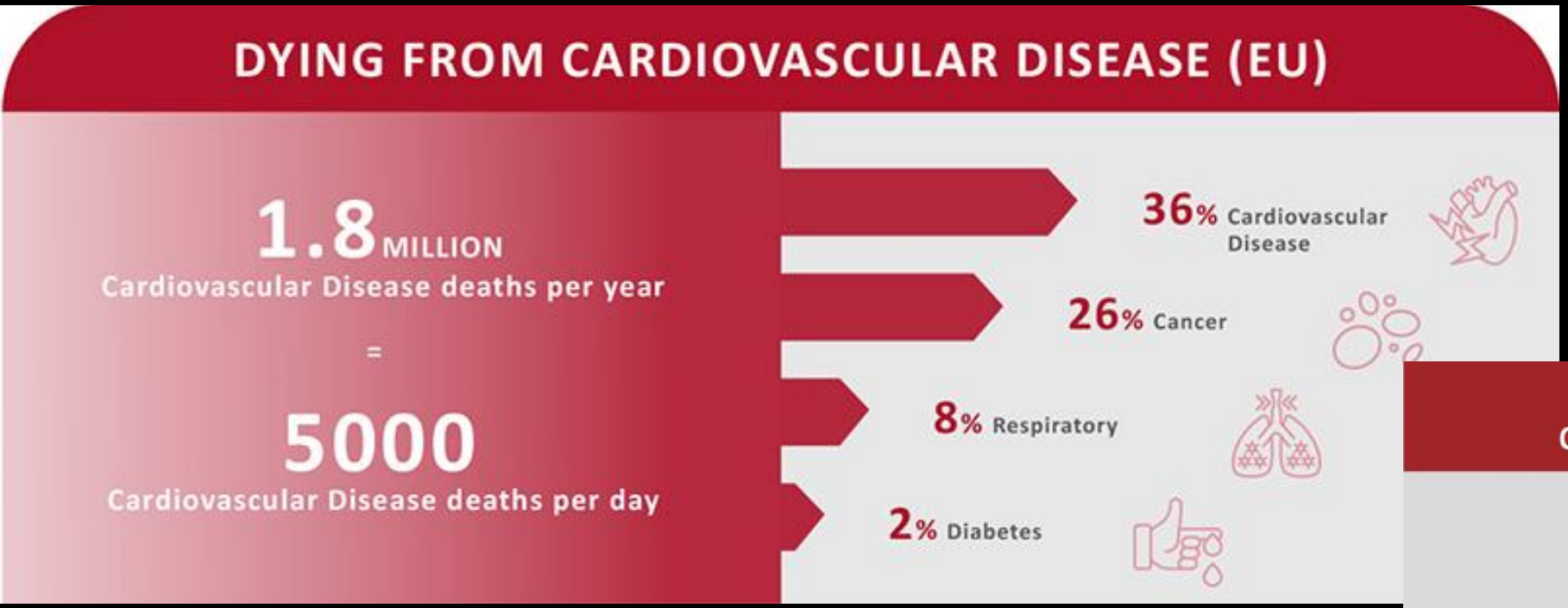
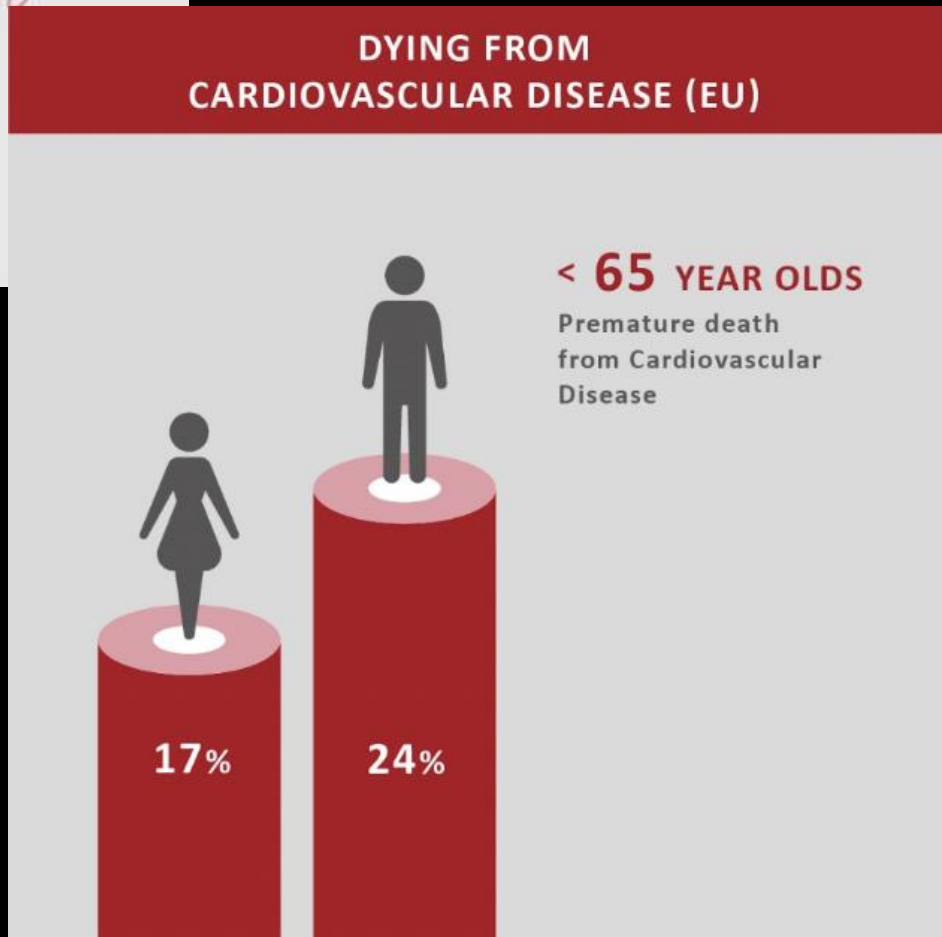

iDNA
GENOMICS

Στα επόμενα 60’,
14 άνθρωποι
θα αυτοκτονήσουν στην Ευρώπη
κυρίως λόγω κατάθλιψης...



Στα επόμενα 60’,
205 άνθρωποι
θα πεθάνουν στην Ευρώπη
λόγω καρδιαγγειακών παθήσεων...




Precision Medicine
Prevention, Diagnosis and Treatment

DNA: We are all different !

Although we share a large amount of our DNA, we all have differences in our genomes

On average, a person's genome sequence is ~99.6% identical to a reference human genome sequence; that person's set of genomic variants accounts for the ~0.4% difference

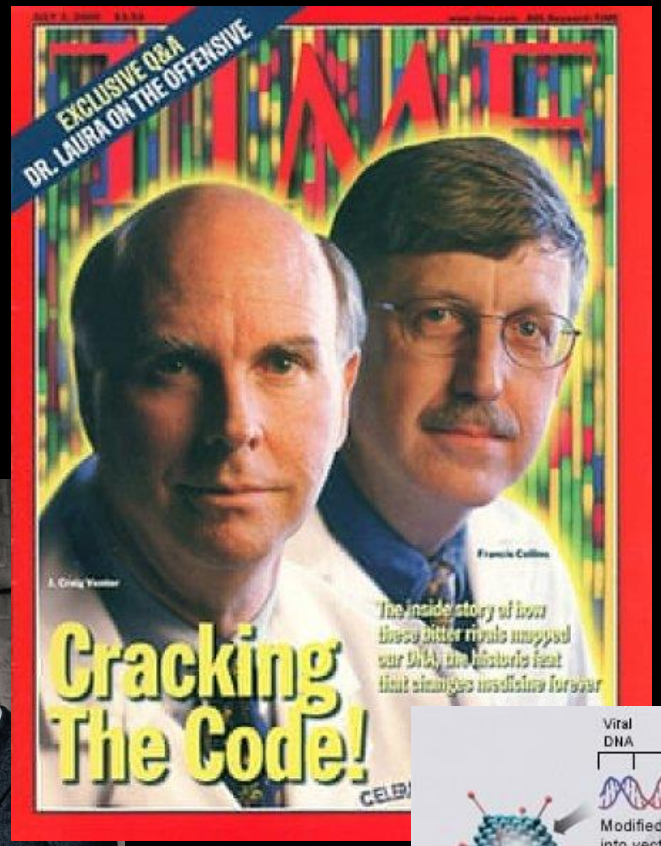
Our DNA Could Change the Future of Health

Precision medicine focuses on identifying optimal care based on a unique personal profile and constitutes a world class shift in HealthCare

