximetry + PE versus PE Alone after 1 year of birth



Decision tree model for cost-effectiveness Pulse Oximetry + PE versus PE Alone after 1 year of birth



Model Inputs for COST

Item	Cost (PhP)	Range (PhP)	Source
Pulse Oximetry Screening (POS) (using handheld type pulse oximeter) ***Setting:*** *Public health facilities (i.e., primary birthing facilities and all government hospital levels)*	452.81	362.25 - 543.37	*UNICEF catalogue (2024); DBP salary grade table (2022)*
Physical Examination Screening (PE)	268.62	214.89 - 322.34	*DBP salary grade table (2022)*
Confirmatory test (2D-echocardiography)	3,580.00	2,864.00 - 4,296.00	*Philippine Heart Center website*
Hospital costs for CCHD patients until definitive treatment	15,080.00	12,064.00 - 18,096.00	*PhilHealth (2022)*
Costs for managing the most common complication from delayed diagnosis (ex: congestive heart failure)	27,422.78	25,170.60 - 29, 674.96	*PhilHealth (2022)*
Surgical procedure costs	99,792.00	79,833.78 - 119,750.68	*PhilHealth (2022)*

Model Inputs for EPIDEMIOLOGIC PARAMETERS

Parameter	Point estimate	Range	Source
Number of registered live births in 2022	1,455,393	N/A	*Philippine Statistics Authority (2024)*
Number of births delivered in public HF	816,475	N/A	*2021 National Demographic and Health Survey (NDHS)* *56.1% of births delivered in public HF*
Prevalence of CCHD (95% CI)	0.00425	0.0023 - 0.0071	*Del Rosario et. al., , 2024 (submitted for publication)*
Percentage of those with CCHD who will not undergo surgical or catheterization intervention*	0.2308	0.1846- 0.277	*Del Rosario et. al., , 2024 (submitted for publication)*
Percentage of those with CCHD who will undergo surgical or catheterization intervention*	0.7692	0.723- 0.8154	*Del Rosario et. al., , 2024 (submitted for publication)*
CCHD mortality (case fatality ratio; 95% CI)- timely diagnosis and intervention given	0.1429	0.026 - 0.51	*Del Rosario et. al., , 2024 (submitted for publication)*
CCHD mortality (case fatality ratio; 95% CI)- timely diagnosis but no corrective intervention	0.67	0.3 - 0.9	*Del Rosario et. al., , 2024 (submitted for publication)*
CCHD mortality (CFR; 95% CI) - delayed diagnosis and intervention	0.27	0.18 - 0.39	*Eckersley, 2015*
CCHD mortality (CFR; 95% CI)- delayed diagnosis, no intervention	0.99	0.98 - 0.99	*Del Rosario et. al., , 2024 (submitted for publication)*
General mortality rate of under 1 year old (95%CI)	0.0205	0.0144 - 0.0279	*WHO website (2024)*

Model Inputs for POS + PE and PE Alone

Parameter	Point estimate	Range	Source
Sensitivity of PE alone	0.588	0.115 to 0.892	*Trujillo, 2019 (Colombia)*
Specificity of PE alone	0.863	0.4 to 0.99	*Trujillo, 2019 (Colombia)*
Sensitivity of POS + PE	0.71	0.53 to 0.85	*PHEX Review, 2021*
Specificity of POS + PE	0.9999	0.9998 to 1	*PHEX Review, 2021* /Assumption

Other Model Parameters

Parameter	Value/Inputs	Source
Perspective	Government Perspective	
Time Horizon	1 week and 1 year	
CE Threshold [PHP [USD])	PHP 155,441 (USD 2,794.19)	*75% of the GDP per capita of the Philippines for 2023 (World Bank Group, 2024)*
USD to PHP Exchange Rate 2025	1 USD = 57.30 PHP	*Bangko Sentral ng Pilipinas, April 2025*

Results

1. *Cost-effectiveness of POS + PE vs PE alone at 1 week*
   - *Deterministic CE analysis*
   - *Probabilistic sensitivity analysis*
     - *CE plane, mean ICER, CEA curve,*
   - *One-way sensitivity analysis*

2. *Cost-effectiveness of POS + PE vs PE alone at 1 year*
   - *Deterministic CE analysis*
   - *Probabilistic sensitivity analysis*
     - *CE plane, mean ICER, CEA curve,*
   - *One-way sensitivity analysis*
   -

RESULT: *Cost-effectiveness of POS + PE vs PE alone at 1 week*

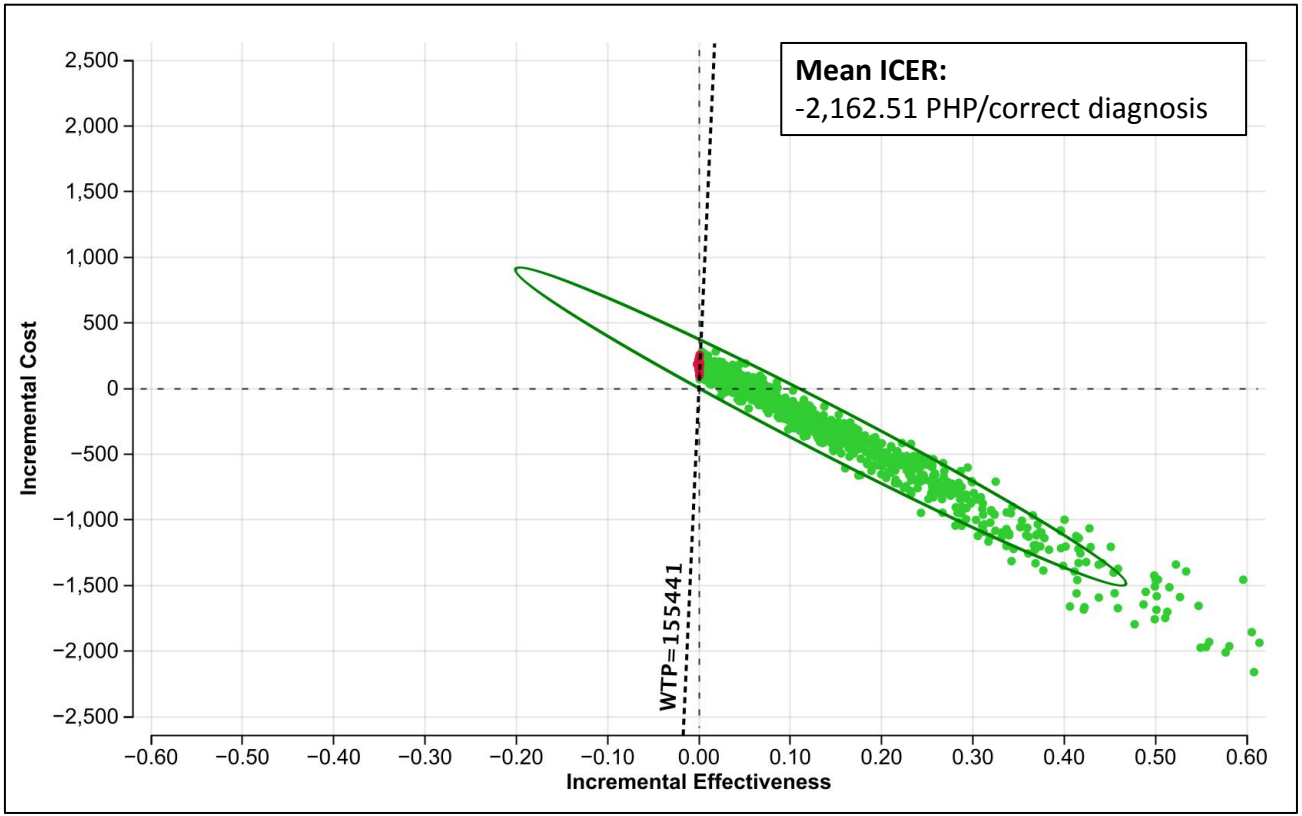
Deterministic cost-effectiveness analysis

Strategy	Cost (PhP)	Incremental cost (PhP)	Effectiveness (Correctly diagnosed case)	Incremental Effectiveness	ICER (PhP/correct diagnosis)
POS + PE	463.97	-301.61	0.999	0.137	-2,205.78
PE alone	765.58	--	0.862	--	--

WTP: PHP 155,441(USD 2,794.19) *[75% of 2023 GDP per capita of Philippines]*

- POS + PE is less costly and more effective than PE only, resulting in a negative ICER
- The negative ICER indicates the POS + PE is cost-saving
- The higher cost of PE only stems from its lower specificity values compared to pulse oximetry plus PE which results in higher false positive cases that will incur costs for confirmatory 2D echocardiography.

