# Může neinvazivní prenatální diagnostika zlepšit záchyt Downova syndromu v České populaci?

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# Zdroje dat

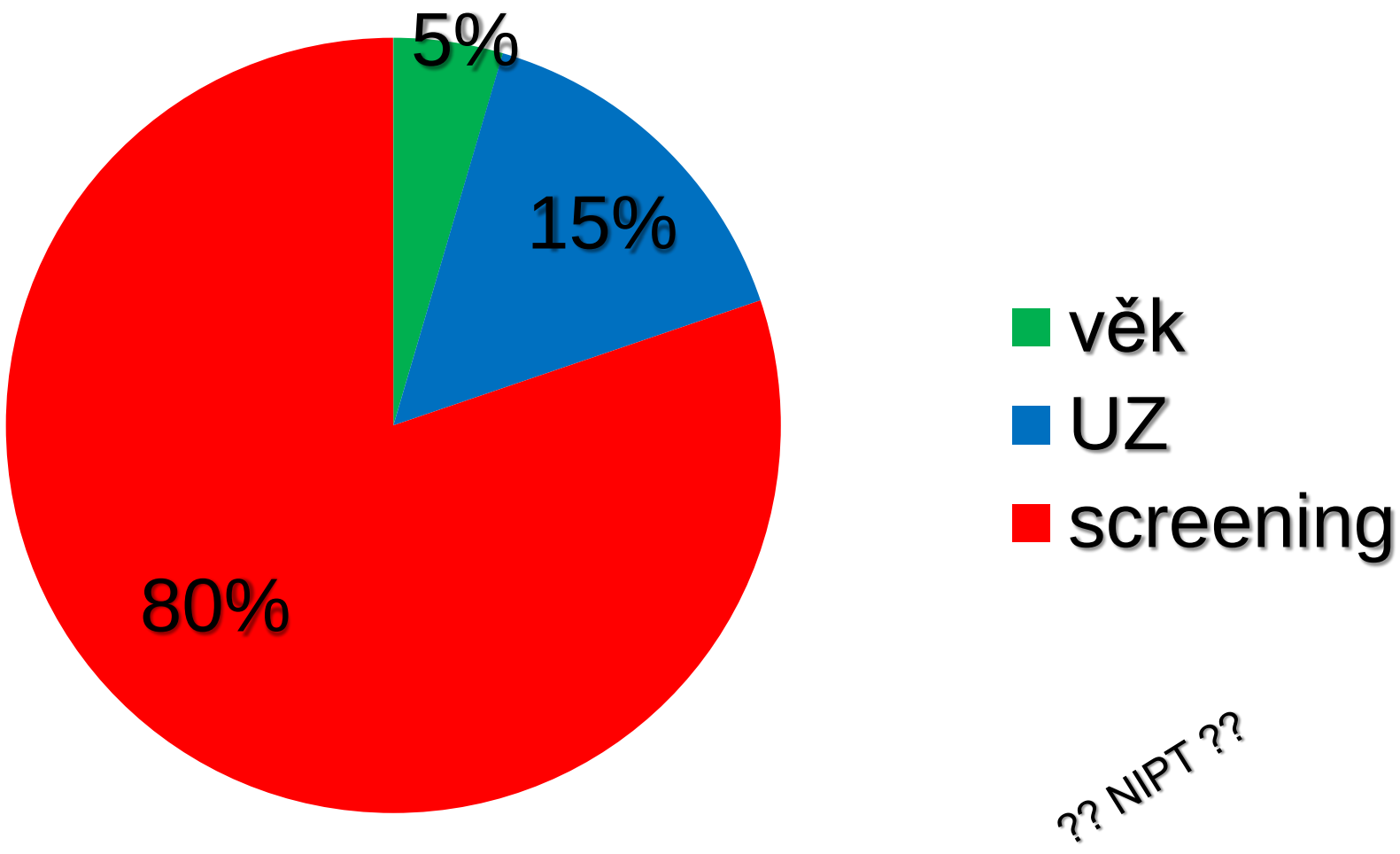
**Data o chromozomových aberacích v České republice v období 1994 – 2014 (21 let).**

**Data o narozených – zdroj: ÚZIS**

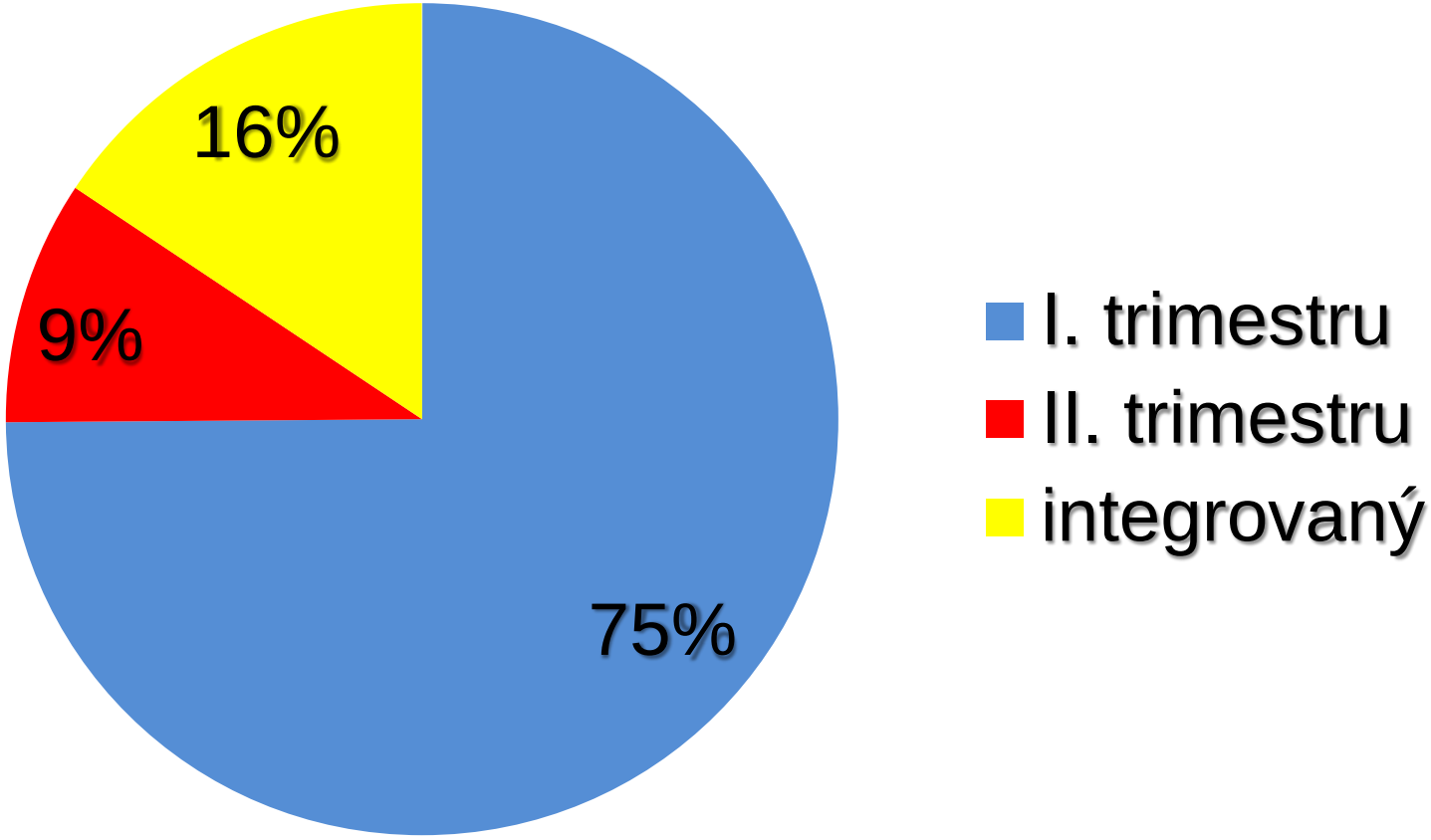
**Data o prenatálně diagnostikovaných případech: SLG**