NIH National Human Genome Research Institute

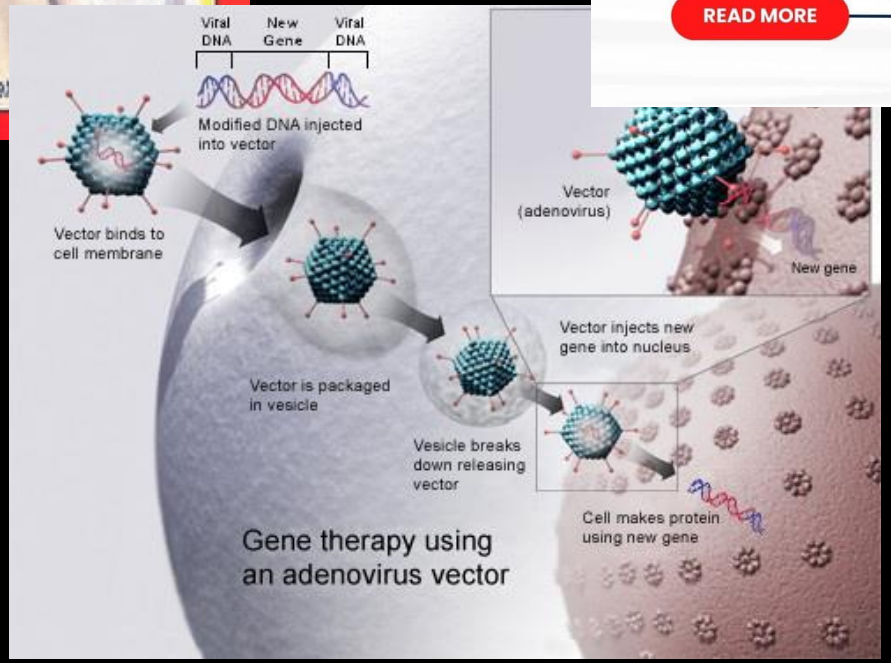
iDNA GENOMICS

1953



2003

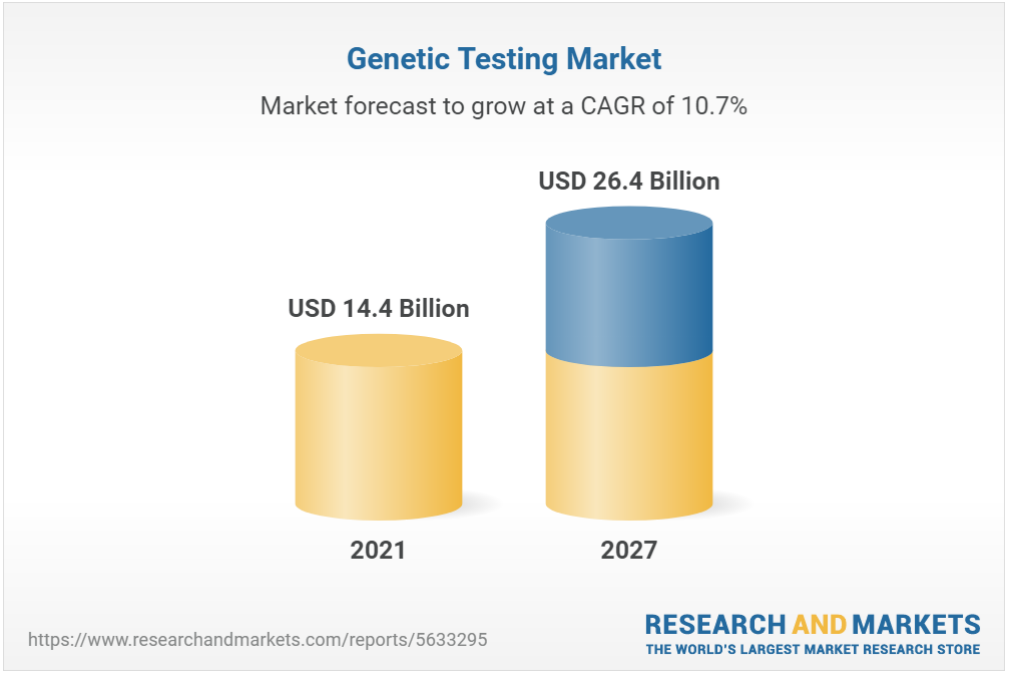
2017

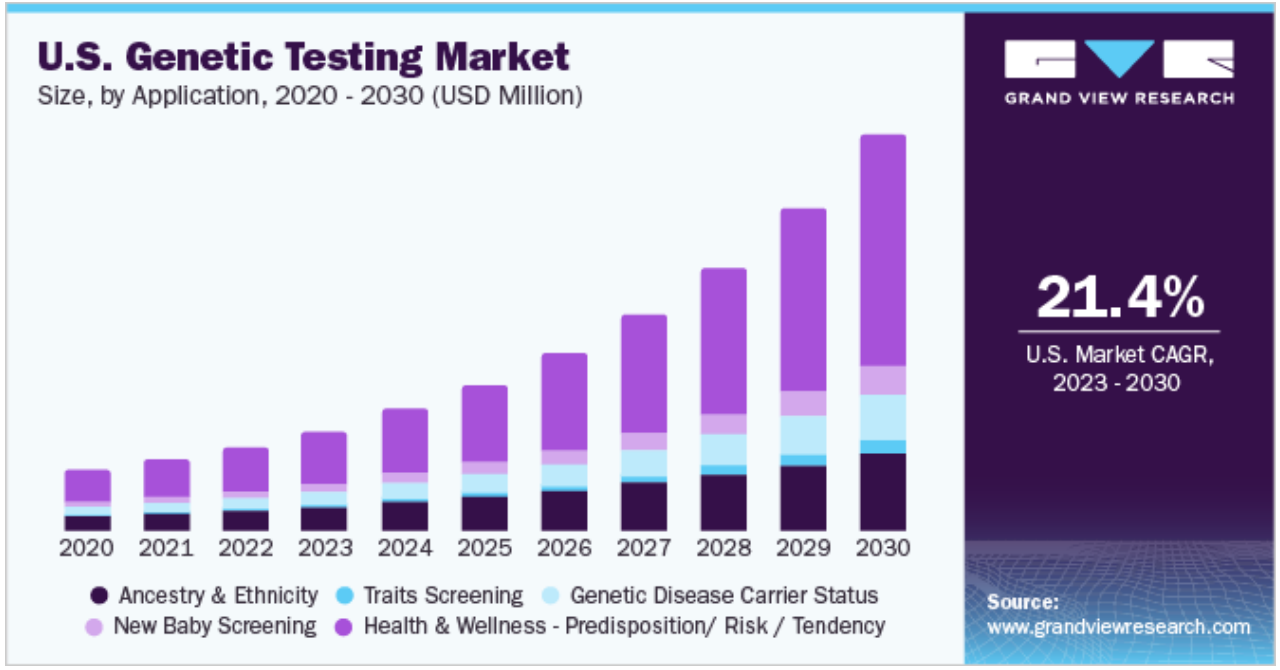


2023

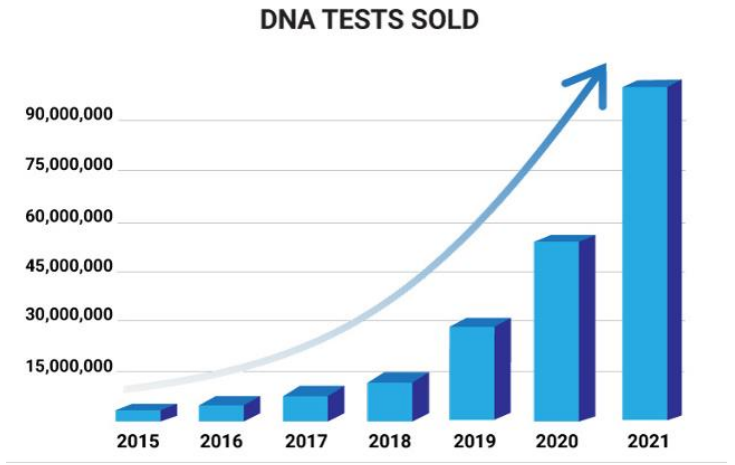
Industry evolution

Genetic Testing Market





- Booming market
- Health &Wellness-Predisposition/Risk/Tendency is the fastest growing segment



iDNA GENOMICS

The company

1. Structure
   - iDNA Laboratories: Medical company, Licensed Diagnostic Laboratory
   - iDNA Genomics: Commercial company
2. Fully integrated company, from concept to product
   - Unique certified in vitro Diagnostics (IVD) DNA tests available
   - New DNA tests development expertise
3. Advanced Science
   - Combined Genetic & Epigenetics concepts
   - Own algorithms
   - Bioinformatics platform
4. Regulatory clearance
   - CE IVD Status
   - ISO 9001:2015, ISO 13485:2016, ISO 27001:2013
5. Competitive Pricing
6. Team
   - Successful track record & expertise, int'l know how
   - Opinion leaders on board

iDNA GENOMICS

iDNA LABORATORIES

ΕΘΝΙΚΑ ΒΡΑΒΕΙΑ ΝΕΟΦΥΟΥΣ ΕΠΙΧΕΙΡΗΜΑΤΙΚΟΤΗΤΑΣ

ELEVATE GREECE national startup point

National Award for Entrepreneurship

LRQA CERTIFIED ISO 9001-2015

ISO 13485 TÜV NORD TÜV HELLAS SYSTEM CERTIFICATION

Information Security DQS ISO/IEC 27001

Quality Management DQS ISO 9001:2015

Quality Management DQS MED ISO 13485

Industry challenges & our solutions

We meet the needs

	4 Key challenges		Our solutions
1.	New global regulatory requirements	→	Regulatory clearance in EU
2.	Privacy of data	→	ISO 27001:2013 – Data Protection
3.	Genetics only are not enough	→	Combined genetics with phenotype* for lifetime health monitoring -UNIQUE
4.	Pricing & Reimbursement	→	Highly competitive pricing & Reimbursement option in pharmacogenetics

** Phenotype is defined as any observable trait such as blood pressure, body weight etc., that can be affected by lifestyle*

iDNA GENOMICS

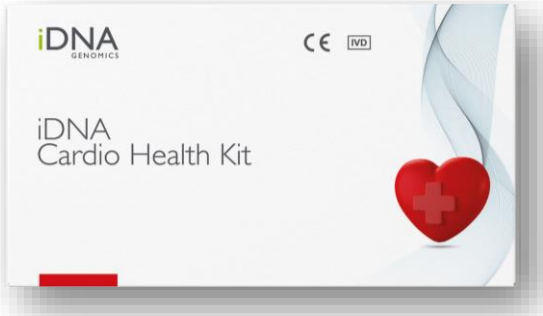
Our Products

Medical Genomics

1. Pharmacogenetics - iDNA PGx CNS
DEPRESSION

- 322 million people suffer from Depression

2. Genetic Predisposition - iDNA Cardio Health
CARDIOVASCULAR DISEASES



- 523 million suffer from CVD

3. Personalized Nutrigenetic Analysis - iDNA NutriGenetix
OBESITY

- 650 million people are obese

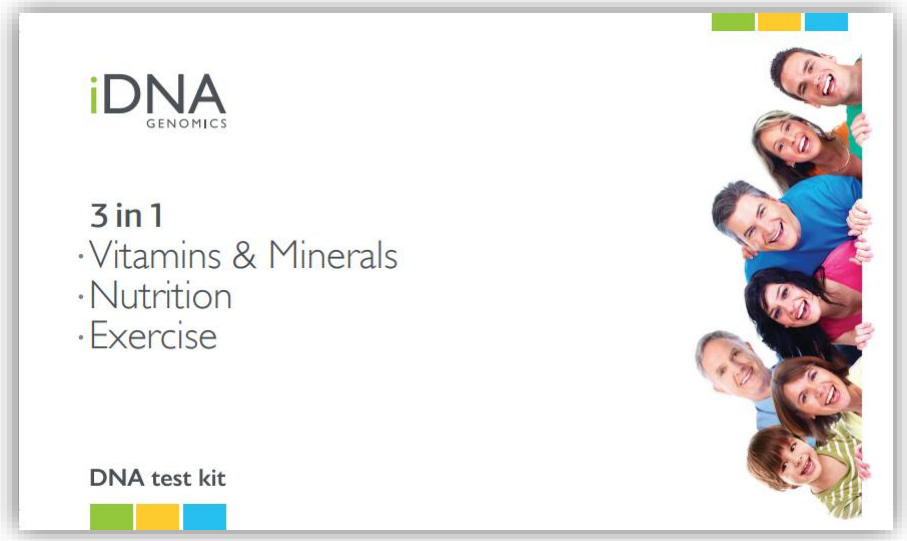
iDNA GENOMICS

Our Products

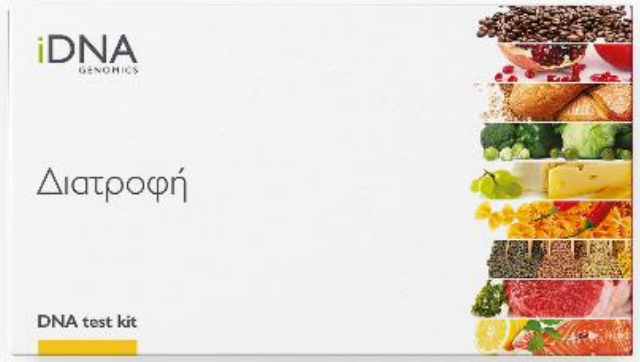
Scientific Wellness Genomics

3 in 1 holistic genetic report on :

- **Nutrition**
- **Vitamins & minerals**
- **Exercise**



47% of people are overwhelmed by conflicting advice on health & wellness.