RESULT: *Probabilistic sensitivity Analysis of POS + PE versus PE alone at 1 week*



The scatterplot shows that after 1,000 simulations, ***POS + PE remained cost-saving or cost-effective in 97.2% of iterations*** *as shown by the larger quantity of green points that is simulating one patient per point.*

WTP: PHP 155,441(USD 2,794.19) [75% of 2023 GDP per capita of Philippines]

RESULTS: *Proportion of POS + PE iterations being cost-effective at 1 week according to CET*

CE Threshold Threshold (PHP)	Proportion of POS+PE iterations as cost-effective (%)
207,254 (1x GDP)	97.7
155,441 (0.75x GDP)	97.2
103,627 (0.5x GDP)	96.3

RESULT: *Probabilistic sensitivity Analysis of POS + PE versus PE only at 1 week (CET = PHP 207,255 [1x GDP])*

Incremental Cost	Incremental Effectiveness	ICER	No. of Iterations	Proportion	Interpretation
IC<0	IE>0	**Superior**	628	0.628	**POS + PE is cost-saving**
IC>0	IE>0	**ICER<207,255**	349	0.349	**POS + PE is cost-effective**
IC<0	IE<0	**ICER>207,255**	0	0	**PE is cost-effective**
IC>0	IE>0	**ICER>207,255**	12	0.012	**PE is cost-effective**
IC<0	IE<0	**ICER<207,255**	0	0	**POS + PE is cost-effective**
IC>0	IE<0	**Inferior**	11	0.011	**PE is cost-effective**

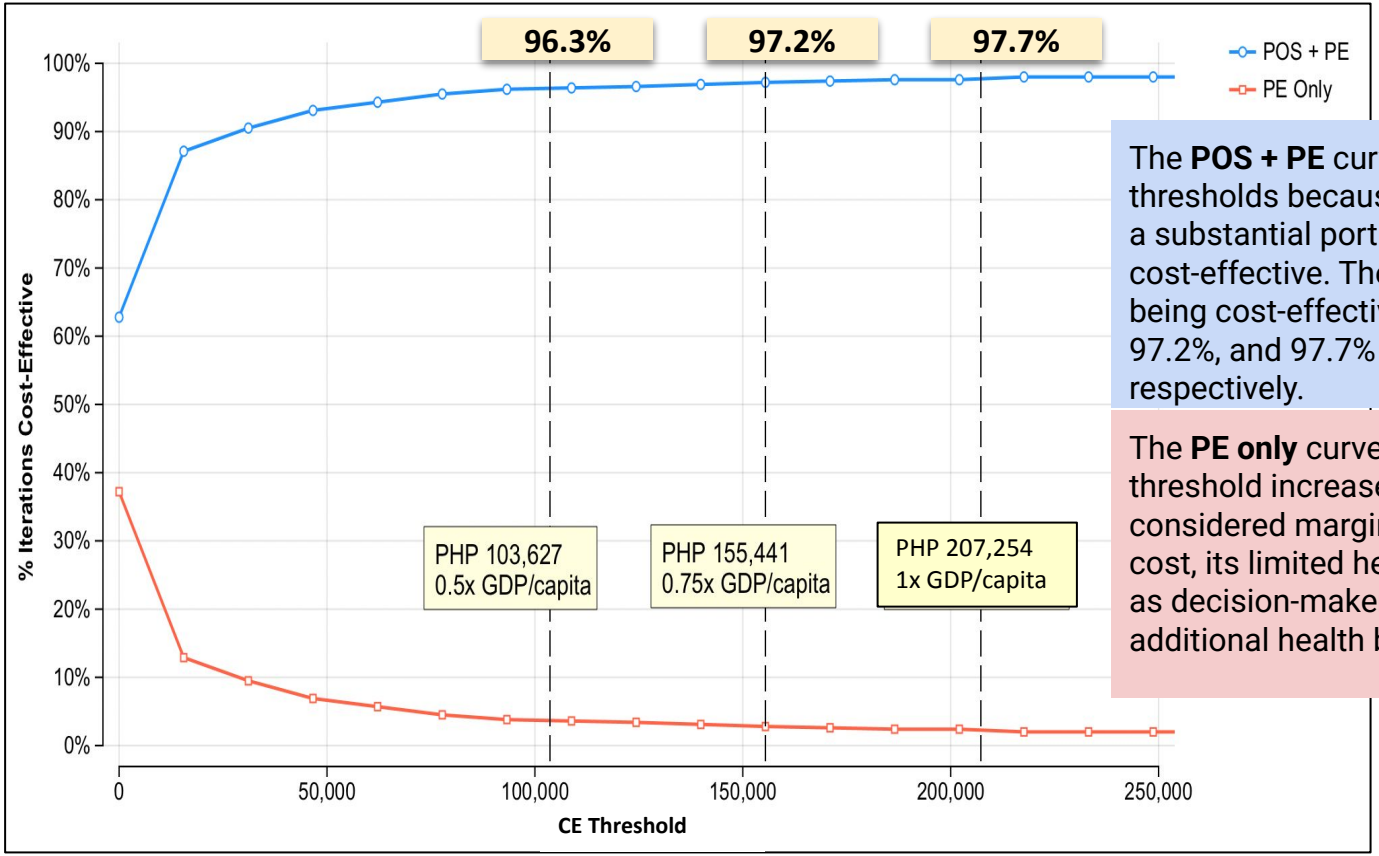
RESULT: *Probabilistic sensitivity Analysis of POS + PE versus PE only at 1 week [CET: (Php 155,441) 0.75x GDP]*

Incremental Cost	Incremental Effectiveness	ICER	No. of Iterations	Proportion	Interpretation
IC<0	IE>0	**Superior**	628	0.628	**POS + PE is cost-saving**
IC>0	IE>0	**ICER<155,441**	344	0.344	**POS + PE is cost-effective**
IC<0	IE<0	**ICER>155,441**	0	0	**PE is cost-effective**
IC>0	IE>0	**ICER>155,441**	17	0.017	**PE is cost-effective**
IC<0	IE<0	**ICER<155,441**	0	0	**POS + PE is cost-effective**
IC>0	IE<0	**Inferior**	11	0.011	**PE is cost-effective**

RESULT: *Probabilistic sensitivity Analysis of POS + PE versus PE only at 1 week (CET = PHP 103,627 [0.5x GDP])*

Incremental Cost	Incremental Effectiveness	ICER	No. of Iterations	Proportion	Interpretation
IC<0	IE>0	**Superior**	628	0.628	**POS + PE is cost-saving**
IC>0	IE>0	**ICER<103,627**	335	0.335	**POS + PE is cost-effective**
IC<0	IE<0	**ICER>103,627**	0	0	**PE is cost-effective**
IC>0	IE>0	**ICER>103,627**	26	0.026	**PE is cost-effective**
IC<0	IE<0	**ICER<103,627**	0	0	**POS + PE is cost-effective**
IC>0	IE<0	**Inferior**	11	0.011	**PE is cost-effective**

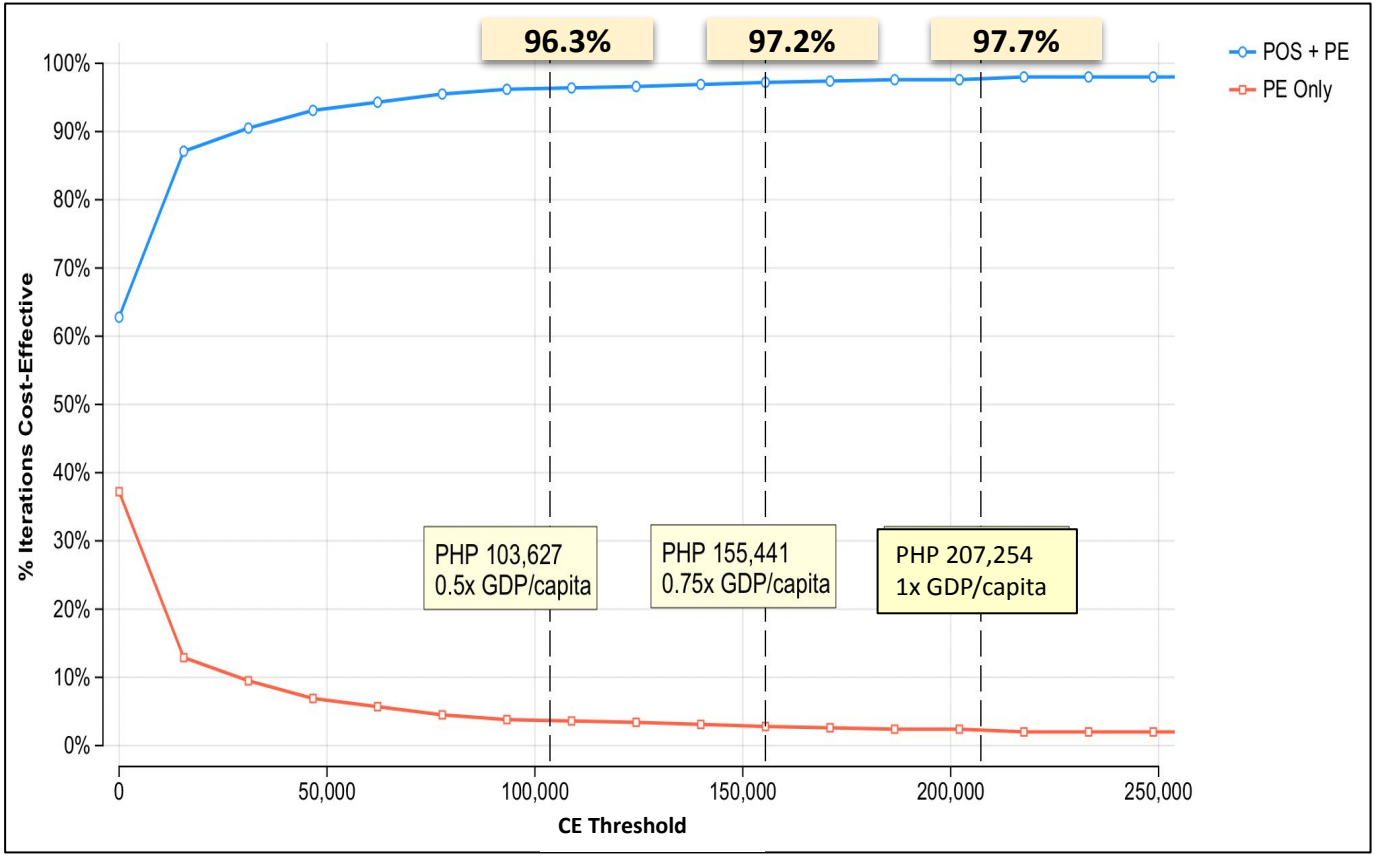
RESULTS: *CE acceptability curve of POS + PE vs PE alone at 1 week*



The **POS + PE** curve starts at 60% at very low CE thresholds because, even when resources are limited, a substantial portion of simulations already find it cost-effective. The proportion of iterations of POS+PE being cost-effective for this outcome are 96.3%, 97.2%, and 97.7% at 0.5x, 0.75x, and 1x the GDP, respectively.