**Diagnózy: *Downův syndrom***

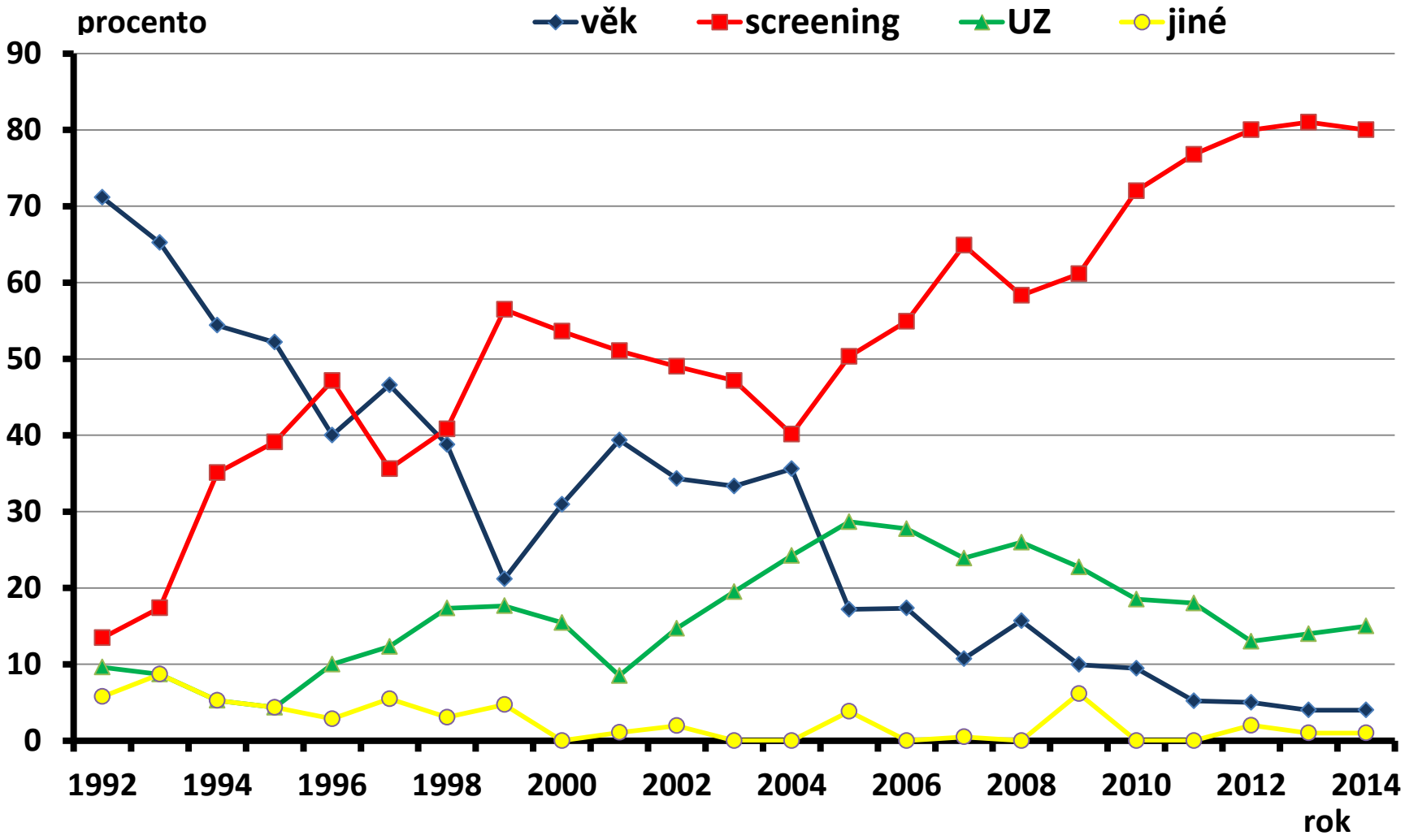
# Diagnostika Downova syndromu v České republice v roce 2014