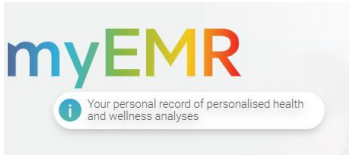
iDNA GENOMICS

What is our process

From saliva DNA to personalized Health report

Kit Supply

- Online
- Physical



Kit Registration

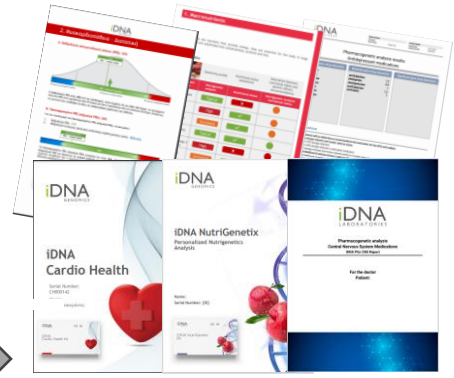
- On MyEMR platform by serial number
- B2B: By Health professionals
- B2C: By End users

Saliva sample

- To be sent to the certified genetic lab free of logistics charge
- Genotyping of the sample by certified scientists

Bioinformatics

- AI analysis
- Genetic report development



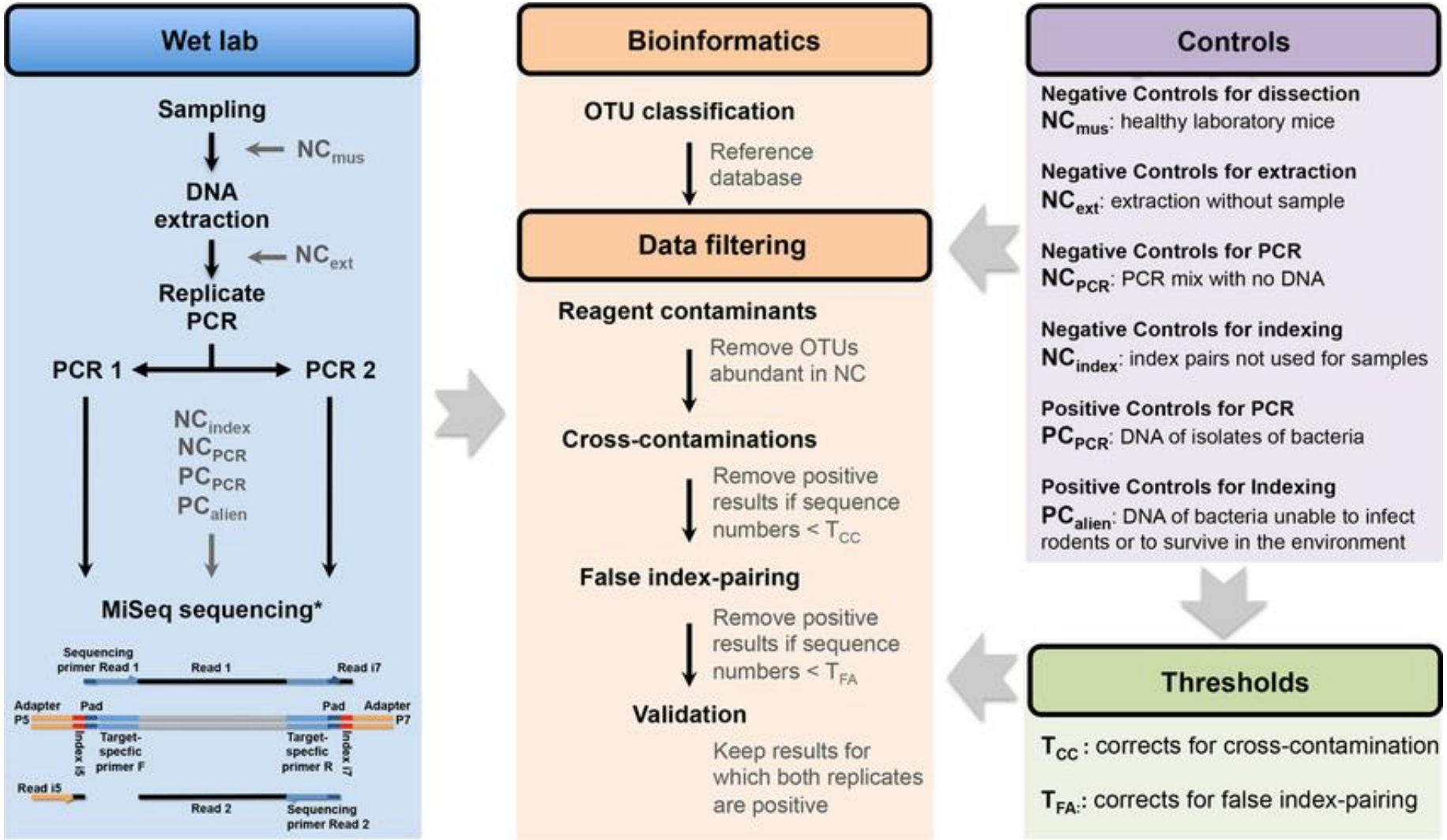
MyEMR platform

- B2B: Personalized Reports uploaded to Health professionals' profile
- B2C: Personalized Report uploaded to End Users' profile