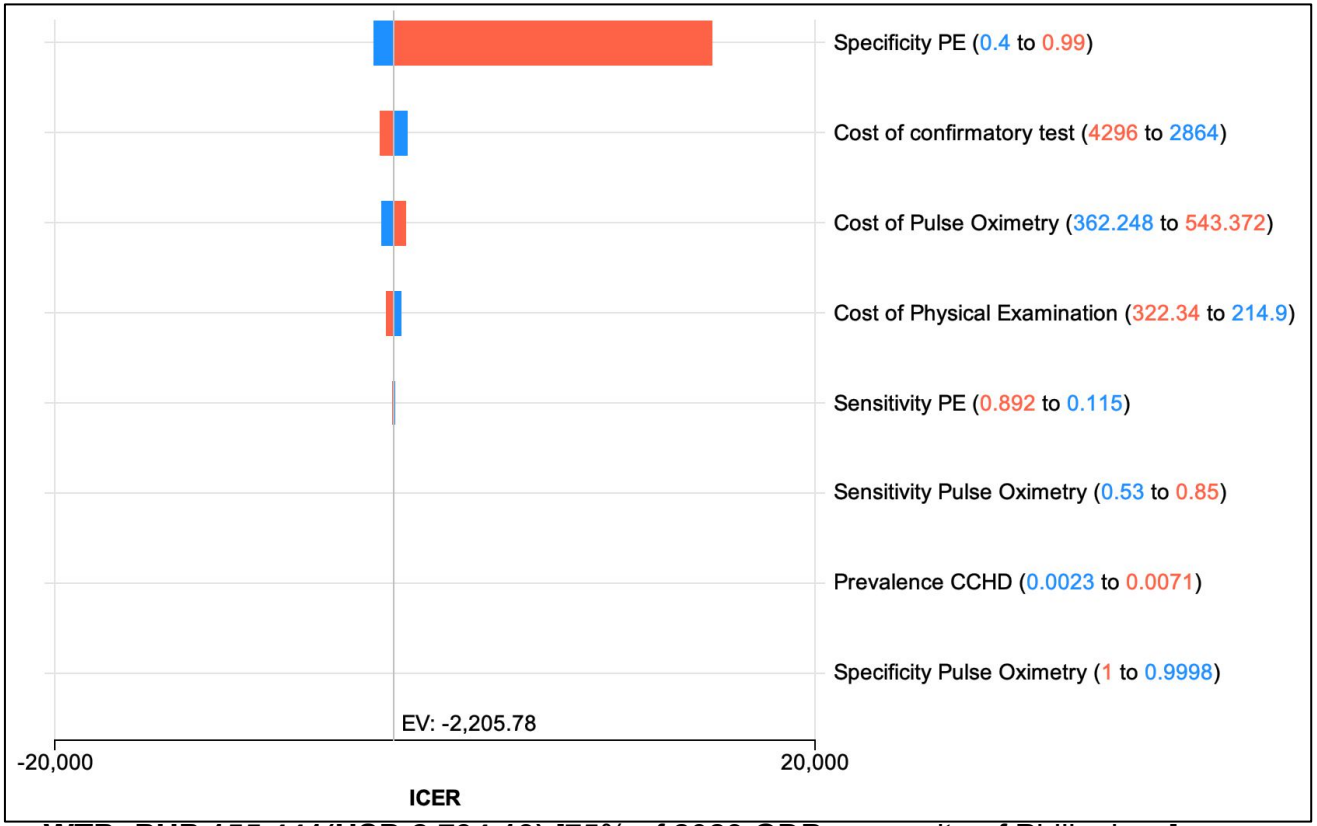
The **PE only** curve begins at 40% but declines as CE threshold increases indicating that, while initially considered marginally cost-effective due to its lower cost, its limited health benefit becomes less justifiable as decision-makers become more willing to invest in additional health benefits.

RESULTS: *CE acceptability curve of POS + PE vs PE alone at 1 week*



- **At all CE thresholds, more than 96% of simulations find POS + PE to be cost-effective.**
- As CE threshold increases, the additional cost associated with added benefits of POS + PE becomes more acceptable, leading to a rapid rise of the curve, which eventually plateaus as CE thresholds approaches 1× GDP and beyond.
- Overall, the CEAC shows the **POS+PE strategy consistently delivers better value and greater health benefits,** even when accounting for economic constraints and uncertainties.

RESULT: *Sensitivity Analysis of POS + PE versus PE only at 1 week*



WTP: PHP 155,441(USD 2,794.19) [75% of 2023 GDP per capita of Philippines]

- *The **specificity of PE is the most influential variable, significantly affecting the ICER** followed by the cost of POS, cost of confirmatory tests, and the cost of PE .*
- *Overall, the diagram shows that **POS remains a cost-effective screening method despite variations in the values of sensitivity, specificity, and costs**.*

Results

1. *Cost-effectiveness of POS + PE vs PE alone at 1 week*
   - *Deterministic CE analysis*
   - *Probabilistic sensitivity analysis*
     - *CE plane, mean ICER, CEA curve,*
   - *One-way sensitivity analysis*

2. *Cost-effectiveness of POS + PE vs PE alone at 1 year*
   - *Deterministic CE analysis*
   - *Probabilistic sensitivity analysis*
     - *CE plane, mean ICER, CEA curve,*
   - *One-way sensitivity analysis*

RESULT: *Cost-effectiveness of POS + PE vs PE alone at 1 year*

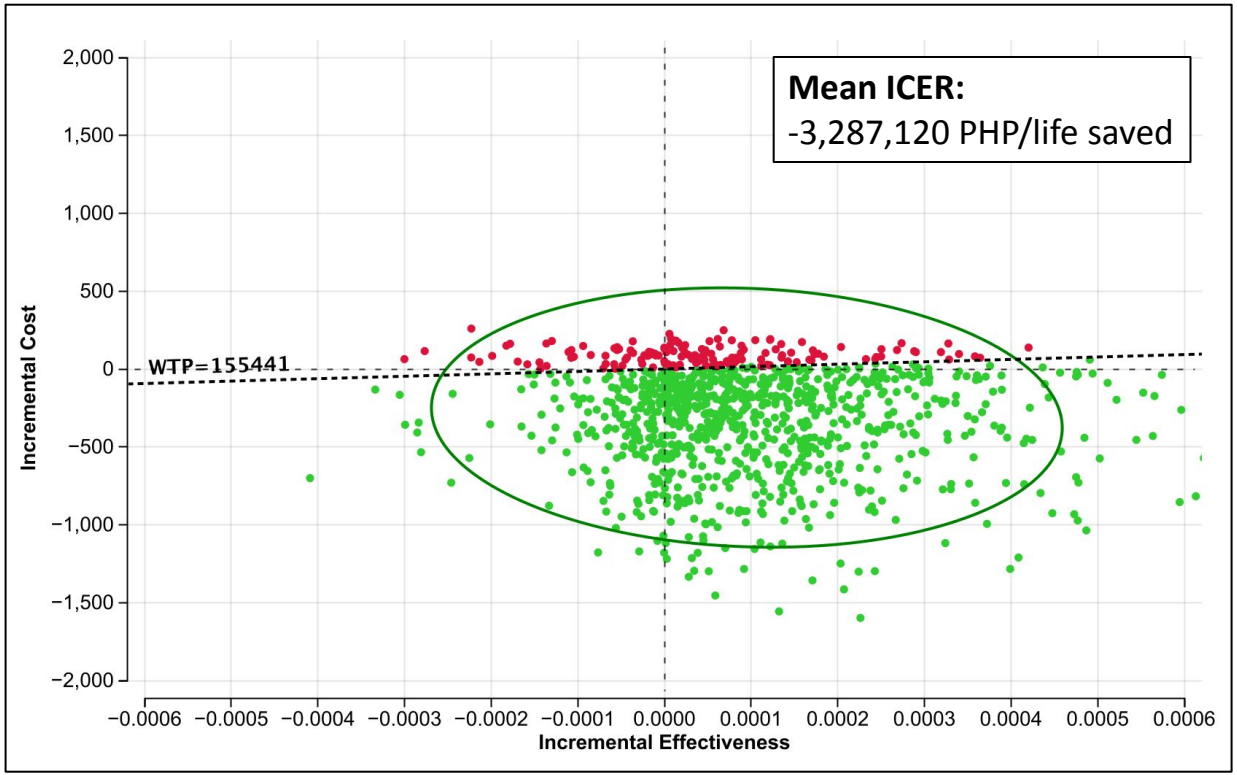
Deterministic cost-effectiveness analysis

Strategy	Cost (PhP)	Incremental cost (PhP)	Effectiveness (Lives saved at 1 year)	Incremental Effectiveness	ICER (PhP/life saved)
POS + PE	892.50	-371.71	0.978281	0.000089	-3,564,559
PE Only	1,210.21	--	0.978192	--	--

WTP: PHP 155,441(USD 2,794.19) *[75% of 2023 GDP per capita of Philippines]*

- POS + PE is less costly and slightly more effective than PE only resulting in a negative ICER (cost-saving strategy)
- For the outcome of survival at year 1, PO in addition to PE compared to PE alone showed marginal incremental effectiveness since after diagnosis is already confirmed, the main driver for reducing mortality is the effect of surgery rather than the screening test

RESULT: *Probabilistic sensitivity Analysis of POS + PE versus PE alone at 1 year [CET: 0.75x GDP]*



The scatterplot shows that after 1,000 simulations, **POS+PE remains cost-effective in 85.4% of the time** as shown by the larger quantity of green points representing one iteration or one simulated patient per point

WTP: PHP 155,441(USD 2,794.19) [75% of 2023 GDP per capita of Philippines]

RESULTS: *Sensitivity Analysis of POS + PE versus PE only at 1 year (CET = PHP 207,254 [1x GDP])*

Incremental Cost	Incremental Effectiveness	Incremental Cost Effectiveness Ratio	No. of iterations	Proportion	Interpretation
IC<0	IE>0	Superior	651	0.651	**POS + PE is cost-saving**
IC>0	IE>0	ICER<207,255	26	0.026	**POS + PE is cost-effective**
IC<0	IE<0	ICER>207,255	0	0	**PE is cost-effective**
IC>0	IE>0	ICER>207,255	93	0.093	**PE is cost-effective**
IC<0	IE<0	ICER<207,255	181	0.181	**POS + PE is cost-effective**
IC>0	IE<0	Inferior	49	0.049	**PE is cost-effective**