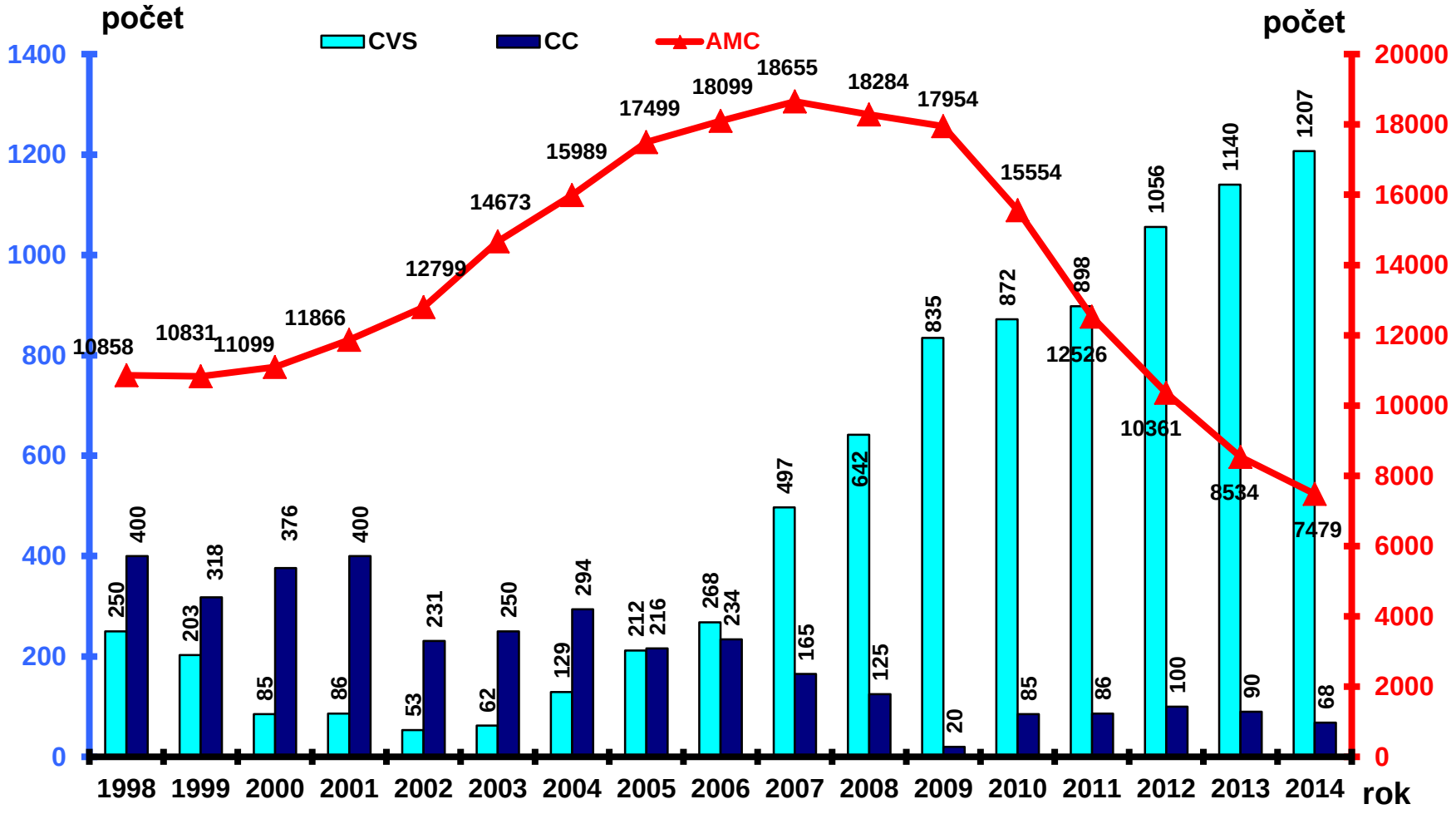
# Diagnostika Downova syndromu v České republice v roce 2014: screening



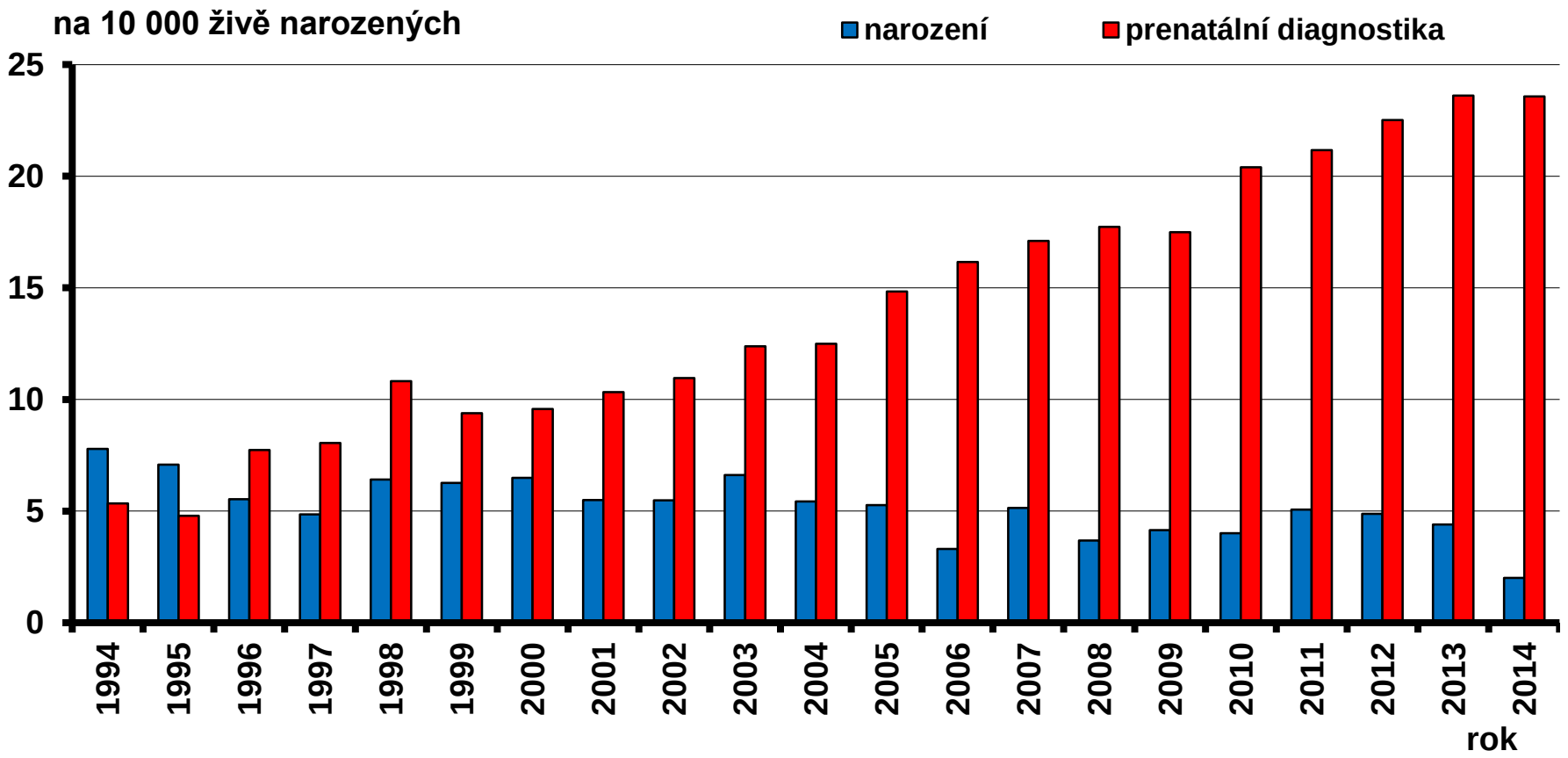
# Indikace k invazivní prenatální diagnostice u plodů s diagnostikovaným DS, ČR 1992 - 2014