iDNA GENOMICS

What is our process

From saliva DNA to personalized Health report



iDNA GENOMICS

```
[Header]
GSGT Version    2.0.4
Processing Date 9/7/2023 7:27 AM
Content         GSAMD-24v3-0-EA_20034606_A2.bpm
Num SNPs        730059
Total SNPs      730059
Num Samples     92
Total Samples   92
File    1 of 92
[Data]
Sample ID       RsID    GC Score        SNP Name        SNP Index       Sample Index    Sample Name     Sample Group    SNP Aux Chr     Position        GT
Score   Cluster Sep     SNP     ILMN Strand     Customer Strand Top Genomic Sequence    Plus/Minus Strand       Allele1 - AB    Allele2 - AB    Allele1 -
Top     Allele2 - Top   Allele1 - Plus  Allele2 - Plus  Allele1 - Forward       Allele2 - Forward       Allele1 - Design        Allele2 - Design
        Theta   R       X       Y       X Raw   Y Raw   B Allele Freq   Log R Ratio     CNV Value       CNV Confidence
WL008951        rs577266494     0.8339  1:103380393     1       1       WL008951                0       1       102914837       0.8123  0.9535  [T/C]   BOT
        TOP             -       B       B       G       G       G       G       G       C       C       0.974   0.816   0.032   0.783   327     1978
        1.0000  0.0721
WL008951        rs577315876     0.8355  1:106737318     2       1       WL008951                0       1       106194696       0.8133  0.5527  [A/C]   TOP
        BOT             -       A       B       A       C       T       G       T       G       A       C       0.416   0.491   0.278   0.213   1540    563
        0.5330  -0.0192
WL008951        rs755970517     0.4783  1:109439680     3       1       WL008951                0       1       108897058       0.8776  1.0000  [A/G]   TOP
        TOP             +       A       A       A       A       A       A       A       A       A       A       0.042   0.690   0.647   0.042   3160    142
        0.0037  -0.1924
WL008951        .       0.1810  1:110228436_CNV_GSTM1   4       1       WL008951                0       1       109685814       0.5536  0.3024  [A/G]   TOP
        BOT             -       B       B       G       G       C       C       C       G       G       0.815   0.277   0.064   0.213   494     608
        1.0000  0.1866
WL008951        .       0.2214  1:110228505_CNV_GSTM1   5       1       WL008951                0       1       109685883       0.5798  0.2299  [A/C]   TOP
        TOP             +       A       B       A       C       A       C       A       C       A       C       0.622   0.092   0.037   0.055   337     206
        0.6634  -1.0783
WL008951        .       0.4582  1:110228615_CNV_GSTM1   6       1       WL008951                0       1       109685993       0.8614  0.9994  [T/C]   BOT
        BOT             +       A       A       A       A       T       T       T       T       T       T       0.073   0.426   0.382   0.044   2180    195
        0.0260  -0.7740
WL008951        rs1419817467    0.3448  1:110228695_CNV_GSTM1   7       1       WL008951                0       1       109686073       0.7621  0.5021
        [T/G]   BOT     BOT             +       B       B       C       C       G       G       G       G       0.791   0.120   0.030
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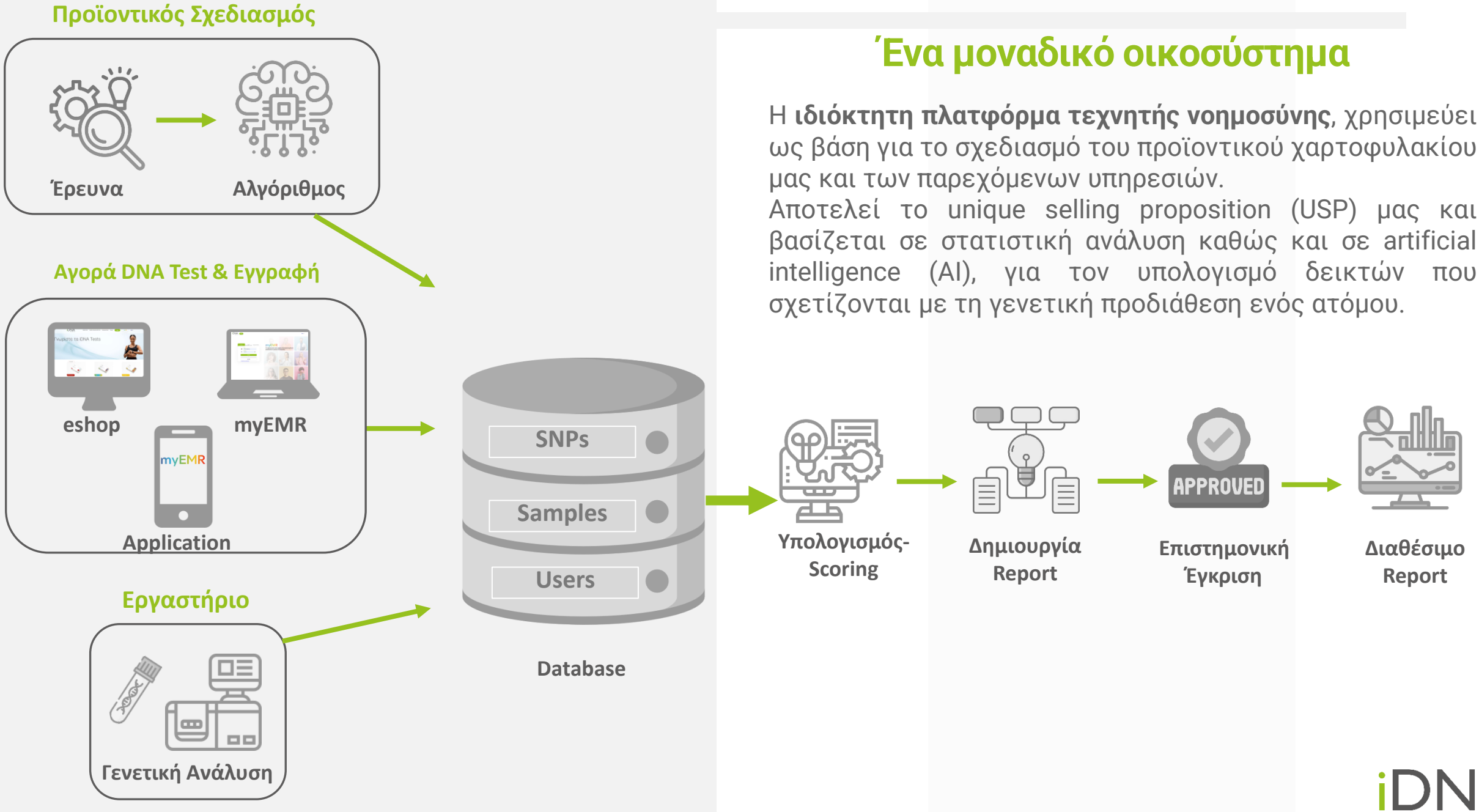
Ln 1, Col 1 | 126,348,820 characters | 100% | Windows (CRLF) | UTF-8



Ένα μοναδικό οικοσύστημα

Η **ιδιόκτητη πλατφόρμα τεχνητής νοημοσύνης**, χρησιμεύει ως βάση για το σχεδιασμό του προϊοντικού χαρτοφυλακίου μας και των παρεχόμενων υπηρεσιών.
Αποτελεί το unique selling proposition (USP) μας και βασίζεται σε στατιστική ανάλυση καθώς και σε artificial intelligence (AI), για τον υπολογισμό δεικτών που σχετίζονται με τη γενετική προδιάθεση ενός ατόμου.

iDNA GENOMICS

Deal	Data quantity	Genomic data type	Price per unit (PPU)	Details
DECODE to Amgen for $415M (2012)	300,000	Genotype	$1,383	Company acquisition including genotyped data + medical records.
23andMe to Genentech for $60M (2015)	3000	Whole genome sequence	$20,000	Partnership including whole genome sequence data + self reported info from Parkinson's disease patients + ability to recontact.
FinnGen to group of pharmaceutical companies for $75M (2017)	500,000	Genotype	$150	7 international pharmaceutical companies funding a study to analyse 500,000 Finnish biobank blood samples. Genotype data + medical records + ability to re-contact.
UK Biobank to Regeneron group of pharmaceutical companies (2018)	500,000	Exome	$300	Regeneron group of pharmaceutical companies funding a study to sequence the exomes of 500,000 UK Biobank participants. Exome data + medical information + exclusive access period.
23andMe to GSK for $300M (2018)	4,000,000	Genotype	$75	Ownership stake in 23andMe with 4 year exclusive access to genotype + survey data.
Genomic Medicine Ireland to WuXi NextCODE for $400M (2018)	400,000	Whole genome sequence	$1000	Company acquisition including whole genome sequence data + medical records + ability to re-contact.
UK Biobank to group of pharmaceutical companies for $200M (2019)	500,000	Whole genome sequence	$400	4 international pharmaceutical companies funding a study to sequence the whole genomes of 500,000 UK Biobank participants. Whole genome sequence data + medical information + exclusive access period.

"34% of CNS drugs side effects are caused by gene – drug interactions and not by drug – drug interactions."

CE IVD

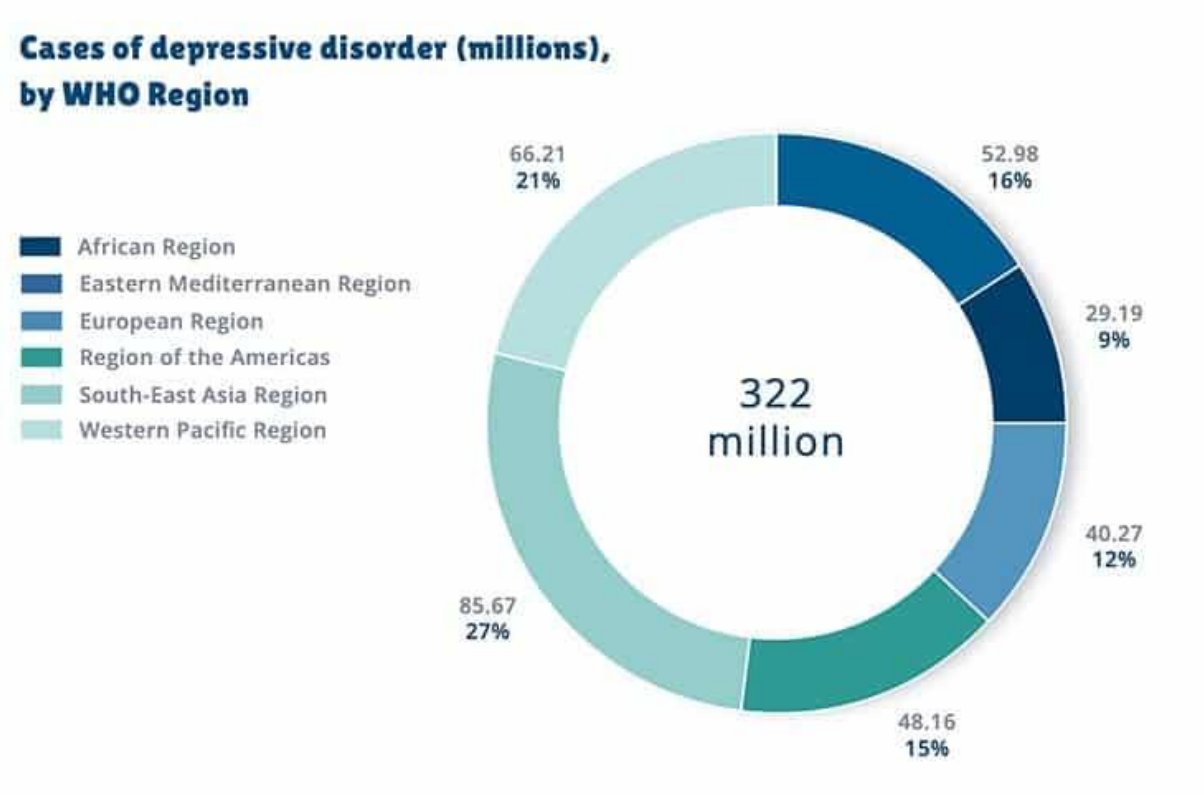
iDNA PGx CNS Test

Pharmacogenetics of Central Nervous System Drugs

iDNA GENOMICS

The problem

1/3 of patients with depression don't respond to selected drug treatment



- Depression is no 1 cause of Suicide
- 322 million people suffer from Depression
- > 35% of them don't respond even to the 2nd drug treatment
- Doctors until today select an antidepressant by *"Trial and Error "*
- Besides the social burden, there is a huge economic one for the Health Systems

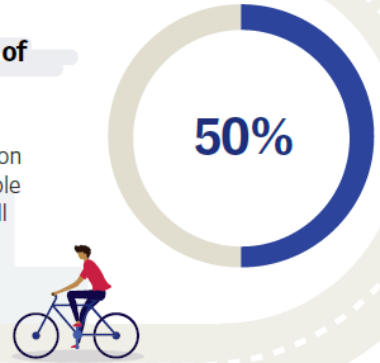
Source: 2017 World Health Organization (WHO) Depression and Other Common Mental Disorders report

iDNA GENOMICS

The problem in Europe

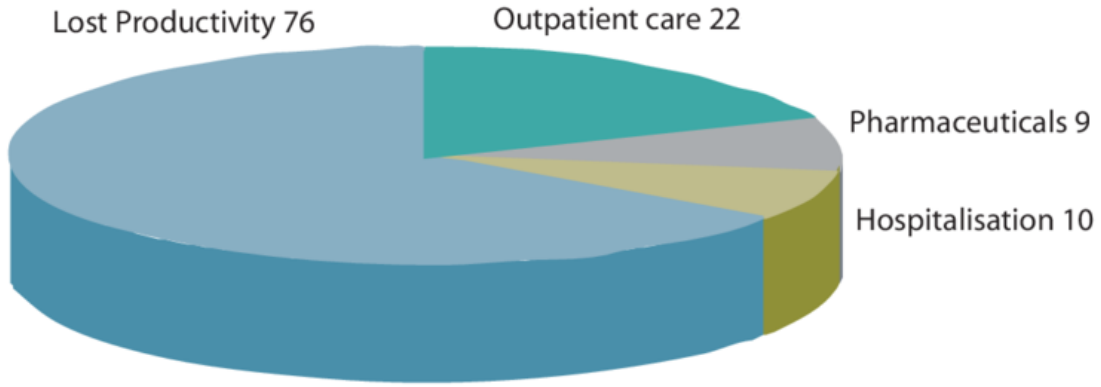
Depression accounts for up to 50% of chronic sick leaves in the EU.

People with depression are less likely to be employed compared to the general population for all EU countries. Even when at work people with depression may not function to their full abilities, and are estimated to be 6% less productive than usual.



€41 billion direct costs