RESULTS: *Sensitivity Analysis of POS + PE versus PE only at 1 year (CET = PHP 155,441 [0.75x GDP])*

Incremental Cost	Incremental Effectiveness	Incremental Cost Effectiveness Ratio	No. of iterations	Proportion	Interpretation
IC<0	IE>0	Superior	651	0.651	**POS + PE is cost-saving**
IC>0	IE>0	ICER<155,441	22	0.022	**POS + PE is cost-effective**
IC<0	IE<0	ICER>155,441	0	0	**PE is cost-effective**
IC>0	IE>0	ICER>155,441	97	0.097	**PE is cost-effective**
IC<0	IE<0	ICER<155,441	181	0.181	**POS + PE is cost-effective**
IC>0	IE<0	Inferior	49	0.049	**PE is cost-effective**

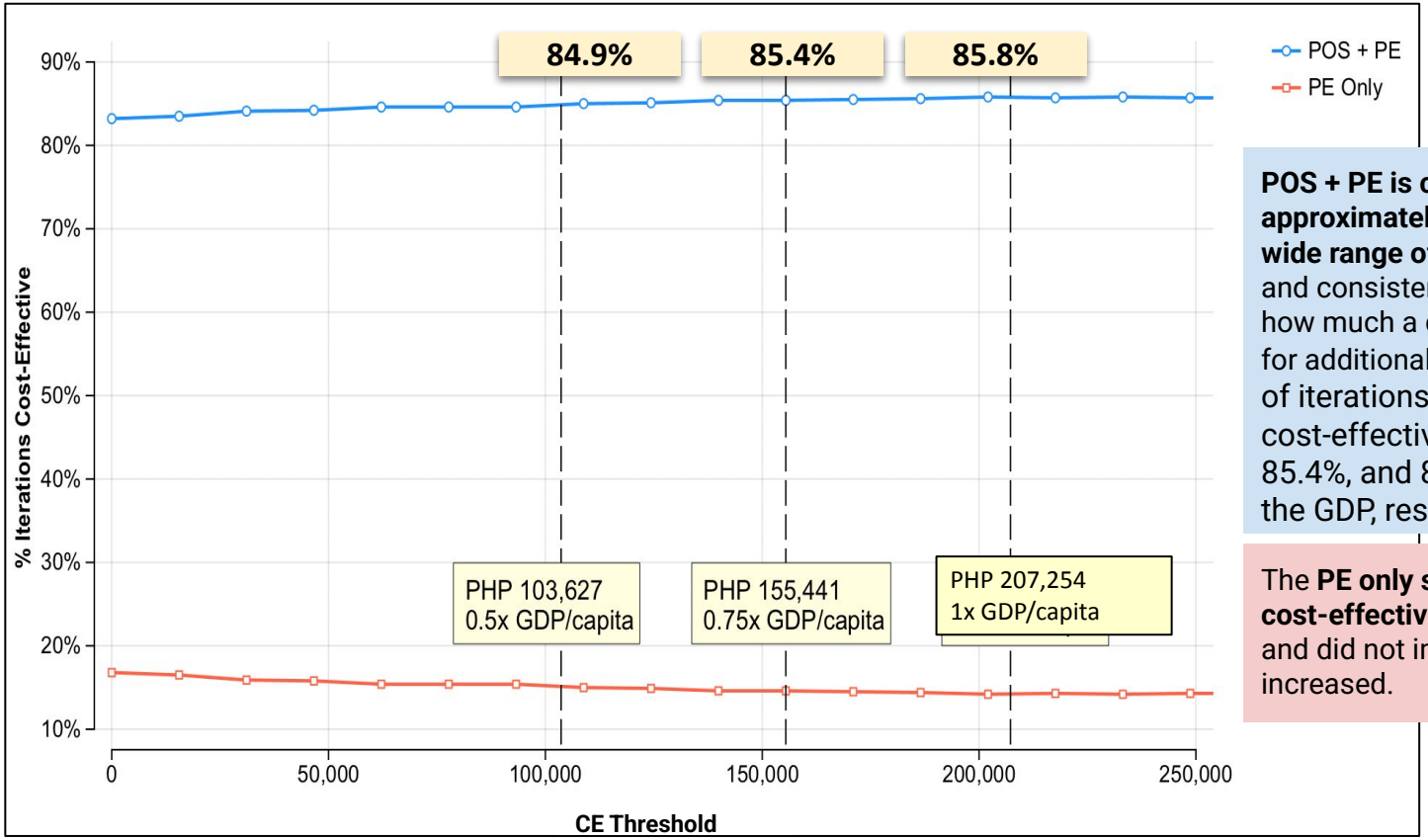
RESULTS: *Sensitivity Analysis of POS + PE versus PE only at 1 year (WTP = PHP 103,627 [0.5x GDP])*

Incremental Cost	Incremental Effectiveness	Incremental Cost Effectiveness Ratio	No. of iterations	Proportion	Interpretation
IC<0	IE>0	Superior	651	0.651	**POS + PE is cost-saving**
IC>0	IE>0	ICER<103,627	17	0.017	**POS + PE is cost-effective**
IC<0	IE<0	ICER>103,627	0	0	**PE is cost-effective**
IC>0	IE>0	ICER>103,627	102	0.102	**PE is cost-effective**
IC<0	IE<0	ICER<103,627	181	0.181	**POS + PE is cost-effective**
IC>0	IE<0	Inferior	49	0.049	**PE is cost-effective**

RESULTS: *Proportion of POS + PE iterations being cost-effective at 1 year according to CET*

CE Threshold Threshold (PHP)	Proportion of POS+PE iterations as cost-effective (%)
207,254 (1x GDP)	85.8
155,441 (0.75x GDP)	85.4
103,627 (0.5x GDP)	84.9

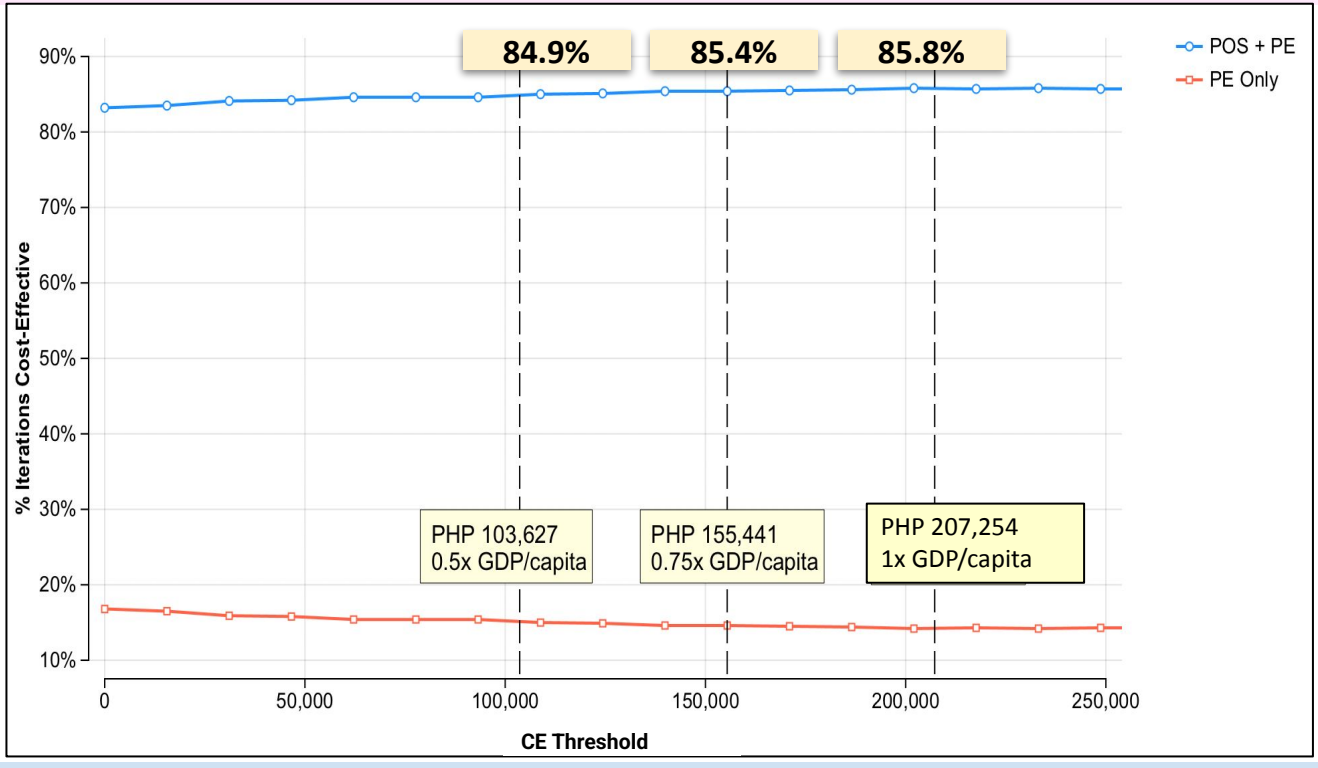
RESULTS: *CE acceptability curve of POS + PE versus PE alone at 1 year*



POS + PE is consistently cost-effective in approximately 85% of simulations across a wide range of CE thresholds indicating strong and consistent value for money, regardless of how much a decision-maker is willing to pay for additional health benefits. The proportion of iterations of POS+PE being cost-effective for this outcome are 84.9%, 85.4%, and 85.8 % at 0.5x, 0.75x, and 1x the GDP, respectively.