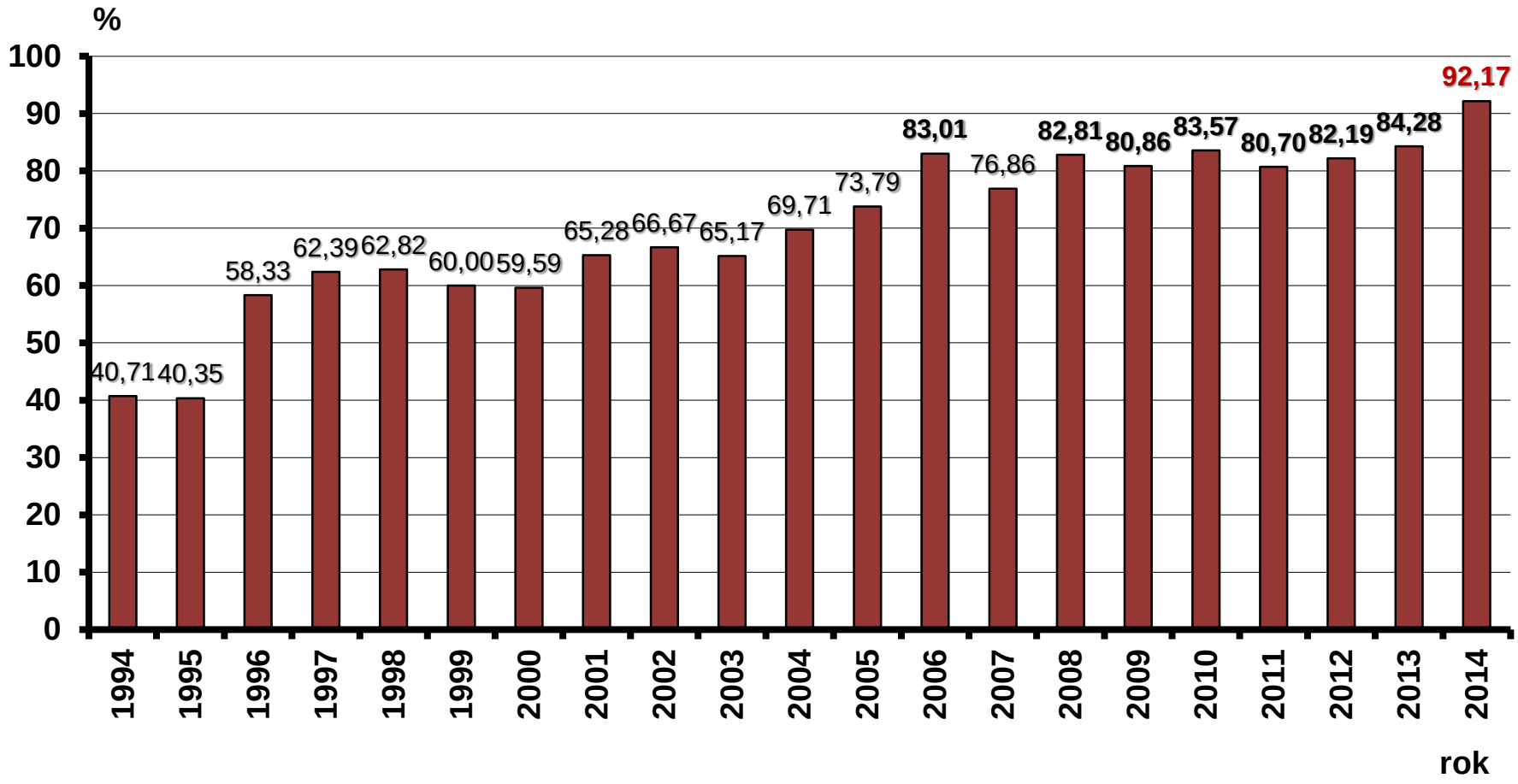
# Vývoj prenatální diagnostiky vrozených vad v České republice, 1998 - 2014