€77 billion productivity losses



120,000

Depression is the primary risk factor associated with suicide and suicidal ideation. An estimated 120,000 people take their own lives every year in the WHO European Region, equivalent to 1.3% of all deaths in 2019

iDNA GENOMICS

The solution

7NA PGx CNS is an *in vitro* diagnostic (IVD) medical device bearing the CE mark

Through a simple saliva genetic test, the physician gets the genetic information needed to select **the most appropriate medication for each patient:**

- Faster remission of symptoms
- Less side effects
- Increased compliance
- Higher efficacy

Strong competitive advantage

- The only in Europe with CE mark *in vitro* diagnostic medical device
- Under reimbursement in Greece
- > 3000 patients already
- Pharmacogenetic analysis for 30 drugs

iDNA GENOMICS

Gene-drug interactions

13 genes, 24 SNPs

Gene	SNP
ANKK1, DRD2	rs1800497
CYP2C19	rs12248560
	rs28399504
	rs4244285
	rs4986893
CYP2C9	rs1057910
	rs1799853
CYP2D6	rs1065852
	rs28371725
	rs35742686
	rs3892097
	rs5030655
	rs5030656
DRD2	rs1799978
DRD3	rs963468
EPHX1	rs1051740
	rs2234922
FKBP5	rs4713916
GRIK1	rs2832407
HTR2C	rs1414334
MC4R	rs17782313
	rs489693
SCN1A	rs3812718
UGT2B7	rs7668258

Out of scientifically validated selected genes & SNPs, PGx analysis is provided for 30 CNS drugs

30 common CNS active substances

Antipsychotics
Quetiapine
Risperidone
Olanzapine
Aripiprazole
Paliperidone
Haloperidol
Clozapine
Amilsupride
Ziprasidone

Antidepressants
Escitalopram
Citalopram
Venlafaxine
Sertraline
Fluoxetine
Mirtazapine
Paroxetine
Duloxetine
Clomipramine
Fluvoxamine
Amitriptyline
Vortioxetine

Antiepileptics
Lamotrigine
Topiramate
Valproic acid
Carbamazepine
Phenytoin

Other
Diazepam
Clobazam
Donepezil
Galantamine

Pharmacogenetic associations are regularly updated according to the latest scientific literature, pharmacogenetic databases, dosing recommendations, and drug labels

iDNA LABORATORIES

iDNA GENOMICS

Στοιχεία ασθενούς
Ονοματεπώνυμο
Ημερομηνία Γέννησης

Πληροφορίες δείγματος
Ημερομηνία αποτελέσματος
Κωδικός δείγματος - Barcode

Αποτελέσματα Φαρμακογονιδιωματικής Ανάλυσης
Αντικαταθλιπτικά Φάρμακα

Ελάχιστη αλληλεπίδραση γονιδίου-φαρμάκου	Μέτρια αλληλεπίδραση γονιδίου-φαρμάκου		Σημαντική αλληλεπίδραση γονιδίου-φαρμάκου	
citalopram	duloxetine	6,8	amitriptyline	4,9
escitalopram	fluoxetine	1,8	clomipramine	4,9
	fluvoxamine	1,2		
	mirtazapine	1,2,6,8		
	paroxetine	6,8		
	sertraline	1,2,6		
	venlafaxine	1,2,6,8		
	vortioxetine	2		

Κλινικές Συμβουλές

1. **Ξεκινήστε τη θεραπεία με τη συνιστώμενη στο Φύλλο Οδηγιών Χρήσης αρχική δοσολογία και αναπροσαρμόστε.**
2. **Εξετάστε μείωση της δοσολογίας και σταθμίστε τις ανεπιθύμητες ενέργειες.**
3. Εξετάστε μείωση της δοσολογίας συντήρησης κατά 25%.
4. **Εξετάστε μείωση της δοσολογίας κατά 50%, ή εναλλακτική θεραπεία.**
5. Εξετάστε αύξηση της δοσολογίας και σταθμίστε τις ανεπιθύμητες ενέργειες, ή επιλέξτε εναλλακτική θεραπεία.
6. **Αυξημένη πιθανότητα ανεπιθύμητων ενεργειών, ή μειωμένης αποτελεσματικότητας.**
7. Αυξημένη πιθανότητα αύξησης βάρους.
8. **Συμβουλευτείτε την ερμηνευτική ανάλυση και προσαρμόστε τη δοσολογία.**
9. **Αποφύγετε τη χρήση αυτής της κατηγορίας φαρμάκων. Εξετάστε εναλλακτικό φάρμακο.**

Clinical **Application**

Before: One-dose-fits-all approach → PGx → **After:** Personalised medicine (from genotype to phenotype)

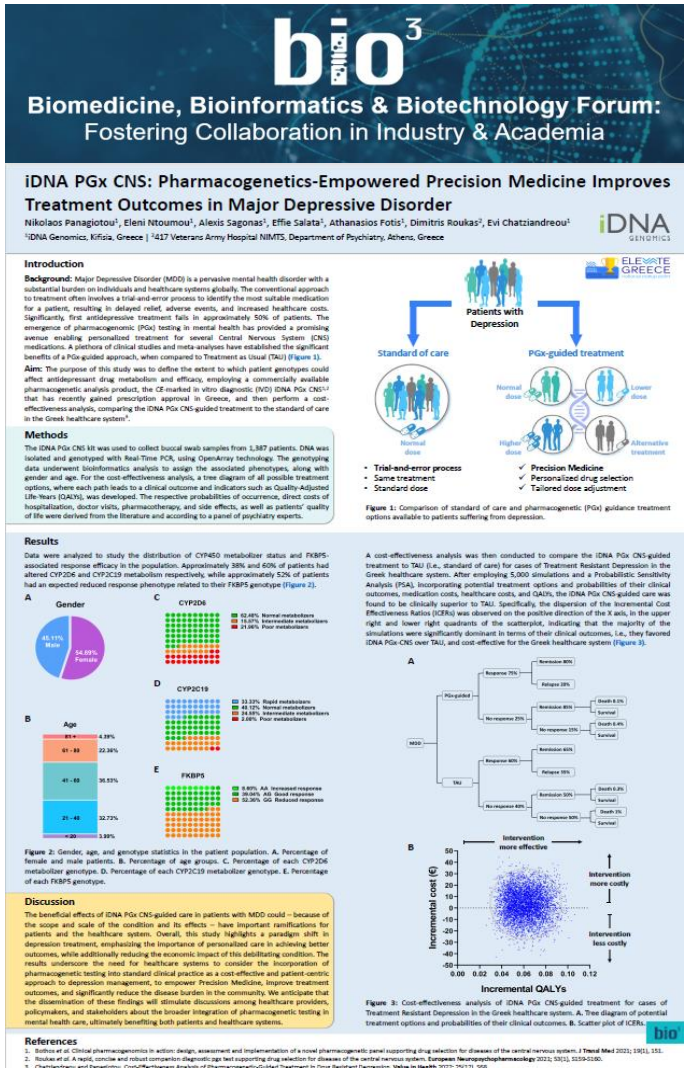
The evidence

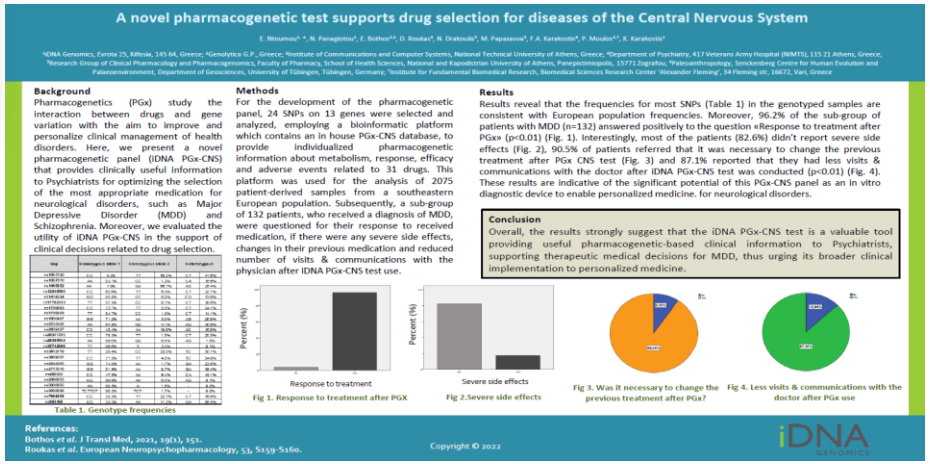
Key findings in >3000 Greek patients

- **Patient satisfaction** *(Gkouvas et al. 2022 and Ntoumou et al. 2022):*
  - 96% of patients responded to their personalized treatment.
  - 83% reported no serious side-effects.
  - 90% reported a change in medication, including dosage adjustments or selection of alternative medication by their doctor.
  - 87% reported fewer visits and communications with their doctor.
- **Cost-effectiveness** *(Chatziandreou & Panagiotou 2022):*
  - PGx-guided therapy was associated with 0.712 Quality-Adjusted Life Years (QALYs), while Treatment as Usual (TAU) was
  - associated with 0.651 QALYs.
  - PGx was found to be highly cost-effective with an Incremental Cost-Effectiveness Ratio (ICER) of 55 €/QALY.
  - Over a 5-year period, suicides to be reduced by approximately 25%.
- **Gene-drug interactions** *(Panagiotou et al. 2023 and Bothos et a.l 2021):*
  - PGx guidance towards dosage adjustment benefits 38% and 60% of patients with altered CYP2D6 and CYP2C19 metabolism respectively, as well as 52% of patients with a reduced response phenotype related to FKBP5.
  - PGx guided therapy benefits over 70% of patients, where a moderate or significant gene-drug interaction was discovered.
- **Product Status**
  - CE IVD
  - Under Reimbursement in MDD in Greece

The scientific publications

FENS Forum 2022





ISPOR Europe 2022
6-9 NOVEMBER 2022 | VIENNA | AUSTRIA

the International Society for Pharmacoeconomics and Outcomes Research

iDNA GENOMICS

iDNA
Cardio Health Prevention

CE IVD

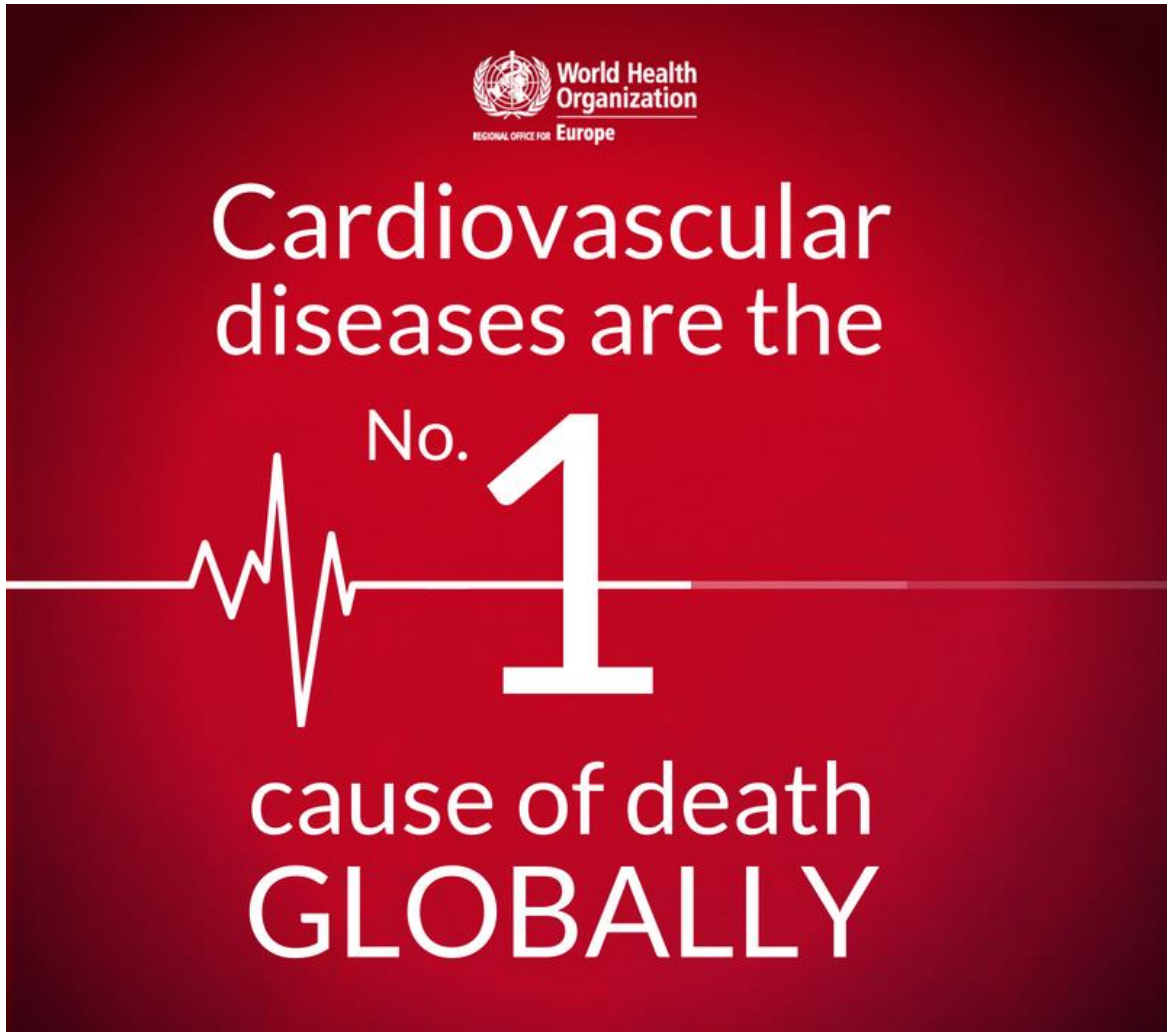
Genetic Predisposition to Cardiovascular Diseases – Polygenic Risk Score (PRS)

> PRS is associated with the prospect of intervention, including prioritization of preventive measures and presymptomatic testing, initiation and frequency of testing, as well as lifestyle modification and clinical decision-making.

iDNA GENOMICS

The problem

No early detection of the risk

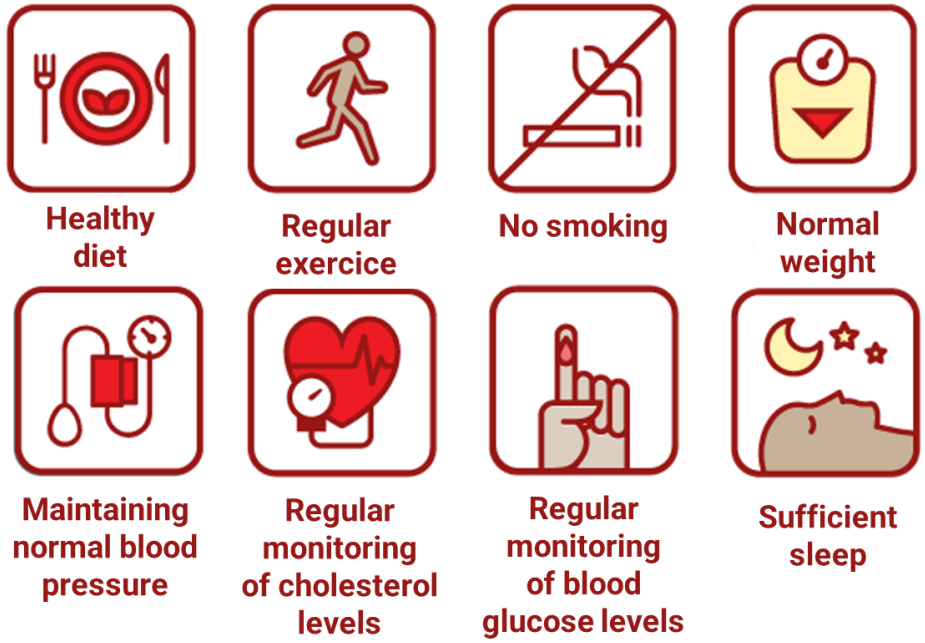


Source: 2023 World Heart Report, World Heart Federation

iDNA GENOMICS

The problem

Risk underestimation



iDNA GENOMICS

Ερωτηματολόγιο: Φαινοτυπικά χαρακτηριστικά

Ημερομηνία γέννησης:	1961-12-09
Φύλο:	Άνδρας
Φυλετική καταγωγή:	Λευκή ή Καυκάσια
Καπνιστικές συνήθειες:	Έκοψα το κάπνισμα περισσότερο από 12 μήνες πριν
Ύψος (cm):	190
Βάρος (kg):	82
ΜΟ εβδομαδιαίας σωματικής άσκησης:	Μέτρια Άσκηση: 210 λεπτά Έντονη Άσκηση: 0 λεπτά
ΜΟ ημερήσιας κατανάλωσης φρούτων & λαχανικών:	Λιγότερα από 4,5 φλυτζάνια
ΜΟ ημερήσιας κατανάλωσης μερίδων (30γρ.) από τρόφιμα ολικής άλεσης:	Λιγότερες από 3 μερίδες
ΜΟ εβδομαδιαίας κατανάλωσης αναψυκτικών (350ml):	Λιγότερα από 3
ΜΟ εβδομαδιαίας κατανάλωσης μερίδων (100γρ.) ψάρι:	2 ή περισσότερες μερίδες
Ημερήσια κατανάλωση αλατιού:	Καταναλώνω περισσότερο από 1/3 κουταλάκι του γλυκού αλάτι ημερησίως
Συστολική (μεγάλη) αρτηριακή πίεση (mm/Hg):	130
Διαστολική (μικρή) αρτηριακή πίεση (mm/Hg):	85
Φαρμακευτική αγωγή για τη μείωση της αρτηριακής πίεσης:	Ναι
Ολική χοληστερόλη (mg/dL):	190