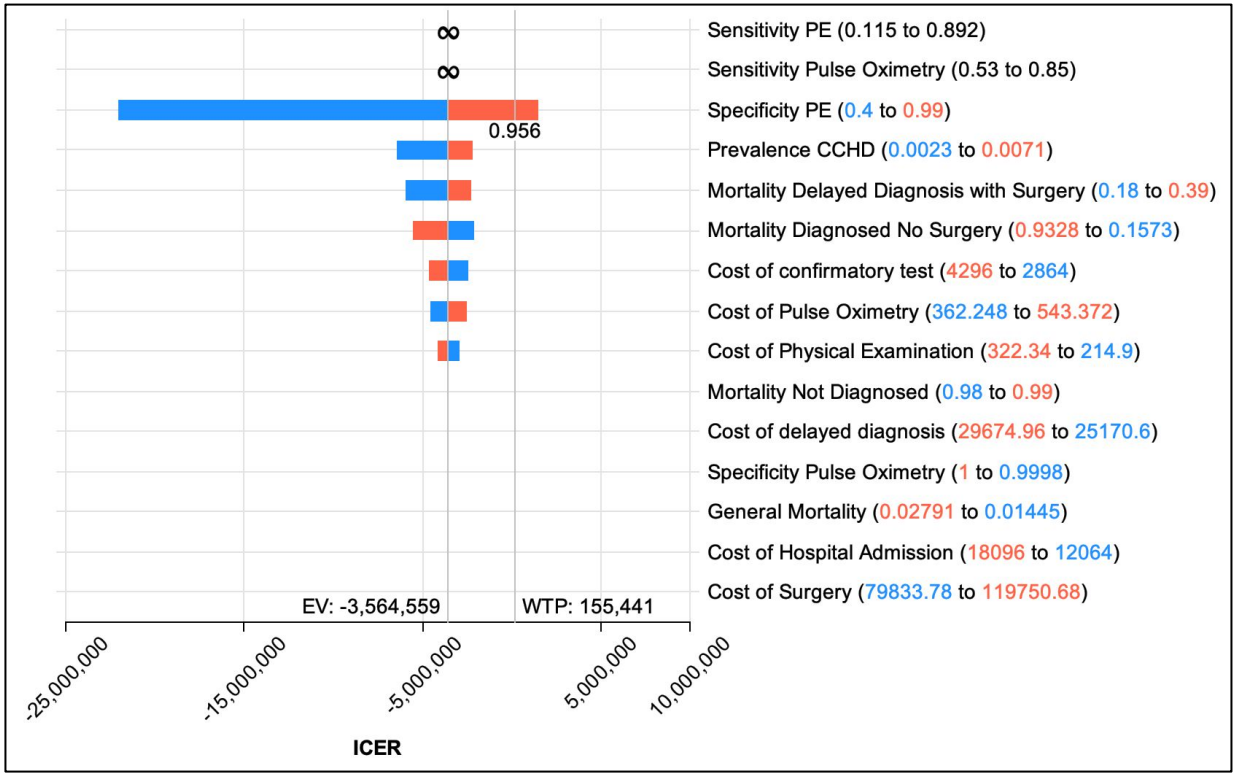
The **PE only strategy showed that it is cost-effective in only 14-15% of simulations** and did not improve even when CE threshold increased.

RESULTS: *CE acceptability curve of POS + PE versus PE alone at 1 year*



- Across all iterations and all CE thresholds, **POS + PE is the more cost-effective choice under both constrained and generous budget scenarios.**
- These results suggest that investing in POS + PE is likely to lead to better health outcomes and more efficient use of resources, even when accounting for uncertainty in the model.

RESULTS: *Sensitivity Analysis of POS + PE vs PE only at 1 year*



- **The tornado diagram shows that ICER at one year is most sensitive to the following parameters: sensitivity of Pulse Oximetry + PE and sensitivity of PE Only**
- The specificity of PE is a significant variable influencing the cost-effectiveness of PO. If the specificity of PE is above 0.956, Pulse Oximetry + PE no longer becomes cost-effective as shown in the diagram with the bar crossing the CE threshold.

WTP: PHP 155,441(USD 2,794.19) [75% of 2023 GDP per capita of Philippines]

Economic analysis

Limitations:

- Model only assessed short-term outcomes because of the lack of long-term data and hence cannot determine the lifetime costs, benefits, cost-effectiveness of the intervention
- Used data from other sources when local data was not available or had limitations as to its accuracy
  - There are no local registries for CCHD; used expert opinion and data from a local multicenter study
  - Study was limited to 16 health facilities in 6 regions with a setup that is not reflective of many areas in the country
  - Therefore, the data used may not accurately reflect the actual outcomes which can be affected by accessibility and availability of necessary healthcare personnel.
- Did not include certain costs in the management of CCHD patients such as transportation and costs incurred when a patient has to be referred and transferred to another health facility; Sensitivity analysis was done to address these limitations
- Model used static population estimates and does not include indirect costs and productivity losses. It assumes consistent sensitivity, specificity, and costs for PE and POS, which may vary across regions and over time.

Economic analysis

Comparison with other cost-effectiveness studies

- Trujillo et al. 2019 cost-effectiveness study set in Colombia:
  - POS + PE was not cost-effective for the 1-year time horizon
- This analysis:
  - POS + PE was cost-saving.
- Possible reasons for the difference in results:
  - Differences in prevalence, costs and sensitivity and specificity values for the interventions.
  - Perspective and costing of treatments used in the Trujillo study
    - Societal perspective vs government perspective
    - Addition of indirect costs vs only the cost of the interventions and the costs borne by the government through PhilHealth case rates
- Systematic review of cost-effectiveness studies of PO screening in newborns by Nargesi et al.2020:
  - 6/7 studies showed POS + PE to be cost-effective
  - 1/7 was not cost-effective in the 1-year time horizon
  - Most commonly used outcome: timely diagnosis of CCHD
  - Either high-income or upper-middle-income countries; no cost-effectiveness study in a lower-middle-income or lower-income country.

Economic evaluation

- **Conclusion**
  - The economic evaluation showed that pulse oximetry screening in addition to physical examination is cost-saving compared to physical examination alone in the timely diagnosis of CCHD infants and in improving survival of CCHD infants at one year of age.

C4: BUDGET IMPACT ANALYSIS

Budget Impact Analysis

Objective: *To determine the budget impact of routine use of pulse oximetry in addition to physical examination in the first 24 hours of life to screen for CCHD*

Budget Impact Analysis

Assumptions:

- All target government healthcare facilities (i.e., primary birthing facilities and all levels of government hospital) will be provided with one handheld pulse oximetry machine
- The cost and epidemiological input parameters from the CEA were also used in the BIA

Budget Impact Analysis

Base computation of using the intervention for all newborns

Gradual shifting strategy	Year 1	Year 2	Year 3	Year 4	Year 5
	20% POS +PE and 80% PE alone	40% POS +PE and 60% PE alone	60% POS +PE and 40% PE alone	80% POS +PE and 20% PE alone	100% POS +PE
Cost of POS + PE Screening (PHP)	131,803,301.00	267,560,701.00	407,361,167.00	551,295,446.00	699,456,097.00
Cost of PE Screening (PHP)	312,758,134.00	238,087,130.00	161,105,624.00	81,761,104.00	0.00

Budget Impact Analysis

Computation of interventions including the cost of outcomes based on the timing of detection and treatment

Gradual shifting strategy	Year 1	Year 2	Year 3	Year 4	Year 5
	20% POS +PE and 80% PE alone	40% POS +PE and 60% PE alone	60% POS +PE and 40% PE alone	80% POS +PE and 20% PE alone	100% POS +PE
Cost of POS + PE Screening (PHP)	259,886,435	527,569,464	803,224,508	1,087,030,501	1,379,169,948
Cost of PE Screening (PHP)	1,409,465,435	1,072,955,562	726,033,264	368,461,881	0
TOTAL COST	**1,669,351,870**	**1,600,525,026**	**1,529,257,772**	**1,455,492,383**	**1,379,169,948**

The total cost of the gradual 5-year shift to 100% POS+PE screening starts at approximately PHP 1.67 billion in Year 1 and decreases to PHP 1.40 billion in Year 5, reflecting reduced costs as detection becomes more efficient.

Budget Impact Analysis (Comparator: Summary of Cost of PE Only)

		Year 1	Year 2	Year 3	Year 4	Year 5
Live Births and Prevalence of CCHD	Annual Live Births	1,455,393	1,477,224	1,499,382	1,521,873	1,544,701
	Population with CCHD	6,185	6,278	6,372	6,468	6,565
Cost of Screening and Treatment with PE Only	Population screened	**100% PE Only**	**100% PE Only**	**100% PE Only**	**100% PE Only**	**100% PE Only**
	Cost of Screening and Treatment (POS + PE)	--	--	--	--	--
	Cost of Screening and Treatment (PE Only)	1,761,831,794	1,788,259,271	1,815,083,160	1,842,309,407	1,869,944,048
	TOTAL COST	**1,761,831,794**	**1,788,259,271**	**1,815,083,160**	**1,842,309,407**	**1,869,944,048**

Budget Impact Analysis of Shifting to POS + PE versus PE Only

		Year 1	Year 2	Year 3	Year 4	Year 5
Live Births and Prevalence of CCHD	Annual Live Births	1,455,393	1,477,224	1,499,382	1,521,873	1,544,701
	Population with CCHD	6,185	6,278	6,372	6,468	6,565
Incremental Cost of Shifting to POS + PE	Total Cost of Intervention: POS + PE and PE only	1,669,351,870	1,600,525,026	1,529,257,772	1,455,492,383	1,379,169,948
	Total Cost of comparator: PE only	1,761,831,794	1,788,259,271	1,815,083,160	1,842,309,407	1,869,944,048
	Incremental Cost of shifting to POS + PE versus PE only	-92,479,924	-187,734,245	-285,825,388	-386,817,025	-490,774,100
	Percentage Change of shifting to POS + PE versus PE only	-5.25%	-10.50%	-15.75%	-21.00%	-26.25%

Economic analysis

Limitations:

- The BIA also has several limitations. It assumes a gradual, linear shift from PE to POS over five years, which may not reflect real-world implementation challenges, such as logistical barriers or disparities in healthcare access, and changes in health policies.