# Downův syndrom v České republice, 1994 - 2014

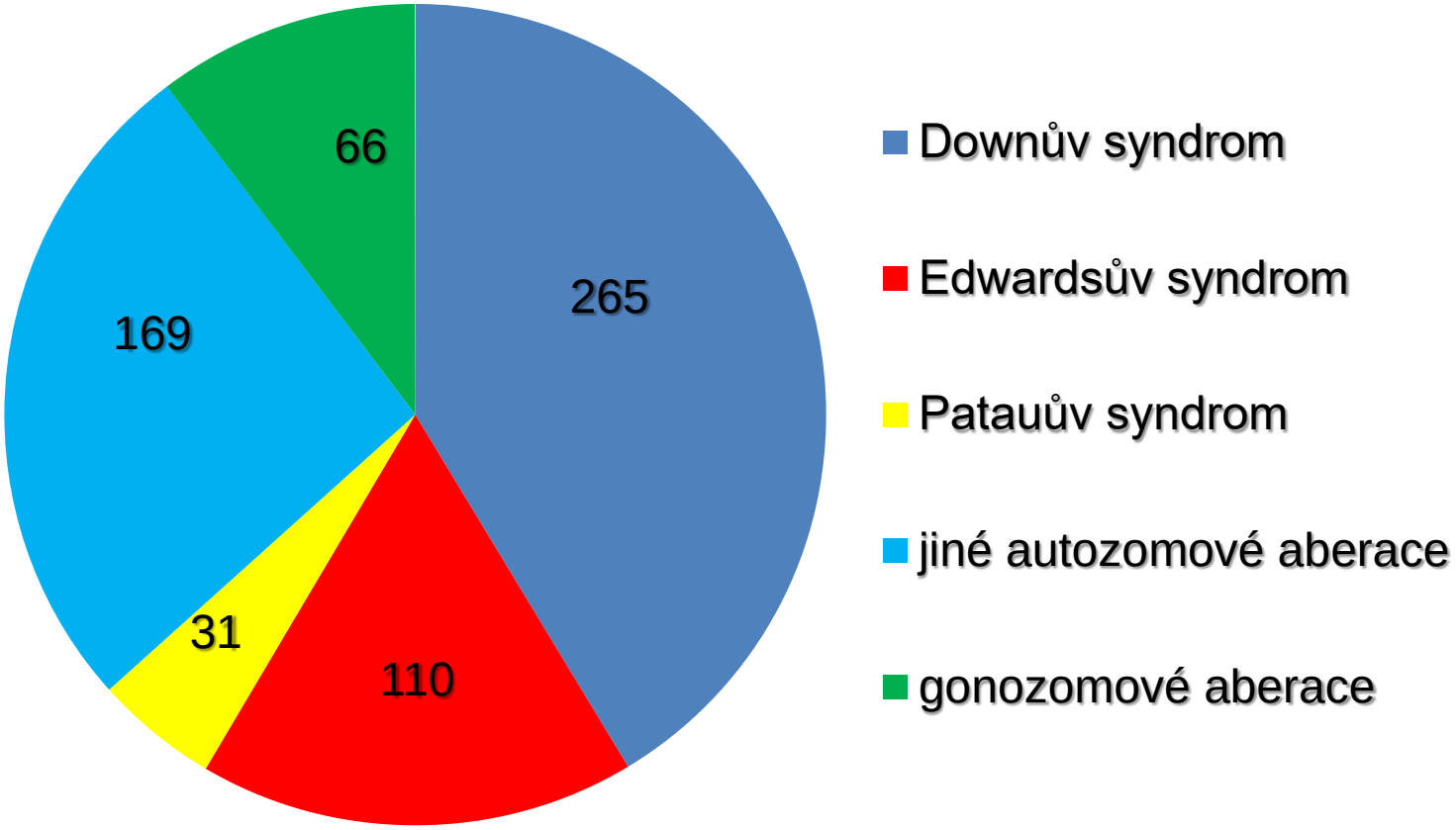


# Downův syndrom v České republice, 1994 – 2014, procento prenatálně diagnostikovaných a ukončených případů z celku



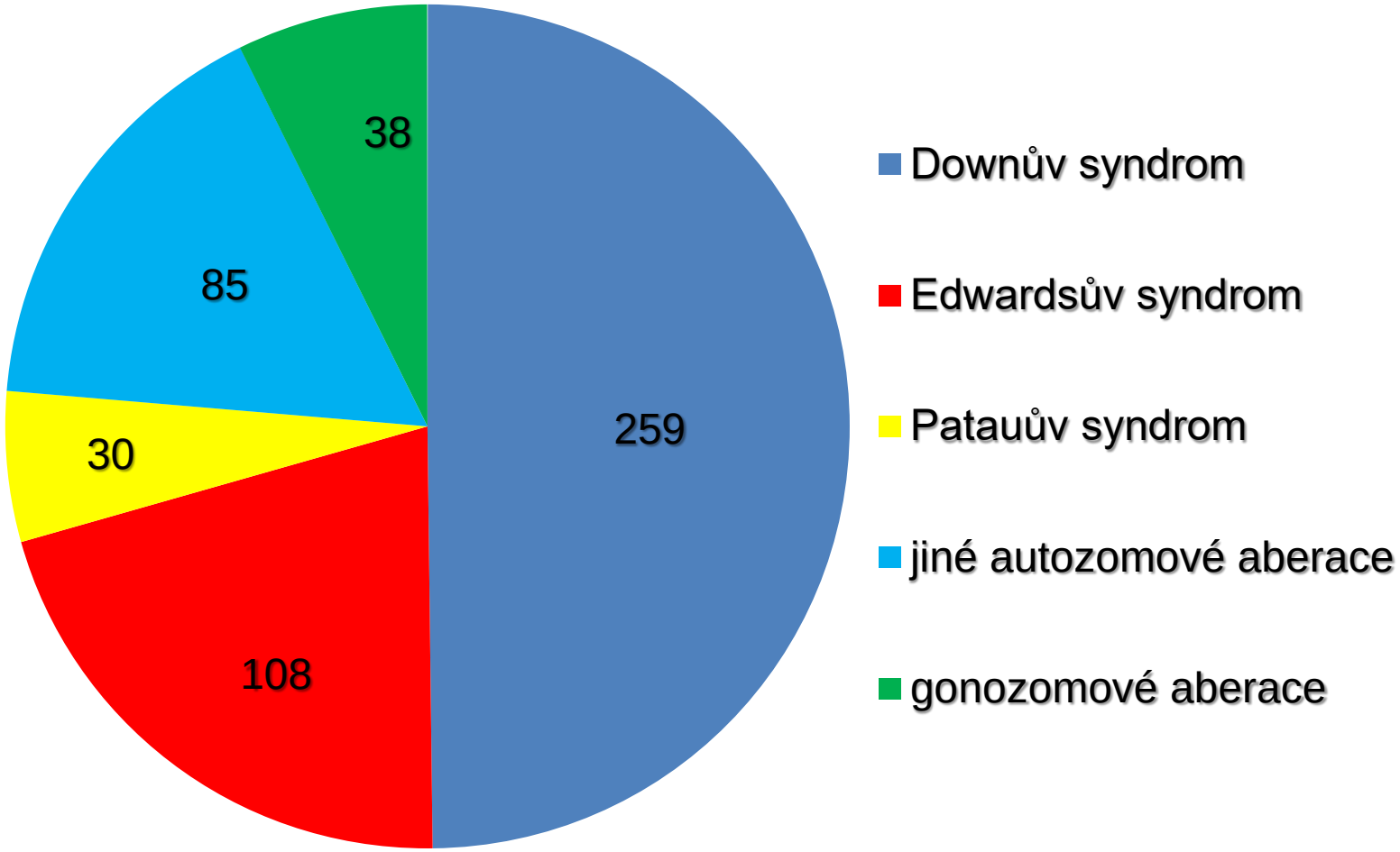
Vrozené vady