Φαρμακευτική αγωγή για τη μείωση της χοληστερόλης:	Ναι
Σάκχαρο / γλυκόζη αίματος νηστείας (mm/dL):	70
Φαρμακευτική αγωγή για τη μείωση του σακχάρου:	Όχι

Source: American Heart Association
https://www.heart.org/en/healthy-living/healthy-lifestyle/lifes-essential-8

iDNA GENOMICS

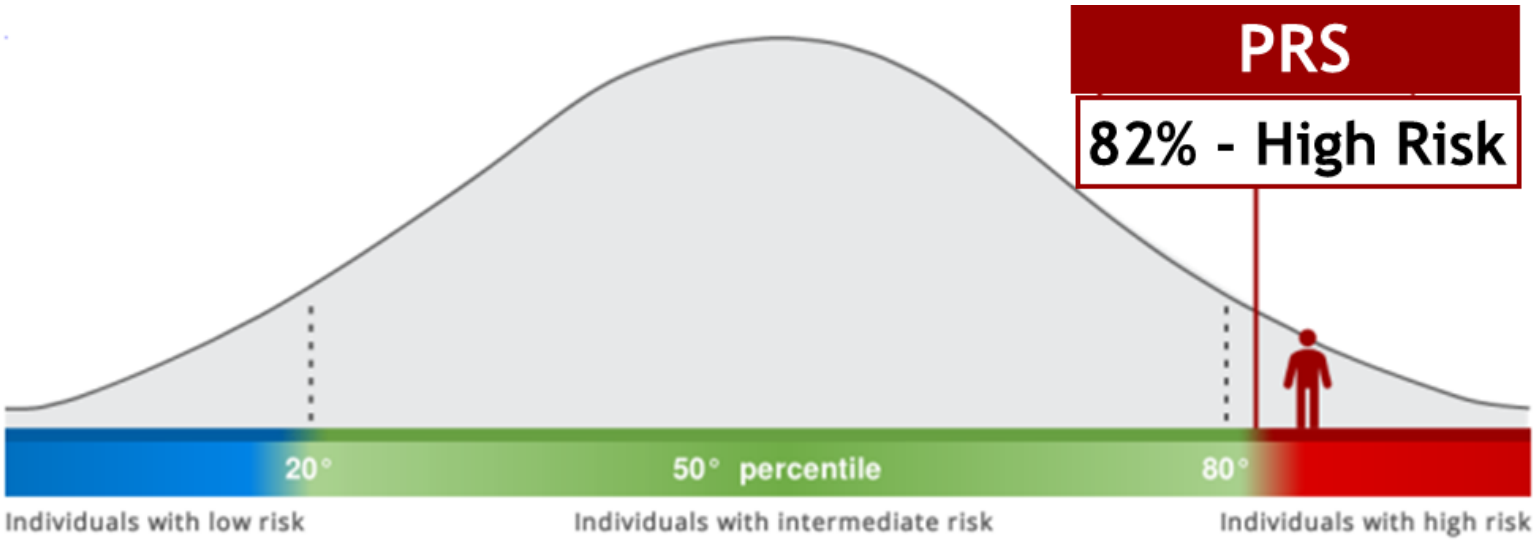
The solution

(Lots of genes)

Polygenic Risk Score

Stroke :
What is your Genetic Predisposition?

PRS: 82% relative to the population



iDNA GENOMICS

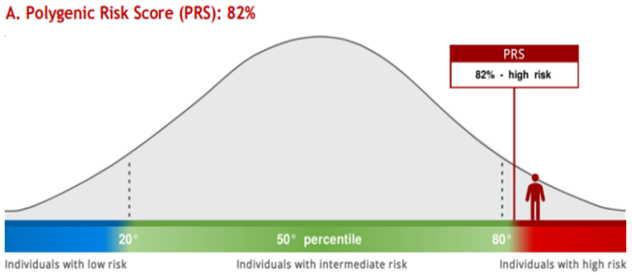
The solution

The report provides PRS and PRS adjusted for 6 cardiovascular diseases. Next to PRS, PRS adjusted reflects the lifestyle impact on disease occurrence

1. Coronary Artery Disease
2. Cardiomyopathy – Dilated
3. Cardiomyopathy – Hypertrophic
4. Heart Failure
5. Arrhythmia - Atrial fibrillation
6. Ischemic stroke

Phenotype + Polygenic Risk Score (PRS) = PRS adjusted

+



= DELAY/AVOID Cardio disease

- **The only *in vitro* diagnostic (IVD) medical device with CE mark**
- **The only one that combines the phenotypic with the genetic profile and comes up with the Adjusted PRS**

iDNA GENOMICS

The solution

iDNA GENOMICS

5. Ισχαιμικό εγκεφαλικό επεισόδιο

A. Βαθμολογία πολυγονιδιακού ρίσκου (PRS): 93%

Η Βαθμολογία PRS είναι 93% επί του πληθυσμού. Αυτό σημαίνει ότι σε κάθε 100 άτομα, το εκτιμώμενο δικό σου PRS είναι υψηλότερο από 93 άτομα και ίδιο ή χαμηλότερο από τα υπόλοιπα 7 άτομα. Επομένως, το γενετικό σου υπόβαθρο σε θέτει σε αυξημένο ρίσκο εμφάνισης της πάθησης.

B. Προσαρμοσμένη Βαθμολογία πολυγονιδιακού ρίσκου (Adjusted PRS): 31%

Για τον υπολογισμό του Προσαρμοσμένου PRS (Adjusted PRS), συνεκτιμάται:

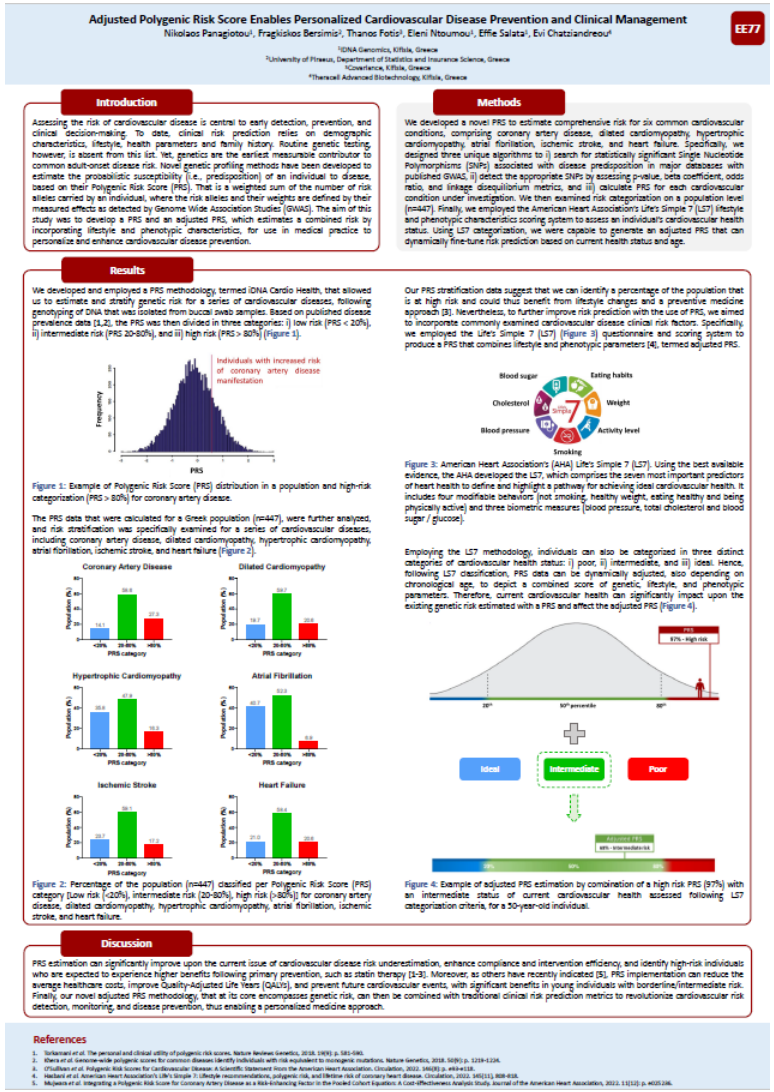
1. Βαθμολογία PRS: 93%
2. Βαθμολογία εκτίμησης τρέχουσας κατάστασης καρδιαγγειακής υγείας: Βέλτιστη

Το Προσαρμοσμένο PRS (Adjusted PRS) εκτιμάται ότι είναι 31%, δηλαδή μειωμένο σε σχέση με την Βαθμολογία PRS και βρίσκεται σε τυπικά επίπεδα ρίσκου σε σχέση με το γενικό πληθυσμό. Η τήρηση υγιεινών συνηθειών και η συμμόρφωση με τις οδηγίες του γιατρού σου, μπορεί να συμβάλουν στη βέλτιστη καρδιαγγειακή υγεία και στην πρόληψη καρδιαγγειακών παθήσεων.

Ένα επεισόδιο συμβαίνει όταν διακόπτεται ή μειώνεται η παροχή αίματος σε μέρος του εγκεφάλου, εμποδίζοντας με αυτό τον τρόπο τον εγκεφαλικό ιστό να πάρει οξυγόνο και θρεπτικά συστατικά. Αποτελεί μια επείγουσα ιατρική κατάσταση της οποίας έγκαιρη αντιμετώπιση είναι ζωτικής σημασίας.

(Πηγή: https://www.mayoclinic.org/diseases-conditions/stroke/symptoms-causes/syc-20350113)

Our scientific publications



Adjusted Polygenic Risk Score Enables Personalized Cardiovascular Disease Prevention and Clinical Management EE77

Nikolaos Panagiotou[1], Fragkiskos Bersimis[2], Thanos Fotis[3], Eleni Ntoumou[1], Effie Salata[3], Evi Chatziandreou[4]

[1]iDNA Genomics, Kilfisia, Greece
[2]University of Piraeus, Department of Statistics and Insurance Science, Greece
[3]Covariance, Kilfisia, Greece
[4]Theracell Advanced Biotechnology, Kilfisia, Greece

Introduction

Assessing the risk of cardiovascular disease is central to early detection, prevention, and clinical decision-making. To date, clinical risk prediction relies on demographic characteristics, lifestyle, health parameters and family history. Routine genetic testing, however, is absent from this list. Yet, genetics are the earliest measurable contributor to common adult-onset disease risk. Novel genetic profiling methods have been developed to estimate the probabilistic susceptibility [i.e., predisposition] of an individual to disease, based on their Polygenic Risk Score (PRS). That is a weighted sum of the number of risk alleles carried by an individual, where the risk alleles and their weights are defined by their measured effects as detected by Genome Wide Association Studies (GWAS). The aim of this study was to develop a PRS and an adjusted PRS, which estimates a combined risk by incorporating lifestyle and phenotypic characteristics, for use in medical practice to personalize and enhance cardiovascular disease prevention.

Methods

We developed a novel PRS to estimate comprehensive risk for six common cardiovascular conditions, comprising coronary artery disease, dilated cardiomyopathy, hypertrophic cardiomyopathy, atrial fibrillation, ischemic stroke, and heart failure. Specifically, we designed three unique algorithms to i) search for statistically significant Single Nucleotide Polymorphisms (SNPs) associated with disease predisposition in major databases with published GWAS, ii) detect the appropriate SNPs by assessing p-value, beta coefficient, odds ratio, and linkage disequilibrium metrics, and iii) calculate PRS for each cardiovascular condition under investigation. We then examined risk categorization on a population level (n=447). Finally, we employed the American Heart Association's Life's Simple 7 (LS7) lifestyle and phenotypic characteristics scoring system to assess an individual's cardiovascular health status. Using LS7 categorization, we were capable to generate an adjusted PRS that can dynamically fine-tune risk prediction based on current health status and age.

Results

We developed and employed a PRS methodology, termed iDNA Cardio Health, that allowed us to estimate and stratify genetic risk for a series of cardiovascular diseases, following genotyping of DNA that was isolated from buccal swab samples. Based on published disease prevalence data [1,2], the PRS was then divided in three categories: i) low risk (PRS < 20%), ii) intermediate risk (PRS 20-80%), and iii) high risk (PRS > 80%) (Figure 1).

Figure 1: Example of Polygenic Risk Score (PRS) distribution in a population and high-risk categorization (PRS > 80%) for coronary artery disease.

The PRS data that were calculated for a Greek population (n=447), were further analyzed, and risk stratification was specifically examined for a series of cardiovascular diseases, including coronary artery disease, dilated cardiomyopathy, hypertrophic cardiomyopathy, atrial fibrillation, ischemic stroke, and heart failure (Figure 2).

Figure 2: Percentage of the population (n=447) classified per Polygenic Risk Score (PRS) category [Low risk (<20%), intermediate risk (20-80%), high risk (>80%)] for coronary artery disease, dilated cardiomyopathy, hypertrophic cardiomyopathy, atrial fibrillation, ischemic stroke, and heart failure.