Conclusion:

- There will be substantial financial impact in the budget in the introduction of pulse oximetry screening in all hospitals and birthing facilities, especially in the first few years of its introduction.
- In summary, adopting POS+PE not only leads to improved clinical outcomes but also results in substantial savings in cost over time compared to PE only, supporting the value of investment in expanded screening.

C5: HOUSEHOLD FINANCIAL IMPACT

Household Financial Impact of CCHD

Methodology

- Source of data is from PhilHealth claims from 2018 to 2023 for the following medical case rate groups:
  - **Congenital malformations of cardiac chambers and connections** (*ICD Q20.0 to Q20.9*)
  - **Congenital malformations of cardiac septa** (*ICD Q21.0 to Q21.9*)
  - **Congenital malformations of pulmonary and tricuspid valves** (*ICD Q22.0 to Q22.9*)
  - **Congenital malformations of aortic and mitral valves** (*ICD Q23.0 to Q23.9*)
  - **Other congenital malformations of heart** (*ICD Q24.0 to Q24.9*)
  - **Congenital malformations of great arteries** (*ICD Q25.0 to Q25.9*)
  - **Congenital malformations of great veins** (*ICD Q26.0 to Q26.9*)
- Used PAID claims only

Household Financial Impact of Congenital Heart Disease

	All ages	<1 year old	1-5 years old	6-17 years old	18-59 years old	60 years and above
Total Number of Paid Claims	12,933	4,526	3,295	2,551	2,269	292
Average Hospitalization Cost	₱ 37,893.19	₱ 44,754.45	₱ 29,643.73	₱ 28,463.69	₱ 45,540.97	₱ 47,584.11
Median Hospitalization Cost	₱ 19,691.50	₱ 23,566.88	₱ 16,068.98	₱ 16,088.90	₱ 22,335.00	₱ 28,889.91
Hospitalization Cost Range	₱ 0 to 14,822,600.01	₱ 0 to 3,844,845.31	₱ 0 to 1,167,066.84	₱ 0 to 710,782.93	₱ 0 to 14,822,600.01	₱ 2 to 470,107.12
Median Claims Cost	₱ 11,600.00	₱ 11,600.00	₱ 11,600.00	₱ 11,600.00	₱ 11,600.00	₱ 11,600.00
Claims Cost Range	₱ 1,805.00 to 27,200.00	₱ 2,750.00 to 15,610.00	₱ 3,480.00 to 22,100.00	₱ 1,805.00 to 18,880.00	₱ 3,480.00 to 21,050.00	₱ 6,553.54 to 27,200.00
Median Out-of-Pocket Cost	₱ 7,624.00	₱ 10,857.83	₱ 4,464.84	₱ 4,506.60	₱ 10,701.08	₱ 17,289.91
Out-of-Pocket Cost Range	₱ 0 to 14,811,000.00	₱ 0 to 3,830,495.31	₱ 0 to 1,155,466.84	₱ 0 to 699,182.93	₱ 0 to 14,811,000.01	₱ 0 to 458,507.12
Average % Coverage	61.37%	57.32%	67.13%	67.03%	56.17%	50.39%

Household Financial Impact of Congenital Heart Disease

	All ages	<1 year old	1-5 years old	6-17 years old	18-59 years old	60 years and above
Total Number of Paid Claims	12,933	4,526	3,295	2,551	2,269	292
Average Hospitalization Cost	₱ 37,893.19	₱ 44,754.45	₱ 29,643.73	₱ 28,463.69	₱ 45,540.97	₱ 47,584.11
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Median Claims Cost	₱ 11,600.00	₱ 11,600.00	₱ 11,600.00	₱ 11,600.00	₱ 11,600.00	₱ 11,600.00
Claims Cost Range	₱ 1,805.00 to 27,200.00	₱ 2,750.00 to 15,610.00	₱ 3,480.00 to 22,100.00	₱ 1,805.00 to 18,880.00	₱ 3,480.00 to 21,050.00	₱ 6,553.54 to 27,200.00
Median Out-of-Pocket Cost	₱ 7,624.00	₱ 10,857.83	₱ 4,464.84	₱ 4,506.60	₱ 10,701.08	₱ 17,289.91
Out-of-Pocket Cost Range	₱ 0 to 14,811,000.00	₱ 0 to 3,830,495.31	₱ 0 to 1,155,466.84	₱ 0 to 699,182.93	₱ 0 to 14,811,000.01	₱ 0 to 458,507.12
Average % Coverage	61.37%	57.32%	67.13%	67.03%	56.17%	50.39%

C6: ETHICAL, LEGAL, SOCIAL, AND HEALTH SYSTEMS (ELSHI) IMPLICATIONS

OBJECTIVES

To identify the **ethical, legal, social and health systems implications** of routine use of pulse oximetry in the first 24 hours of life to screen for congenital heart disease including CCHD.

Population	Asymptomatic, apparently healthy newborns
Intervention	Pulse oximetry screening in addition to physical examination
Comparator	Physical examination of the newborn; no POS
Outcomes	Ethical implications Social implications Legal implications Health systems implications

METHODOLOGY

Literature review

- To identify relevant themes related to ELSHI implications.
- PubMed search, handsearching included articles, handsearching references from PHEx 2021
- Search terms: (pulse oximetry screening AND critical congenital heart disease) AND (social OR ethical OR legal or health system implications)

Key informant interviews (KIIs) or Focus group discussions (FGDs)

- To obtain perspectives of parents, public healthcare practitioners, healthcare providers and civil society representatives on the ethical, legal, social, and health systems implications of the including NPOS to the newborn screening tests
- Secured ethical clearance from UPMREB
- Guide questions and/or questionnaires were developed and approved (e.g. acceptability and general attitude towards NPOS).
- Convenience sampling and sent out invitations to target participants.
- Descriptive thematic analysis

METHODS of DATA GATHERING: KIIs and FGDs

	Invited participants	Number of participants	Tool	Platform
Ethical and social implications	• CSOs (patient organizations which cater to children with CHD)	4 representatives from CSOs (either mothers or relatives of a child with CHD who needed surgical intervention)	KII	Online / Zoom
	• Parents of newborns from health facilities (tertiary hospital and RHUs)	5 mothers of newborns in the OB ward of a tertiary hospital (divided in two groups)	FGD	Face-to-face
Legal implications	• Staff from the Legal Office of DOH • Staff from the Disease Prevention and Control Bureau (DPCB) of DOH	3 staff from DPCB Written response from DOH Legal office	FGD	Online FGD written response

Health system implications	• For <u>administrative perspective</u> (e.g. in charge of policy making and program planning), staff from DPCB of DOH, Regional DOH offices
	• For <u>implementer perspective</u>:
	  • Staff from health facilities who had experience in implementing POS (from the Philippine multicenter POS study)
	  • Specialists (pediatric cardiologists and neonatologists)
		Total of 39 participants, 10 sessions with mean of 3-4 participants each sessions (minimum of 2, maximum of 8 per session)	FGD	Online / Zoom

RESULTS: LITERATURE REVIEW (1 of 3)

- 11 articles from the search; themes related mostly to health systems implications and a few on social, ethical and legal implications

Author/Year (Country)	Population	Description of study
Ewer et al 2012 (United Kingdom)	• Parents • Health care staff of the study hospitals	• Structured questionnaire, FGD and email survey on **acceptability of POS as a screening test for CHDs in newborn infants** among parents and hospital staff
Powell et al 2012 (United Kingdom)	• Mothers of newborns from six maternity units	• Main topic: **Acceptability of POS** for congenital heart defects and **factors predictive of participation** in screening among mothers • Executive summary of an HTA on POS • Structured questionnaire on **satisfaction, stress, anxiety, depression, general feelings** about test, **perceptions on what the test meant, perception of the illness being screened**, and **measure of optimism**
Hom et al 2016 (US)		• Expert review • Main topic: **Legal and ethical implications of mandatory POS** (e.g. parental authority over religion and personal beliefs, rights of infants)
Kumar 2016 (India)		• Editorial • Main topic: **Challenges, considerations and possible opportunities** for population-wide POS in low-resource settings

RESULTS: LITERATURE REVIEW (2 of 3)

- 11 articles from the search; themes related mostly to health systems implications and a few on social, ethical and legal implications

Author/Year (Country)	Population	Description of study
Van Niekerk et al 2016 (South Africa)	• Mothers of newborn • Health staff who implemented POS	• Descriptive, prospective implementation of POS in one postnatal ward of a secondary-level maternity hospital • Questionnaires on the implementation **feasibility and acceptability of POS**
McClain et al 2017 (USA)	• Six (6) demonstration project grantees and other state representatives involved in the implementation of CCHD screening programs	• A qualitative review on **implementation challenges** from on the following areas: **legislation, provider and family education, screening algorithms, data collection improvements, home and rural births, neonatal ICUs** • To assist federal and state policymakers and public health to implement CCHD screening. • Data gathered from a monthly technical assistance conference where they shared their experiences with POS implementation.
Murni et al 2022 (Indonesia)	• Hospital personnel who implemented POS were given semi-structured interviews	• Cross sectional study • Main topic: Semi-structured interview on **barriers encountered by hospital personnel** in implementing POS
Kluckow 2018 (Australia)		• Narrative review • Main topic: identifying and reviewing the **barriers and acceptance to the implementation** of pulse oximetry as a screening test for CCHD.

