Economic analysis of the use of Non-Invasive-Prenatal Test (NIPT) Harmony for prenatal screening of trisomy 21, 18, 13 in pregnant women

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BACKGROUND

- A trisomy is a type of aneuploidy (an abnormal number of chromosomes) [1]
- The most common trisomies are: trisomy 21 (Down Syndrome, 1/700 live birth), trisomy 18 (Edward Syndrome, 1/5,000 live birth), trisomy 13 (Patau Syndrome, 1/16,000 live birth) [2]
- The current clinical practice consists in first and second trimester combined ultrasound and biochemical screening tests (FTS and STS, respectively); chorionic villus sampling and amniocentesis as invasive diagnostic tests
- The cell-free DNA Non-Invasive Prenatal Test (NIPT) is highly accurate in the detection of common fetal autosomal trisomy (i.e. T21, T18, T13) in pregnant women [3]
- NIPT is performed on a blood sample of the pregnant woman, which contains cell-free DNA that originates from the lysis of maternal and placental cells [3]

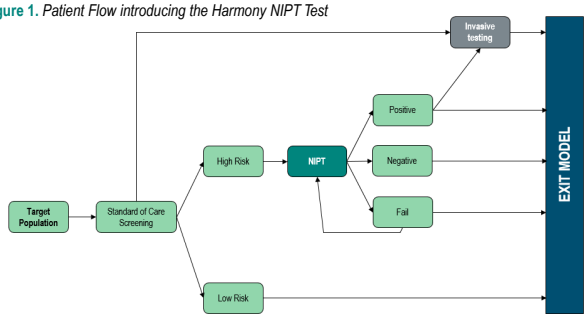
OBJECTIVE

- The aim of this study was to evaluate the financial impact on the Italian NHS of the introduction of the Harmony screening NIPT, in comparison to current clinical practice

METHODS

- A budget impact analysis, with 3-year-time horizon, was developed on short-term period until child birth, adopting the Italian NHS perspective
- The economic impact of adopting the Harmony NIPT Test was determined by comparing two Scenarios: current clinical practice vs introduction of NIPT as a second-level screening test after current clinical practice.
- Two analyses were run:
  - *Standard of Care (SOC)*: clinical and economic inputs of current clinical practice
  - *Intervention (Harmony NIPT Test)*: clinical and economic inputs of current clinical practice with the introduction of NIPT as a second-level screening test
- Both analyses were implemented on the same target population
- The target population was represented by Italian singleton-pregnant screened women (479,709) [4,5,6,7,8]
- The patient flow taken into account introducing the Harmony NIPT Test is shown in **Figure 1**
- The risk cut-off for high risk or low risk was set at 1/1000

Figure 1. *Patient Flow introducing the Harmony NIPT Test*



- Direct costs associated to testing strategies were analyzed: testing costs (i.e. screening costs, Harmony NIPT costs, diagnosis costs) and treatment costs (e.g. complication, miscarriage, termination costs and counseling costs) [9,10]
- Screening costs and counseling costs corresponded to Italian outpatient tariffs; diagnosis costs, complication, miscarriage, termination costs corresponded to Italian inpatient tariffs. Testing costs are reported in **Table 1** [9,10]
- Sensitivity and specificity values were derived from published literature (**Table 2**) [11,12,13]
- For both analyzed Scenarios, according to the relative level of sensitivity and specificity (reported in **Table 2**), the T21, T18, T13, and overall detection rates were determined through the model.

Table 1. *Testing Costs considered in the budget impact analysis*

Screening Costs		
Cost of first trimester serum testing	€	42.46
Cost of NT ultrasound	€	30.99
Cost of second trimester screening	€	23.33
Harmony NIPT Costs		
Cost of the Harmony NIPT Test	€	300.00
Diagnosis Costs		
Cost of chorionic villus sampling (CVS)	€	341.51
Cost of amniocentesis	€	352.66

Table 2. *Sensitivity and specificity values of SOC and the Harmony NIPT Test*

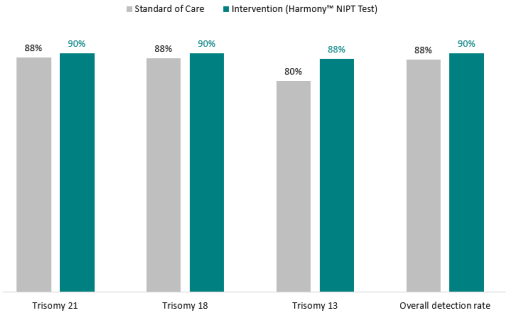
	FTS		STS		Harmony NIPT Test	
	Sensitivity	*Specificity*	*Sensitivity*	*Specificity*	*Sensitivity*	*Specificity*
T21	88,00%	95,00%	80,50%	90,50%	99,30%	99,96%
T18	90,00%	94,00%	63,50%	99,25%	97,40%	99,98%
T13	78,00%	92,00%	50,00%	64,00%	93,80%	99,98%