Our PRS stratification data suggest that we can identify a percentage of the population that is at high risk and could thus benefit from lifestyle changes and a preventive medicine approach [3]. Nevertheless, to further improve risk prediction with the use of PRS, we aimed to incorporate commonly examined cardiovascular disease clinical risk factors. Specifically, we employed the Life's Simple 7 (LS7) (Figure 3) questionnaire and scoring system to produce a PRS that combines lifestyle and phenotypic parameters [4], termed adjusted PRS.

Figure 3: American Heart Association's (AHA) Life's Simple 7 (LS7). Using the best available evidence, the AHA developed the LS7, which comprises the seven most important predictors of heart health to define and highlight a pathway for achieving ideal cardiovascular health. It includes four modifiable behaviors (not smoking, healthy weight, eating healthy and being physically active) and three biometric measures (blood pressure, total cholesterol and blood sugar / glucose).

Employing the LS7 methodology, individuals can also be categorized in three distinct categories of cardiovascular health status: i) poor, ii) intermediate, and iii) ideal. Hence, following LS7 classification, PRS data can be dynamically adjusted, also depending on chronological age, to depict a combined score of genetic, lifestyle, and phenotypic parameters. Therefore, current cardiovascular health can significantly impact upon the existing genetic risk estimated with a PRS and affect the adjusted PRS (Figure 4).

Figure 4: Example of adjusted PRS estimation by combination of a high risk PRS (97%) with an intermediate status of current cardiovascular health assessed following LS7 categorization criteria, for a 50-year-old individual.

Discussion

PRS estimation can significantly improve upon the current issue of cardiovascular disease risk underestimation, enhance compliance and intervention efficiency, and identify high-risk individuals who are expected to experience higher benefits following primary prevention, such as statin therapy [1-3]. Moreover, as others have recently indicated [5], PRS implementation can reduce the average healthcare costs, improve Quality-Adjusted Life Years (QALYs), and prevent future cardiovascular events, with significant benefits in young individuals with borderline/intermediate risk. Finally, our novel adjusted PRS methodology, that at its core encompasses genetic risk, can then be combined with traditional clinical risk prediction metrics to revolutionize cardiovascular risk detection, monitoring, and disease prevention, thus enabling a personalized medicine approach.

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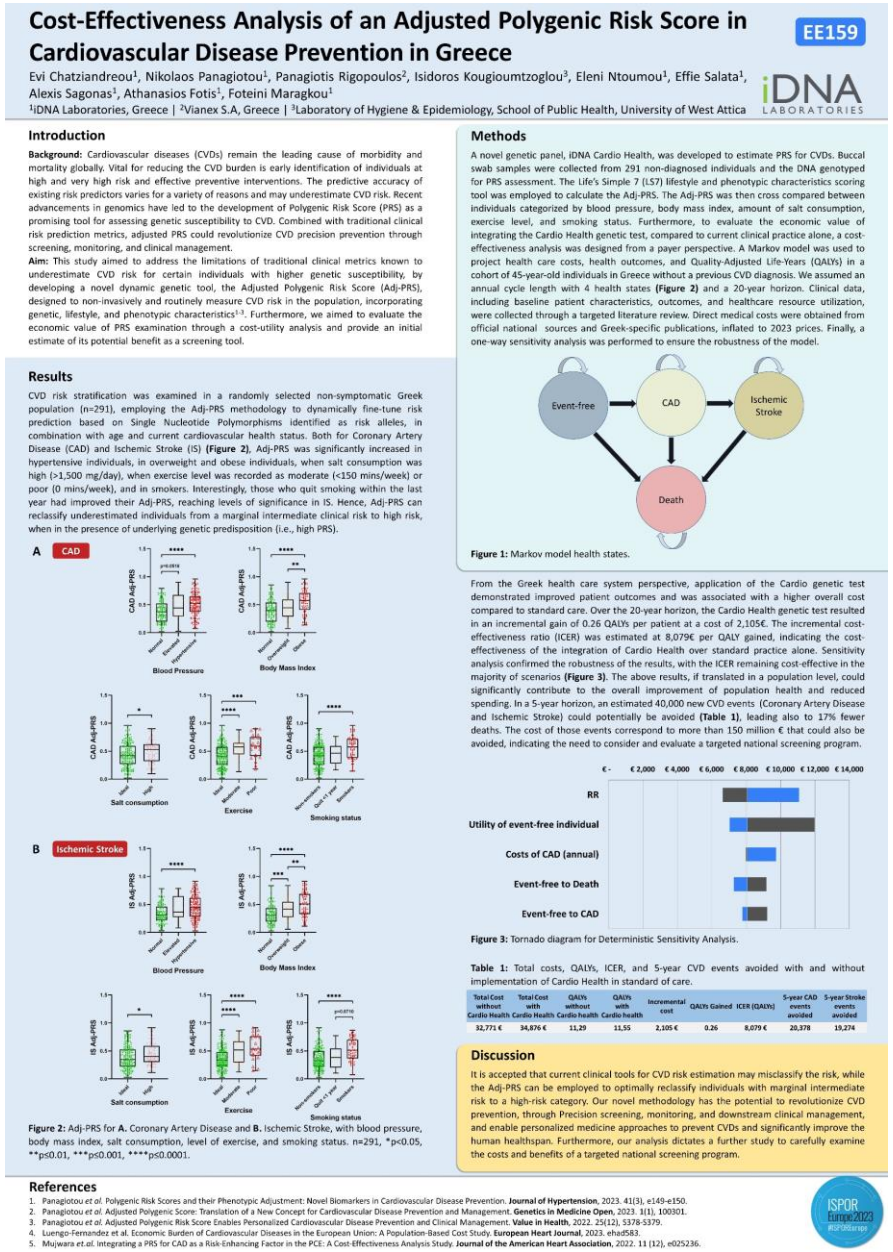

Cost-Effectiveness Analysis of an Adjusted Polygenic Risk Score in Cardiovascular Disease Prevention in Greece EE159

Evi Chatziandreou[1], Nikolaos Panagiotou[1], Panagiotis Rigopoulos[2], Isidoros Kougioumtzoglou[3], Eleni Ntoumou[1], Effie Salata[1], Alexis Sagonas[1], Athanasios Fotis[1], Foteini Maragkou[1]

[1]iDNA Laboratories, Greece | [2]Vianex S.A, Greece | [3]Laboratory of Hygiene & Epidemiology, School of Public Health, University of West Attica

Introduction

Background: Cardiovascular diseases (CVDs) remain the leading cause of morbidity and mortality globally. Vital for reducing the CVD burden is early identification of individuals at high and very high risk and effective preventive interventions. The predictive accuracy of existing risk predictors varies for a variety of reasons and may underestimate CVD risk. Recent advancements in genomics have led to the development of Polygenic Risk Score (PRS) as a promising tool for assessing genetic susceptibility to CVD. Combined with traditional clinical risk prediction metrics, adjusted PRS could revolutionize CVD precision prevention through screening, monitoring, and clinical management.

Aim: This study aimed to address the limitations of traditional clinical metrics known to underestimate CVD risk for certain individuals with higher genetic susceptibility, by developing a novel dynamic genetic tool, the Adjusted Polygenic Risk Score (Adj-PRS), designed to non-invasively and routinely measure CVD risk in the population, incorporating genetic, lifestyle, and phenotypic characteristics[1-3]. Furthermore, we aimed to evaluate the economic value of PRS examination through a cost-utility analysis and provide an initial estimate of its potential benefit as a screening tool.

Results

CVD risk stratification was examined in a randomly selected non-symptomatic Greek population (n=291), employing the Adj-PRS methodology to dynamically fine-tune risk prediction based on Single Nucleotide Polymorphisms identified as risk alleles, in combination with age and current cardiovascular health status. Both for Coronary Artery Disease (CAD) and Ischemic Stroke (IS) **(Figure 2)**, Adj-PRS was significantly increased in hypertensive individuals, in overweight and obese individuals, when salt consumption was high (>1,500 mg/day), when exercise level was recorded as moderate (<150 mins/week) or poor (0 mins/week), and in smokers. Interestingly, those who quit smoking within the last year had improved their Adj-PRS, reaching levels of significance in IS. Hence, Adj-PRS can reclassify underestimated individuals from a marginal intermediate clinical risk to high risk, when in the presence of underlying genetic predisposition (i.e., high PRS).

Figure 2: Adj-PRS for **A.** Coronary Artery Disease and **B.** Ischemic Stroke, with blood pressure, body mass index, salt consumption, level of exercise, and smoking status. n=291, *p<0.05, **p≤0.01, ***p≤0.001, ****p≤0.0001.

Methods

A novel genetic panel, iDNA Cardio Health, was developed to estimate PRS for CVDs. Buccal swab samples were collected from 291 non-diagnosed individuals and the DNA genotyped for PRS assessment. The Life's Simple 7 (LS7) lifestyle and phenotypic characteristics scoring tool was employed to calculate the Adj-PRS. The Adj-PRS was then cross compared between individuals categorized by blood pressure, body mass index, amount of salt consumption, exercise level, and smoking status. Furthermore, to evaluate the economic value of integrating the Cardio Health genetic test, compared to current clinical practice alone, a cost-effectiveness analysis was designed from a payer perspective. A Markov model was used to project health care costs, health outcomes, and Quality-Adjusted Life-Years (QALYs) in a cohort of 45-year-old individuals in Greece without a previous CVD diagnosis. We assumed an annual cycle length with 4 health states **(Figure 2)** and a 20-year horizon. Clinical data, including baseline patient characteristics, outcomes, and healthcare resource utilization, were collected through a targeted literature review. Direct medical costs were obtained from official national sources and Greek-specific publications, inflated to 2023 prices. Finally, a one-way sensitivity analysis was performed to ensure the robustness of the model.