RESULTS: LITERATURE REVIEW (3 of 3)

- 11 articles from the search; themes related mostly to health systems implications and a few on social, ethical and legal implications

Author/Year (Country)	Population	Description of study
Zheleva et al 2020 (India)		• Commentary • Main topic: **Health system readiness**, considerations and recommendations in **implementing POS for CCHD in low-and middle-income countries**
Rajani & Narayanappa, 2020 (India)	Randomly selected health care professionals	• Main topic: Online survey questionnaire on **knowledge, attitudes and practices and opinion** related to NPOS for CHD
Cloete et al 2018 (New Zealand)	Parents of infants who underwent pulse oximetry screening	• Survey on **consumer satisfaction** of services received from health facilities (including hospitals and primary health facilities); qualitative and quantitative analysis (thematic analysis); N=657 (only 4% of those who underwent POS)

ETHICAL IMPLICATIONS

Findings from the literature review and KII or FGDs

Themes for Ethical Implications:

No.	Themes	Sources of evidence
1	Mandatory screening, obtaining consent	Literature review: k=3 KII with CSO representatives FGD with parents of newborns from health facilities (tertiary hospital and RHUs)
2	Equity issues	Literature review: k= 2

Theme 1: Mandatory screening, obtaining consent (1 of 2)

This theme highlights the considerations in obtaining parental consent and communicating relevant information about NPOS among parents.

- The State can override the parents' right to decide which medical procedures can be done to their children to prevent death or serious harm. Nevertheless, parents who refuse POS should be engaged and counseled as to the benefits of POS and risk if it is not performed [Hom, 2016 (expert review, US)].

- To enable engagement during the consent process, some parents think that **more information on how the test is conducted and what will happen after** should be given (Powell et.al 2012, UK).

- However, **the timing of information delivery influenced how the parent retained the information.** Some participants cannot recall the information given about the test because of **fatigue following delivery** (Cloete et al 2018, New Zealand).

Theme 1: Mandatory screening, obtaining consent (2 of 2)

- Mothers interviewed in a OB ward generally had no difficulty during consent procedures. However, one noted that it was **hard to understand the information given related to POS due to the number of post-delivery newborn procedures**.

- CSOs advocating for children with CHD stated the mothers often **struggle to understand the consent information given**. Mothers also often refrain from clarifying due to confusion, fear, or shame.

- Lastly, the stress experienced by mothers because of their child's situation made it **difficult for them to understand the procedures** the hospital staff were explaining.

Theme 2: Equity Issues

Identified possible equity issues are the following:

- A substantial proportion of home births in India was observed and with this, even if POS will be implemented, they will still not be screened and CCHD will still be undetected. Moreover, there are existing limitations in the health system, such as capacity, referral processes, confirmatory testing, and newborn transport, taking into account regional and socioeconomic disparities (Kumar 2016).
- Lack of 2D echocardiography in some rural health facilities and home births which account for more than 10x the incidence of missed CCHD cases in the US (McClain et al 2017).

SOCIAL IMPLICATIONS

Findings from the literature review and KII or FGDs

Themes for Social Implications:

No.	Themes	Sources of evidence
1	Equity Issues	KIIs or FGD findings
2	Acceptability of screening tests	Literature review: k=5 KIIs or FGD findings
3	Barriers to acceptability of screening test	KIIs or FGD findings

Theme: 1. Equity Issues

Findings from the KIIS and FGDs described equity challenges in accessing NPOS, particularly affecting infants and mothers.

- A respondent recalled difficulties of being referred to a hospital in Manila due to the initial facility's inability to handle a newborn with medical issues.

- Similarly, some respondents opted not to do further procedures if they were required to go to another facility, as this would entail additional money and time spent.

- Generally, respondents concluded that health facilities with **NPOS should be available nationwide as routine newborn screening** by PhilHealth. Confirmatory tests should also be free for those who test positive in NPOS and to increase capacity and number of health facilities capable of managing CHDs.

Theme 2: Acceptability of NPOS among parents (1 of 3)

- Most respondents **perceived NPOS positively** (i.e., quick, safe, non-invasive, painless for the baby and reassuring for parents), and as an important health check on to identify early condition and comprehensibility of heart disease (Cloete et al 2018, Ewer et al 2012, Powell et al 2012,).

- **No evidence that mothers given false-positive (FP) results were more anxious** than those given true-negative (TN) results. However, **certain ethnicities (i.e., Asian: Indian, Pakistani, and Bangladeshi; and Black of African and Caribbean origins) presented higher anxiety and depression**, which was associated with **lower overall satisfaction** (Ewer et al 2012).

- Instead of tagging NPOS as a CCHD assessment, Kluckow, 2018 suggested **documenting the oxygen saturation as part of routine vital signs**. This approach can **decrease parental anxiety and expectation**, change the interpretation of false positives and the timing of the test, and removing the pressure to perform an immediate echocardiogram if the test is positive.

- **Majority of those who completed questionnaires (99%) felt the test was explained well**, the duration of the test acceptable, and NPOS beneficial to all children (Van Niekerk, 2016). However, a study had contrasting results wherein they said that **hospital staff should be more reassuring to parents** regarding the results of the test and should have full understanding of the protocol if the test fails (Powell et al 2012). They also wish to be given more information on what happens after a baby 'fails' a test.

Theme 2: Acceptability of NPOS among parents (2 of 3)

- Respondents support the inclusion of the NPOS to the existing newborn care package, encompassing all the healthcare facilities from tertiary hospitals down to lying-in facilities in urban, rural settings, and particularly in remote areas. Benefits identified were:

  (1) early detection and intervention,

  (2) no out-of-pocket expense

  (3) equitable screening delivery in different healthcare institutions,

  (4) more comprehensive newborn care package.

Theme 2: Acceptability of NPOS among parents (3 of 3)

- Given a possible false positive (FP) test, a mother expressed that while she would be relieved that her infant did not have CHD, she thinks it would be a waste of time and resources for them to proceed to a confirmatory test, only for it to turn negative. She suggested that screening test should then be improved to have less FP test results.

- The mothers suggested that they be informed of the possible results (i.e., false negative and false positive) and what it entails when HCPs explain about NPOS

- All the mothers, who had undergone POS at the hospital, felt that the **test was acceptable because it was non-invasive, free and a negative screen gave them assurance of the well-being of their newborns**.

Theme 3: Barriers to acceptability of NPOS among parents

- **Poor communication regarding POS**, including the consequences and parent's concern of different outcomes of POS

- Some respondents **opted not to have confirmatory tests** or further management done if it involved referral to a different health facility and considerable **added expenses** in terms of direct medical costs and travel cost

- **Stigma against cardiac conditions -** some parents, older family members, or family members who provide financial support see "heart defects" as a death sentence and further management as futile, hence the refusal to undergo procedures

- **Lack of information on health services in government hospitals**
  - Respondents equate private hospitals with better service (i.e.. because of better healthcare provider availability, smaller patient-healthcare worker ratio, less waiting time, better facilities) due to previous experiences or experiences of other family members

- **Distance to or accessibility to public health facilities** like RHUs

LEGAL IMPLICATIONS

Findings from the literature review and KII or FGDs

Themes for Legal Implications:

No.	Themes	Sources of evidence
1	Mandates on newborn screening; need for consent	Literature review: k=2 FGD with DPCB and written questionnaire with DOH Legal office
2	Procurement Issues	FGD with DPCB and written questionnaire from the DOH Legal Office
3	Data Privacy and Confidentiality Issues	FGD with DPCB and written questionnaire from the DOH Legal Office

Theme 1: Mandates on newborn screening; need for consent

- RA 9288 or the Newborn (NB) Screening Act of 2004 does not state the need for a written consent specifically for newborn screening.
- While the PH law does not specify pulse oximetry screening, Section 4 indicates that Comprehensive Newborn Screening System is not limited to the current newborn screening.
- Parents or legal guardians have the right to refuse NB screening procedures. However, this refusal should be in a signed document as part of the patient's records. The document should include a statement that refusal of testing puts their newborn at risk for undiagnosed conditions.

Theme 2: Procurement Issues

- According to the Government Procurement Reform Act (RA 9184), "*Specifications for the procurement of Goods shall be based on relevant characteristics, functionality and/or performance requirements.*" This means that *"the use of brand names or tailor-fitting technical specifications to a unique brand name are prohibited under the revised IRR of the Procurement Act, Hence,* ***a generic description of the product or service must be used****"* (GPPB.2016).

- A technical working group (TWG) may be formed to develop the technical specifications for the pulse oximeter to be used in the bidding

Theme 3: Data Privacy and Confidentiality Issues

- NPOS implementation may start a registry for birth defects and could potentially raise concerns related to the Data Privacy Act of 2012 (DPA), its Implementing Rules and Regulations (IRR) and other pertinent issuances of the National Privacy Commission (NPC).

- The DPA considers the data collected from NPOS as **Sensitive Personal Information (SPI) because it relates to the health of a minor**. However, data used in a health registry for birth defects are **exempted from data privacy promulgations as long as the data are anonymized**.

HEALTH SYSTEM IMPLICATIONS

Findings from the literature review and KII or FGDs

Themes for Health Systems Implications:

No.	Themes	Sources of evidence
1	Availability of resources and sustainability- Human resources capacity and training	Literature review: k=2 FGDs with health professionals
2	Availability of resources and sustainability- Healthcare infrastructure	Literature review: k=1 FGDs with health professionals
3	Service delivery- Acceptability of POS among healthcare providers and implementers	Literature review: k=2
4	Service delivery	FGDs with health professionals
5	Sustainability	FGDs with health professionals
6	Barriers and challenges to POS implementation	Literature review: k=2 FGDs with health professionals

Composition of FGDs on Health System Implications

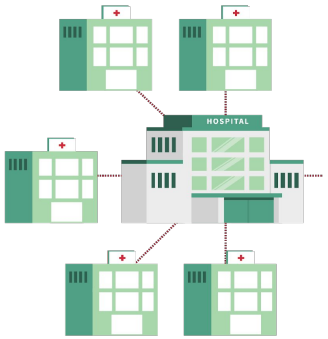
Session No.	No. of Participants	Type of health facility or office	Profession
1	4	Public level 3 hospital	2 MDs, 1 nurse, 1 midwife
2	5	Public level 3 hospital and public university infirmary	4 MDs, 1 nurse
3	4	Public level 3 hospital	4 MDs (1 administrative head)
4	3	DPCB- DOH	2 MDs, 1 nurse (public health specialists)
5	2	1 CHD- Luzon	2 nurses
6	2	1 CHD- Visayas	1 MD, 1 nurse
7	8	All from Mindanao: 2 CHD 2 public level 2 hospitals 3 rural health unit or birthing facility 1 public level 3 Hospital	 2 nurses 1 MD, 1 nurse 3 nurses 1 nurse
9	4	2 private level 3 hospitals- Visayas 1 RHU (Visayas) 1 RHU (Luzon)	1 MD, 1 nurse 1 MD 1 nurse
10	7	1 CHD- Luzon 1 CHD- Luzon Birthing facility- Luzon	2 nurses 1 MD 1 MD; 1 administrative officer, 2 midwives

Theme 1: Availability of resources and sustainability - Human resource capacity and training (1 of 3)

- Healthcare staff should be given training on communicating NPOS screening procedures and results (Ewer 2012, cross-sectional study, UK).