RESULTS

CLINICAL OUTCOMES

- According to *Intervention (Harmony NIPT Test)* analysis, the number of invasive tests performed decreased by **71%** (from 106,488 of the *Standard of Care* analysis to 31,142)
- Using Harmony NIPT Test increases the overall trisomy detection rate by **3%** (see **Figure 2**)
- Introducing the Harmony NIPT Test brings to a lower number of false positive compared to current clinical practice (without NIPT Test) scenario. Consequently, the number of unnecessary invasive tests due to false positives decreases by **72%**
- Moreover, the number of procedure related-miscarriages is about three times lower than the *Standard of Care* scenario (from 532 to 156) because of the decrease of unnecessary invasive tests.

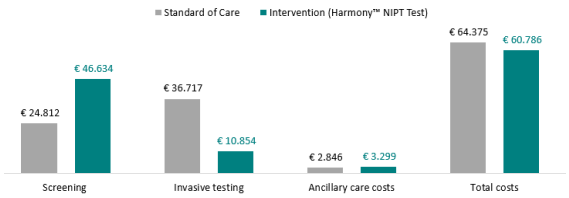
Figure 2. *Clinical outcomes: detection rates*



ECONOMIC OUTCOMES

- Testing costs decrease by **€ 4.1 million** (from million € 61.6 to 57.5)
- Taking into account both testing and treatment costs, total short term costs decrease by **€ 3.6 million** (from million € 64.4 to 60.8) (reported in **Figure 3**)
- Therefore, performing Harmony NIPT Test in prenatal screening programs results in a lower total cost and a greater number of detected trisomies
- In the lights of the budget impact analysis, introducing the Harmony NIPT Test brings to an **incremental saving** of **€ 7.48** per screened woman

Figure 3. *Economic outcomes: total short term costs*



CONCLUSIONS

- The introduction of NIPT as a second-level screening test might be a valuable solution for the NHS. It can produce cost-savings due to a lower number of performed invasive tests than in current clinical practice. These savings could be re-invested in other area, improving patient management in women's health.

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REFERENCES

1. Griffiths AJF, Miller JH, Suzuki DT, et al. An Introduction to Genetic Analysis. 7th edition. New York: W. H. Freeman; 2000. Aneuploidy. Available from: https://www.ncbi.nlm.nih.gov/books/NBK21870/
2. Linee guida ACOG 2013
3. Linee Guida per lo screening pre-natale non invasivo basato sul DNA (May 2015)
4. Dati.istat.it. (2015). Statistiche Istat: Popolazione e famiglie/Natalità/Nati vivi: Serie 2001 - ultimo anno. [online] Available at: http://dati.istat.it/
5. Avalos LA et al. A Systematic Review to Calculate Background Miscarriage Rates using Life Table Analysis. Birth Defects Res A Clin Mol Teratol. 2012 Jul. 2017]
6. Wyatt PR et al. Age-specific risk of fetal loss observed in a second trimester serum screening population. Am J Obstet Gynecol. 2005;192(1):240-6
7. Eurostat Databases - Italy - 2014 Live births by mother's age and newborn's sex [demo_fasec]
8. Istat.it. (2014). Gravidanza, parto e allattamento al seno. [online] Available at: https://www.istat.it/it/archivio/141431 [Accessed 4 Jul. 2017]
9. Ministry of Health (2013). Outpatient Tariffs
10. Ministry of Health (2013). Inpatient DRGTariffs
11. Nicolaides KH et al. Multicenter study of first-trimester screening for trisomy 21 in 75 821 pregnancies: results and estimation of the potential impact of individual risk-orientated two-stage first-trimester screening. Ultrasound Obstet Gynecol 2005; 25: 221–226.
12. Institute of Health Economics (2012). First and Second Trimester Prenatal Screening for Trisomies 13, 18, and 21 and Open Neural Tube Defects. Edmonton AB: Institute of Health Economics
13. Stokowski R et al. Clinical performance of non-invasive prenatal testing (NIPT) using targeted cell-free DNA analysis in maternal plasma with microarrays or next generation sequencing (NGS) is consistent across multiple controlled clinical studies. Prenatal Diagnosis. 2015; 35: 1–4.