# Prenatální diagnostika chromozomových aberací v ČR, 2014:
## Všechny případy pozitivní prenatální diagnostiky

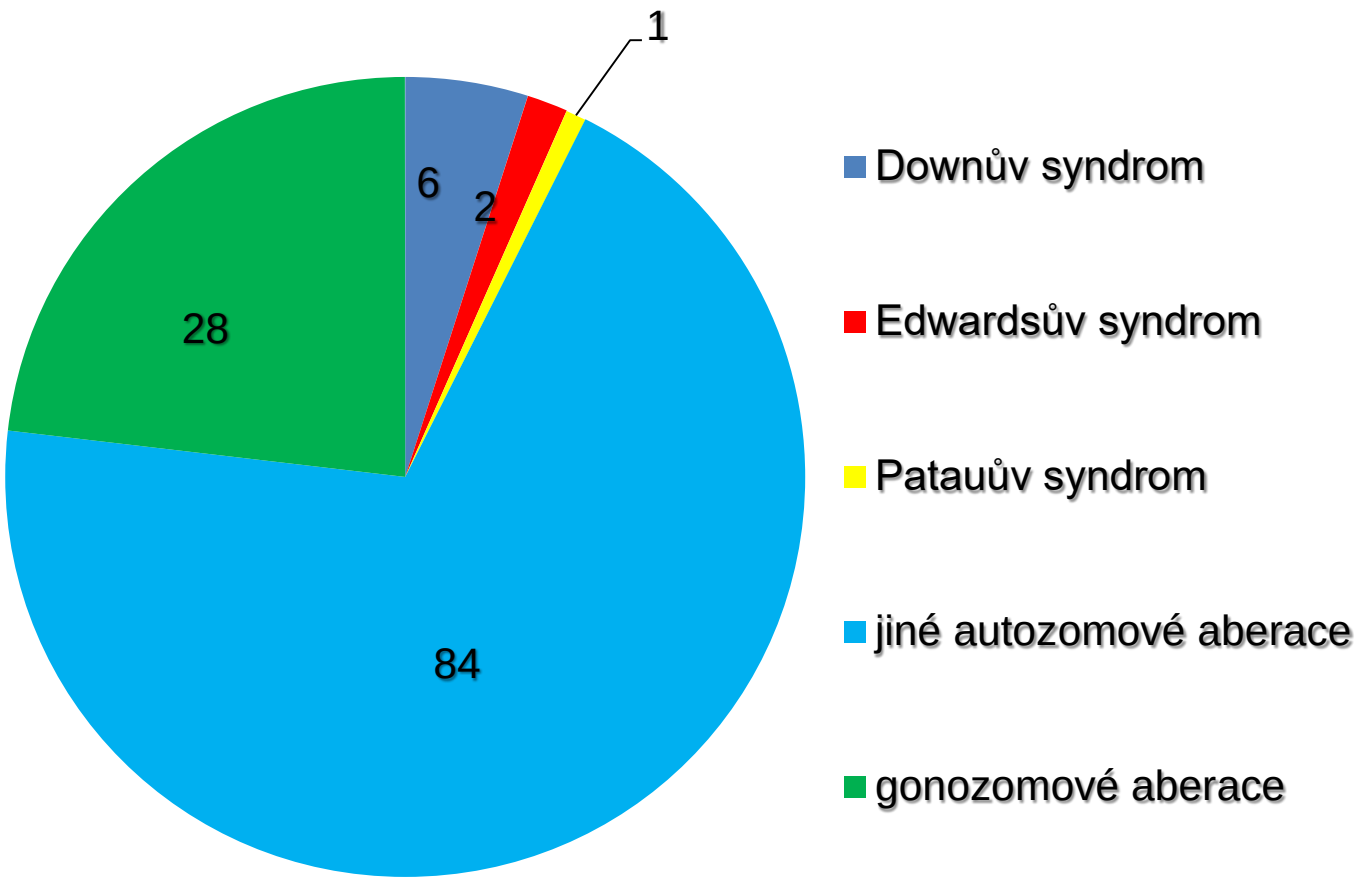


Vrozené vady

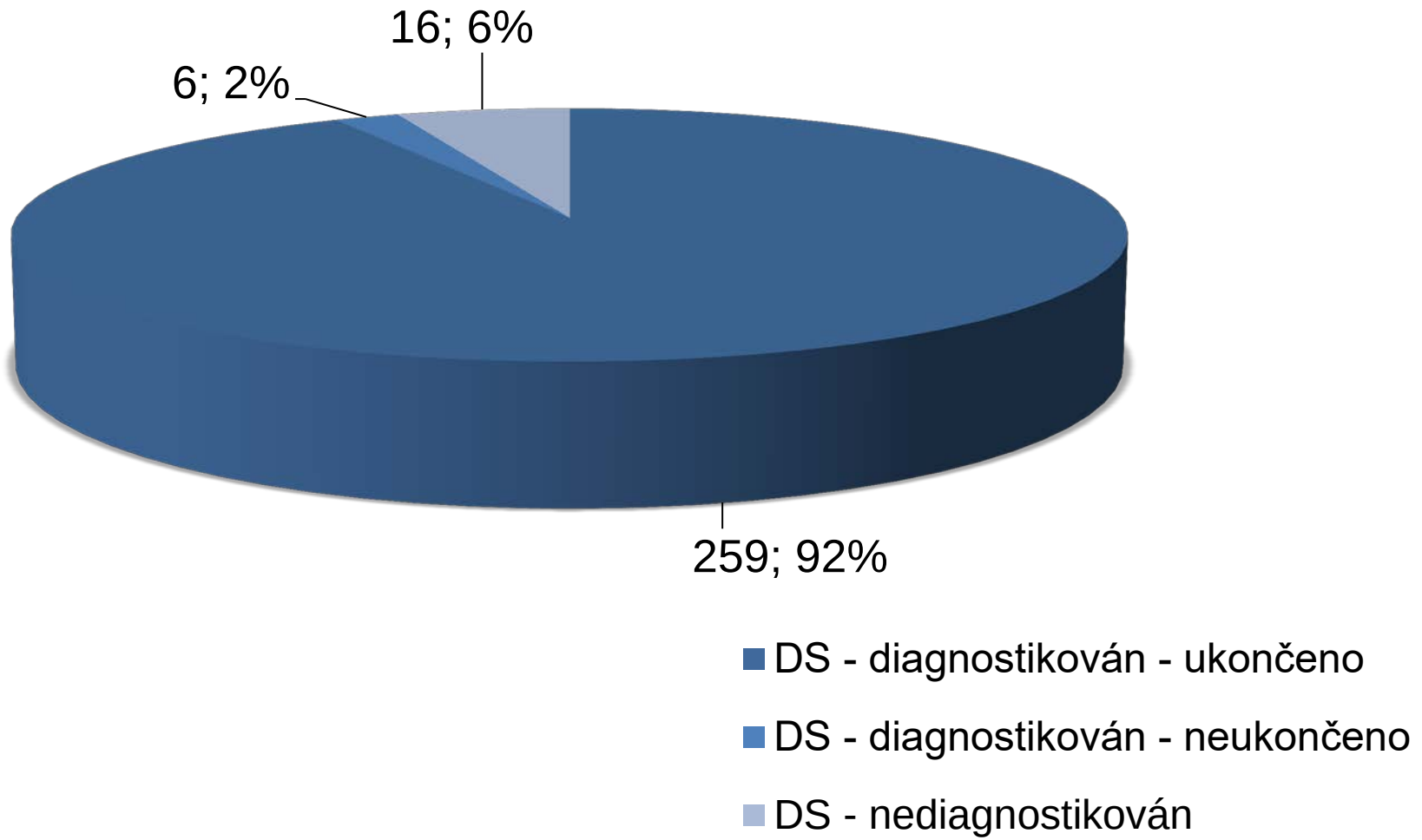
# Prenatální diagnostika chromozomových aberací v ČR, 2014:
## Ukončené případy po pozitivní prenatální diagnostice