- Threshold may vary because children born at different altitude areas and of different skin pigmentation may have different pulse oximetry levels. It was suggested to develop strategies to improve the accuracy of interpretation of results and the ease of use for healthcare providers and implementers [McClain, 2017 (summary of experiences of pilot CCHD screening projects in the US)].

Theme 1: Availability of resources and sustainability - Human resource capacity and training (2 of 3)



Facilitators of screening:

- Staff can be trained with the standard NPOS protocol which will take into account the factors affecting the accuracy of the reading.
- Level 3 hospitals with trained experts (e.g., pediatric cardiologists, neonatologists, interventional cardiologist) should be part of a **referral system** linking them with the HFs without these experts; use of telemedicine to help in interpretation of confirmatory tests

- All participants were willing to implement NPOS but voiced reservations because of sustainability due to device availability, lack of dedicated staff with training, and accessibility of confirmatory testing and medications for management

Theme 1: Availability of resources and sustainability - Human resource capacity and training (3 of 3)

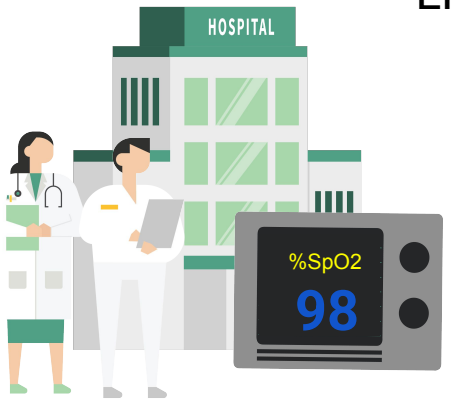
Good communication and counseling training

- The results of a failed initial NPOS should be communicated properly to parents.
- The parents should also be informed of the possibility of a cardiac condition despite passing the test. NPOS limitations must be explained well to avoid disappointment for false negative cases.

Barriers to screening:

- Lack of experts (to read 2D echo, manage CCHD patients, perform procedures)
- Limited number of staff who is assigned to do POS
- Overburdened health staff
- High turnover of staff so new staff has to be trained again

Theme 2: Availability of resources and sustainability - Healthcare infrastructure (1 of 1)



Considerations in widespread implementation of NPOS in LMICs (Zheleva 2020):

- Assessment of health facility capacity
- Assessment of delivery processes and staff training needs
- Data collection on implementations and its outcomes, including surgical outcomes to guide further implementation
- Long-term planning for lifelong care for children with CCHD

Theme 3: Service delivery- Acceptability among healthcare providers and implementers (1 of 2)

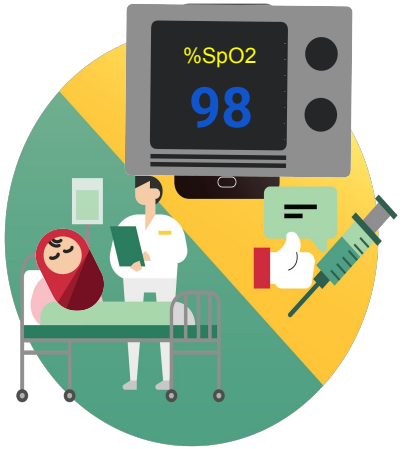
Ewer, 2012 (cross sectional survey, UK)

- Despite additional workload, POS was acceptable because health staff can care and treat CCHD patients while in less critical conditions

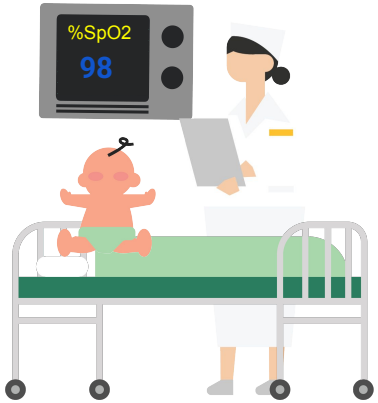
Rajani, 2020 (cross-sectional survey among healthcare providers in India)

- 69% agree POS is a promising method for newborn screening but only few (3%) were using pulse oximetry routinely in their practice.

- Main concerns included the cost effectiveness of POS, availability in rural areas, costs of implementation, availability of adequate staff infrastructure for further confirmatory studies like 2D-echo and longer duration of hospital stay for babies with false-positive which can have psychosocial impact on parents and availability of proper referral services for further management.



Theme 3: Service delivery- Acceptability among healthcare providers and implementers (1 of 2)

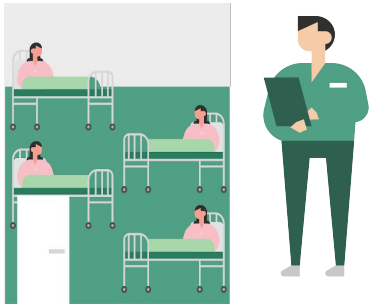


Van Niekerk, 2016 (South Africa)

Views from Health staff on **difficulties in implementation of NPOS**

- **2% found NPOS difficult to perform** because of restless babies and technical issues with the pulse oximeter
- **Few errors on protocol (3.1%),** most were results that were recorded as pass when they should have been failed. All nurses found the protocol to be easy to follow.
- All nurses who implemented NPOS, except one, felt confident in explaining the purpose and limitations of NPOS to the parents.
- **92% of the nurses** said they **did not have enough time to do NPOS** in addition to their other routine tasks.
- 50% of the nurses felt that it would be possible to introduce NPOS as routine procedure

Theme 4: Service delivery (1 of 2)

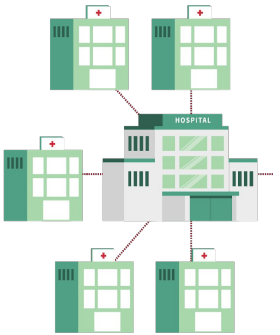


- ***Acceptability among healthcare providers***
  - **Increase in workload** of health staff especially in HF with very high deliveries
  - Suggestions of a **dedicated staff for NB tests** in HFs with high delivery rates

- ***Integration into existing programs***
  - All facilities, except for one center, **incorporated NPOS along with the other newborn screening tests** which they think improved efficiency.
  - One center, NPOS is done by pediatric interns or residents who incorporate NPOS as part of the newborn PE. Integration into other programs also gives more time for the implementing staff to explain the tests to the parents.

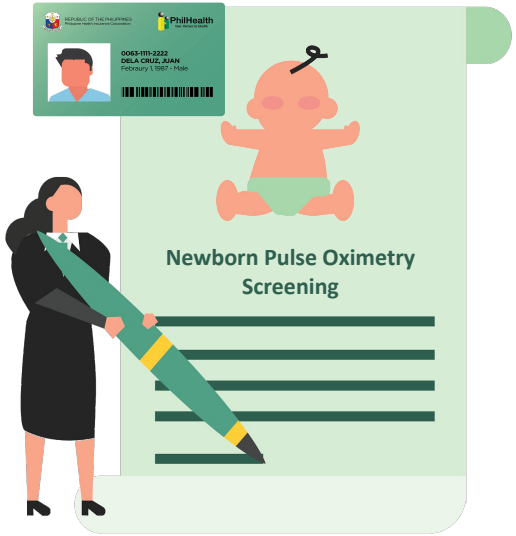
Theme 4: Service delivery (2 of 2)

- ***Referral systems***
  - Even in HFs with existing referral systems, there were times when they were referring a patient but there was no vacancy in the referral hospital (capacity).
    - Suggestion was to **increase the capacity of more hospitals to be referral facilities**
    - **Formal linkages:** Staff from primary care facilities noted in their experience with newborn screening (NBS) roll-out that they have to have **formal memoranda of agreements (MOAs) with a pre-identified referral health facility to facilitate referrals and possible transfers.**



Theme 5: Sustainability

- **Financing** is an important part of sustainability of POS as a national program
- Respondents all agree that **coverage of POS by the PhilHealth** is an important part of this sustainability.
- Sustainability can be achieved through **policy setting and a law institutionalizing** adopting this screening will help in its implementation and sustainability.
- Another way to sustain this is by **involving a network of stakeholders** like professional organizations and CSOs to advocate for its implementation and to inform policymakers and the public of its possible impact.
- Some facilities, in particular the RHUs, noted the **importance of the buy-in and support of local government units (LGUs) to its implementation.**



Theme 6: Barriers and challenges to POS implementation (1 of 2)

Murni, 2022 (Cross sectional study on POS implementation in Indonesia)

- Usual length of postnatal length of stay in apparently well babies is short so POS was done before 24 hours in some cases
- Confirmatory tests could not be done immediately because of unavailability in some hospitals; positive screens had to be referred
- Lack of pulse oximetry devices in all the wards
- Hospital staff preoccupied with their other clinical tasks so some were not able to do POS
- Some newborns were crying and constantly moving which presented difficulty in performing POS

Theme 6: Barriers and challenges to POS implementation (2 of 2)

- Lack of health infrastructure including appropriate POS device, confirmatory tests, facilities for treatment, and medicines for management of cases
- Lack of experts who can diagnose positive screens and manage confirmed cases
- Functioning and responsive referral system including for the smallest health units
- Lack of specialized medical transportation when transferring confirmed cases
- Sustained financing for the program, including financial support for confirmed CCHD cases