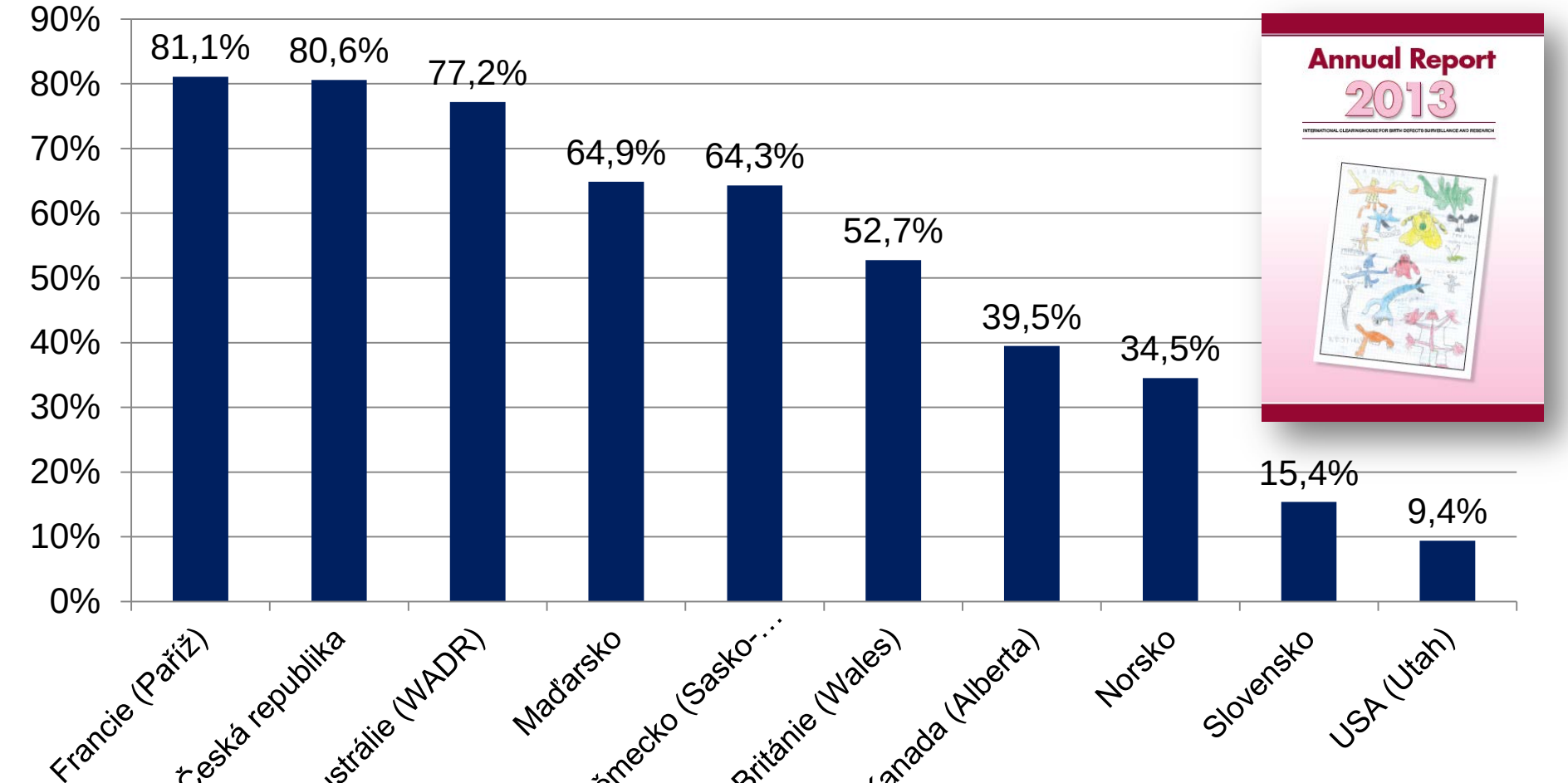
# Prenatální diagnostika chromozomových aberací v ČR, 2014:
## Neukončené případy po pozitivní prenatální diagnostice



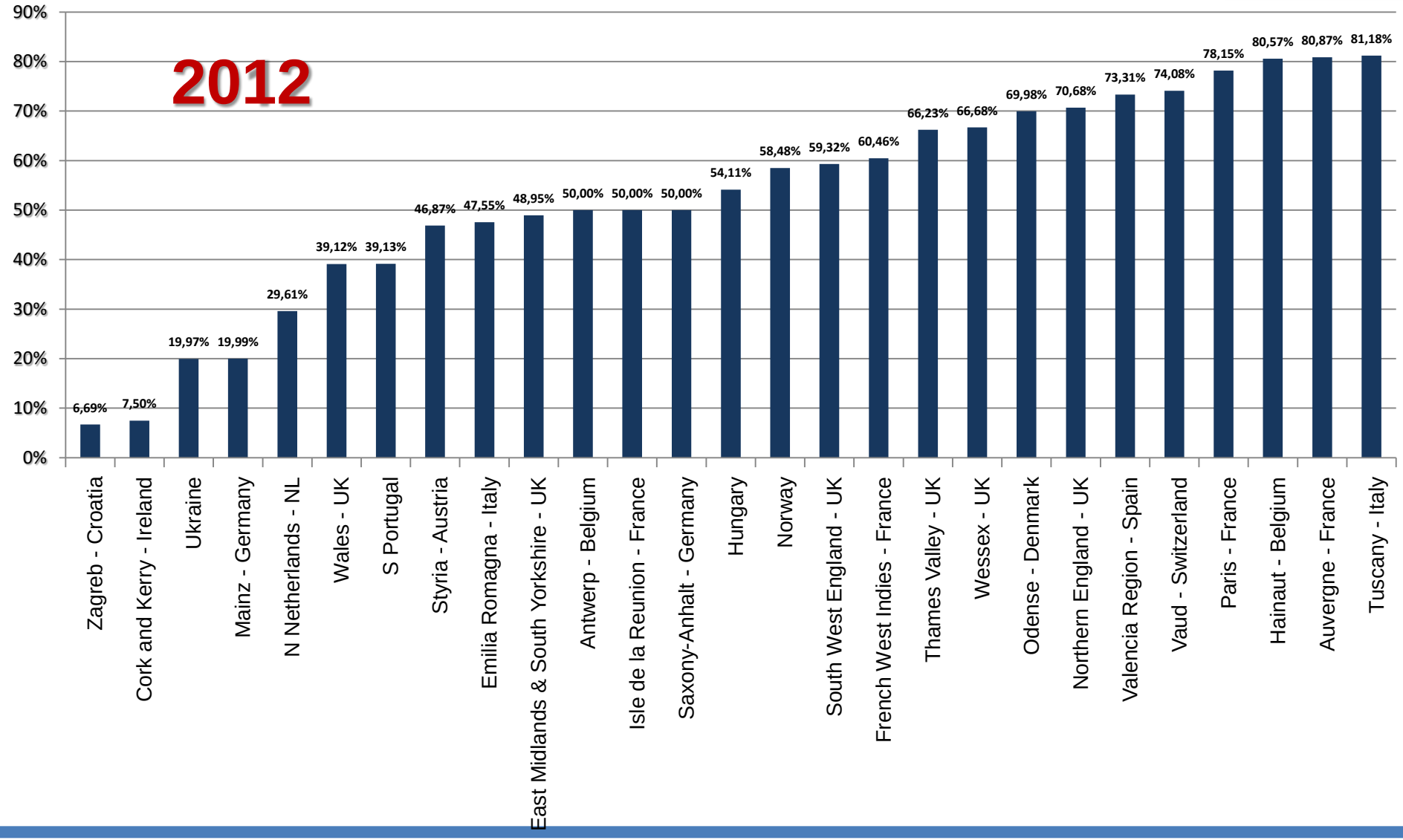
# Downův syndrom v České republice 2014:
# Ukončené vs. neukončené případy po pozitivní prenatální diagnostice



# Downův syndrom (% UUT)



# Downův syndrom (% UUT)



# HTA studie



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## Introducing the non-invasive prenatal test for trisomy 21 in Belgium: a cost-consequences analysis

Mattias Neyt,[1] Frank Hulstaert,[1] Wilfried Gyselaers[2,3]

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### ABSTRACT

**Background:** The first- and second-trimester screening for trisomy 21 (T21) are reimbursed for all pregnant women in Belgium. Using a cut-off risk of 1:300 for T21, about 5% of all pregnant women are referred for definitive prenatal diagnosis using an invasive test, at a sensitivity of (only) 72.5%. The sensitivity and specificity of the non-invasive prenatal test (NIPT) are over 99% but come at a cost of €460 (£373) per test. The objective is to estimate the consequences of introducing NIPT for the detection of T21.

**Methods:** A cost-consequences analysis was performed presenting the impact on benefits, harms and costs. Context-specific real-world information was available to set up a model reflecting the current screening situation in Belgium. This model was used to construct the second and first line NIPT screening scenarios applying information from the literature on NIPT's test accuracy.

**Results:** Introducing NIPT in the first or second line reduces harm by decreasing the number of procedure-related miscarriages after invasive testing. In contrast with NIPT in the second line, offering NIPT in the first line additionally will miss fewer cases of T21 due to less false-negative test results. The introduction of NIPT in the second line results in cost savings, which is not true for NIPT at the current price in the first line. If NIPT is offered to all pregnant women, the price should be lowered to about €150 to keep the screening cost per T21 diagnosis constant.

**Conclusions:** In Belgium, the introduction and reimbursement of NIPT as a second line triage test significantly reduces procedure-related miscarriages without increasing the short-term screening costs. Offering and reimbursing NIPT in the first line to all pregnant women is preferred in the long term, as it would, in addition, miss fewer cases of T21. However, taking into account the government's limited resources for universal reimbursement, the price of NIPT should first be lowered substantially before this can be realised.

### Strengths and limitations of this study

- The major strength of the model is the availability of context-specific real-world information and the ability to reflect the current Belgian screening situation by calibrating the model to the number of women screened, the expected and observed number of children born with Down syndrome and the number of invasive tests performed in Belgium. This calibration assures that the initial screening model reflects the current Belgian screening situation as well as possible.
- The most important limitation of our analysis is that, owing to a lack of reliable data, we were unable to apply a long-term horizon and translate outcomes to incremental cost-effectiveness ratios expressing results in euros per (quality-adjusted) life-year gained. However, by presenting the consequences of screening in a transparent way (which includes the detection of trisomy 21, the number of Down births whether or not after a false-negative screening test, and the number of procedure-related losses), we try to inform policymakers in a transparent way about the possible consequences of introducing NIPT in different settings.
- In order to avoid a 'black box' and to provide other researchers with the possibility to use and adopt the model to their context, details of the full model are included in online supplementary files with a step-by-step explanation for every transition.

### INTRODUCTION

Prenatal diagnosis of Down syndrome allows for informed decision-making with regard to pregnancy continuation or termination. Multiple prenatal trisomy 21 (T21, Down syndrome)/aneuploidy screening strategies in the first and second trimesters have been developed.[1] The most commonly used approach for the first trimester screening in Belgium is the combination of the nuchal translucency (NT) ultrasound measure at week 12 (weeks 11–14), the level of free-β-human chorionic gonadotrophin hormone and pregnancy associated plasma protein-A, in combination with age and medical history. The T21 screening in Belgium is fully reimbursed for all pregnant



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## Model-Based Analysis of Costs and Outcomes of Non-Invasive Prenatal Testing for Down's Syndrome Using Cell Free Fetal DNA in the UK National Health Service

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### Abstract

***Background:*** Non-invasive prenatal testing (NIPT) for Down's syndrome (DS) using cell free fetal DNA in maternal blood has the potential to dramatically alter the way prenatal screening and diagnosis is delivered. Before NIPT can be implemented into routine practice, information is required on its costs and benefits. We investigated the costs and outcomes of NIPT for DS as contingent testing and as first-line testing compared with the current DS screening programme in the UK National Health Service.

***Methods:*** We used a pre-existing model to evaluate the costs and outcomes associated with NIPT compared with the current DS screening programme. The analysis was based on a hypothetical screening population of 10,000 pregnant women. Model inputs were taken from published sources. The main outcome measures were number of DS cases detected, number of procedure-related miscarriages and total cost.

***Results:*** At a screening risk cut-off of 1:150 NIPT as contingent testing detects slightly fewer DS cases, has fewer procedure-related miscarriages, and costs the same as current DS screening (around UK£280,000) at a cost of £500 per NIPT. As first-line testing NIPT detects more DS cases, has fewer procedure-related miscarriages, and is more expensive than current screening at a cost of £50 per NIPT. When NIPT uptake increases, NIPT detects more DS cases with a small increase in procedure-related miscarriages and costs.

***Conclusions:*** NIPT is currently available in the private sector in the UK at a price of £400-£900. If the NHS cost was at the lower end of this range then at a screening risk cut-off of 1:150 NIPT as contingent testing would be cost neutral or cost saving compared with current DS screening. As first-line testing NIPT is likely to produce more favourable outcomes but at greater cost. Further research is needed to evaluate NIPT under real world conditions.

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**Competing Interests:** The authors have declared that no competing interests exist.

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### Introduction

In the UK the National Screening Committee (NSC) sets the standards for antenatal screening and recommends that all pregnant women are offered Down's syndrome (DS) screening. Ideally this is the combined screening test performed between 11 and 14 weeks gestation. In current National Health Service (NHS) practice this has a detection rate of around 85% and a screen positive rate around 2.5% [1]. Women with a risk of 1:150 or greater of the baby having DS are offered an invasive diagnostic test (chorionic villus sampling (CVS) or amniocentesis), providing definitive diagnosis as to whether or not the baby has DS. If full karyotyping or microarray analysis is performed other chromosomal abnormalities may be detected.

Current invasive diagnostic tests have a risk of miscarriage of 0.5–1% [2]. The discovery of cell free fetal DNA (cffDNA) in maternal blood [3] has led to safer non-invasive approaches to prenatal testing where aneuploidies are detected via a maternal blood test from 10 weeks gestation [4]. Several large-scale validity studies have been conducted to evaluate non-invasive prenatal testing (NIPT) for DS based on next generation sequencing [5–12]. Detection rates for DS are typically greater than 99% with a false positive rate of 0.1–1%. NIPT can also detect other aneuploidies including trisomy 18 (99% accurate) and trisomy 13 (up to 90% accurate) [9–12]. The small false positive rate for DS means NIPT should be confirmed by invasive testing [13–15]. NIPT for DS as well as trisomy 18 and 13 is now offered through commercial providers in several countries including the USA,

# Závěry

- Podle dostupných údajů bylo v roce 2014 prenatálně diagnostikováno 94 % případů M. Down, naprostá většina případů (92 %) byla prenatálně ukončena.
- I v mezinárodním srovnání jde o extrémně vysoké procento prenatální záchytnosti M. Down.
- Prostor k rozšiřování prenatální záchytnosti M. Down (stran kvantitativních ukazatelů) je tak již celkově velmi malý.
- Ekonomická otázka plošného zavedení NIPT jako hlavní screeningové metody je složitá.
- V rámci invazivní prenatální diagnostiky jsou zachycovány i jiné aberace autozomů, které jsou možnou indikací UUT a které nejsou v základní variantě NIPT detekovatelné.

# Poděkování

*Závěrem by autoři rádi poděkovali všem osobám, které se podílely, podílejí nebo budou v budoucnosti podílet na procesu registrace vrozených vývojových vad na území České republiky.*

*Bez jejich pečlivé a trpělivé práce by vybudování registru na světové úrovni nebylo nikdy možné.*

# Poděkování

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