Figure 1: Markov model health states.

From the Greek health care system perspective, application of the Cardio genetic test demonstrated improved patient outcomes and was associated with a higher overall cost compared to standard care. Over the 20-year horizon, the Cardio Health genetic test resulted in an incremental gain of 0.26 QALYs per patient at a cost of 2,105€. The incremental cost-effectiveness ratio (ICER) was estimated at 8,079€ per QALY gained, indicating the cost-effectiveness of the integration of Cardio Health over standard practice alone. Sensitivity analysis confirmed the robustness of the results, with the ICER remaining cost-effective in the majority of scenarios **(Figure 3)**. The above results, if translated in a population level, could significantly contribute to the overall improvement of population health and reduced spending. In a 5-year horizon, an estimated 40,000 new CVD events (Coronary Artery Disease and Ischemic Stroke) could potentially be avoided **(Table 1)**, leading also to 17% fewer deaths. The cost of those events correspond to more than 150 million € that could also be avoided, indicating the need to consider and evaluate a targeted national screening program.

Figure 3: Tornado diagram for Deterministic Sensitivity Analysis.

Table 1: Total costs, QALYs, ICER, and 5-year CVD events avoided with and without implementation of Cardio Health in standard of care.

Total Cost without Cardio Health	Total Cost with Cardio Health	QALYs without Cardio health	QALYs with Cardio health	Incremental cost	QALYs Gained	ICER (QALYs)	5-year CAD events avoided	5-year Stroke events avoided
32,771 €	34,876 €	11.29	11.55	2,105 €	0.26	8,079 €	20,378	19,274

Discussion

It is accepted that current clinical tools for CVD risk estimation may misclassify the risk, while the Adj-PRS can be employed to optimally reclassify individuals with marginal intermediate risk to a high-risk category. Our novel methodology has the potential to revolutionize CVD prevention, through Precision screening, monitoring, and downstream clinical management, and enable personalized medicine approaches to prevent CVDs and significantly improve the human healthspan. Furthermore, our analysis dictates a further study to carefully examine the costs and benefits of a targeted national screening program.

References

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European Heart Journal

ESC European Society of Cardiology

Article Contents

JOURNAL ARTICLE

Integration of a polygenic score into guideline-recommended prediction of cardiovascular disease

Ling Li, Shichao Pang, Fabian Starnecker, Bertram Mueller-Myhsok, Heribert Schunkert ✉ Author Notes

European Heart Journal, ehae048,
https://doi.org/10.1093/eurheartj/ehae048
Published: 29 March 2024 **Article history** ▾

iDNA NutriGenetix

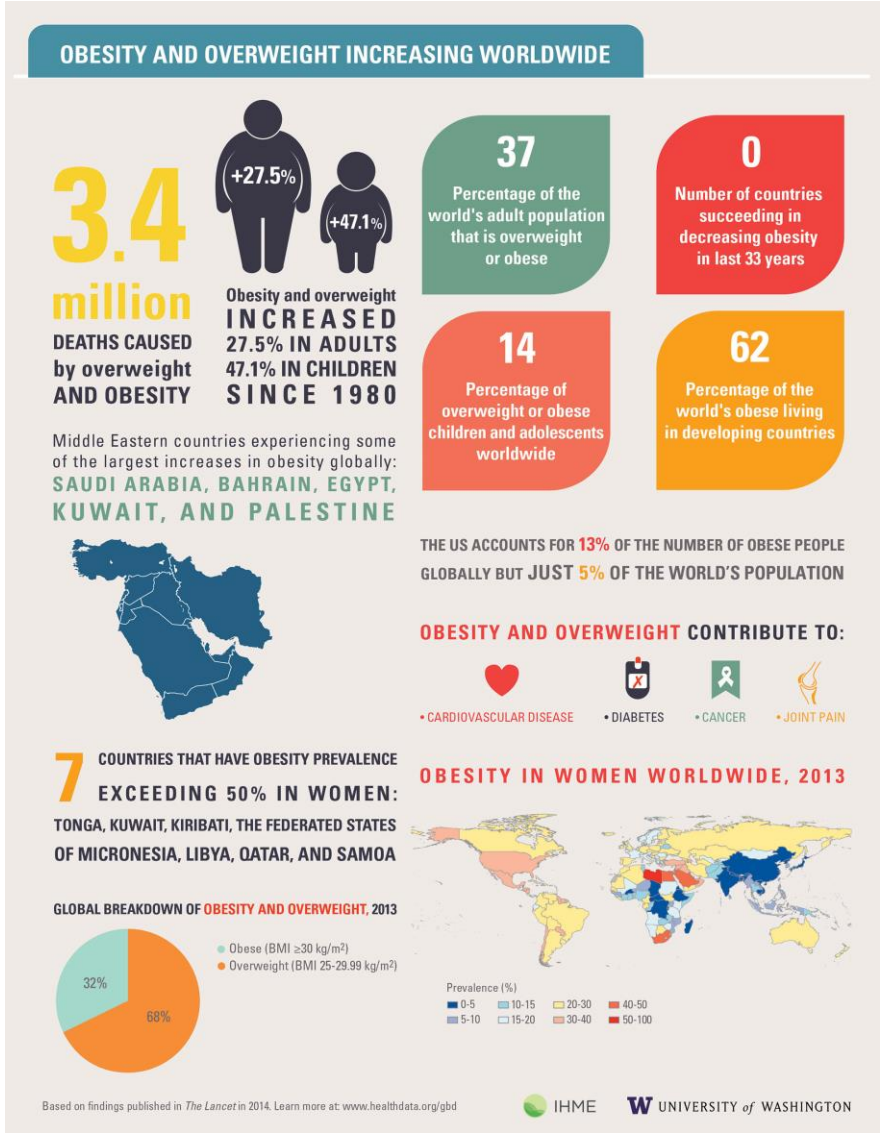
Personalized Nutrigenetic Analysis

CE IVD

iDNA GENOMICS

The problem

No real tailor-made nutritional plan

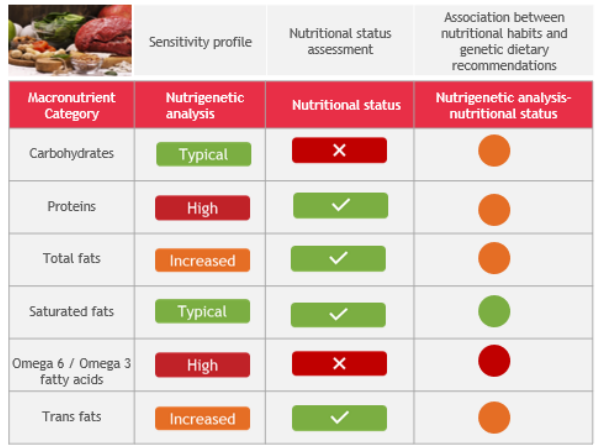


- 1.9 billion people (37% of global population) are overweight
- 1 out of 5 children 5-19 y.o. are overweight
- 650 million people are obese
- Obesity is related to serious health problems i.e., Diabetes, Cardiovascular diseases, musculoskeletal problems
- >50% of obesity risk is genetic
- Current nutritional plans & diets are not based on genetic profile but rather only on phenotype & lifestyle characteristics

iDNA GENOMICS

The solution

The report provides personalized advises and dietery plan combining both phenotype and genetics



Phenotype & lifestyle + Nutrigenetics = Precision Nutrition

- Age, sex, BMI
- Medical history
- Weight goal
- Dietary habits

+

Genetic analysis for specific genetic polymorphisms in 27 nutritional categories

=

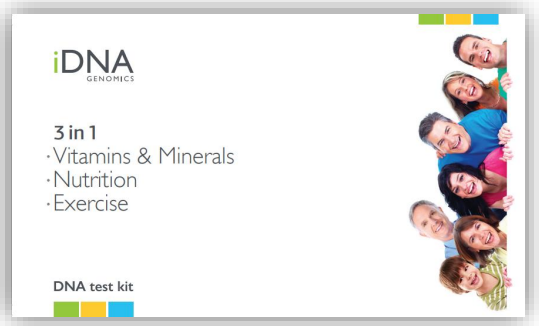
- Tailor made dietary plan
- Actionable interventions
- Long term monitoring & dietary adjustments

- **The only *in vitro* diagnostic (IVD) nutrigenetic with CE mark**
- **The only one that combines the phenotypic with the genetic profile and comes up with tailor made nutritional plan**

iDNA GENOMICS

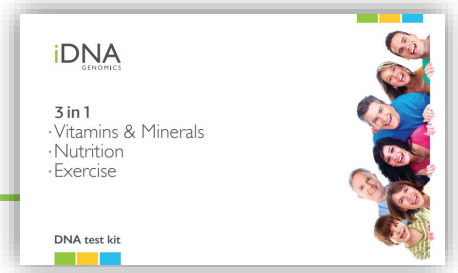
iDNA 3 in 1

Personalized Nutrition, Vitamins & Exercise Genetic Analysis



iDNA GENOMICS

The solution



The 'one-size-fits-all' approach in nutrition and exercise does not suit everyone.
The iDNA 3 in 1 DNA Test includes the genetic information needed to ***personalize our dietary and sports choices****. This offers a deeper understanding of the individual nutrition, vitamins, minerals and exercise needs to achieve* ***optimal health and athletic performance****.*
The iDNA 3 in 1 DNA test offers personalized genetic analysis in 37 categories related to ***Nutrition, Exercise, Vitamins & Minerals.***

The categories

Weight Management
Our genes dictate the optimal diet for weight loss and long-term weight management.

Cardiovascular Health
Cardiovascular health is highly dependent on both our genetic makeup and environmental factors, such as nutrition.

Food sensitivity
Food sensitivity refers mainly to the reduced ability to process or digest certain food components. We will learn if we can process compounds such as caffeine, lactose and gluten, satisfactorily.

Detoxification Capacity & Antioxidant Needs
The detoxification process, which is carried out by the liver and kidneys, may be reduced due to our genes.

Vitamin absorption
Through personalized genetic analysis we will find out what is the recommended vitamin intake for us.

Mineral metabolism
Our genes influence the way we absorb minerals. By receiving this information, we will be able to prevent potential deficiencies.

Athletic Profile
We will be informed in which sports we are genetically predisposed and in which we can achieve maximum performance.

Injury predisposition
Knowing our genetic predisposition will help us choose the right training regimen to avoid injuries.

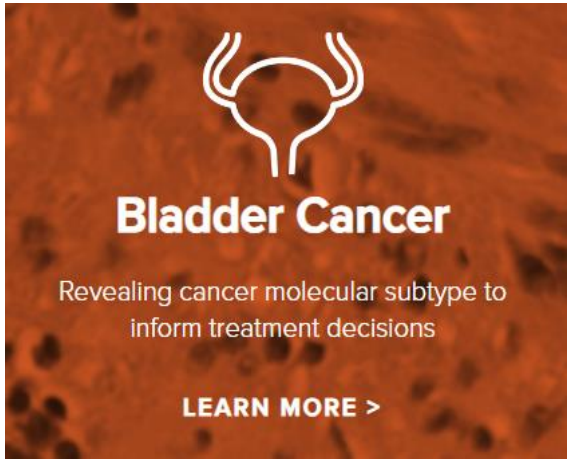
iDNA GENOMICS

Veracyte

Oncology genetics

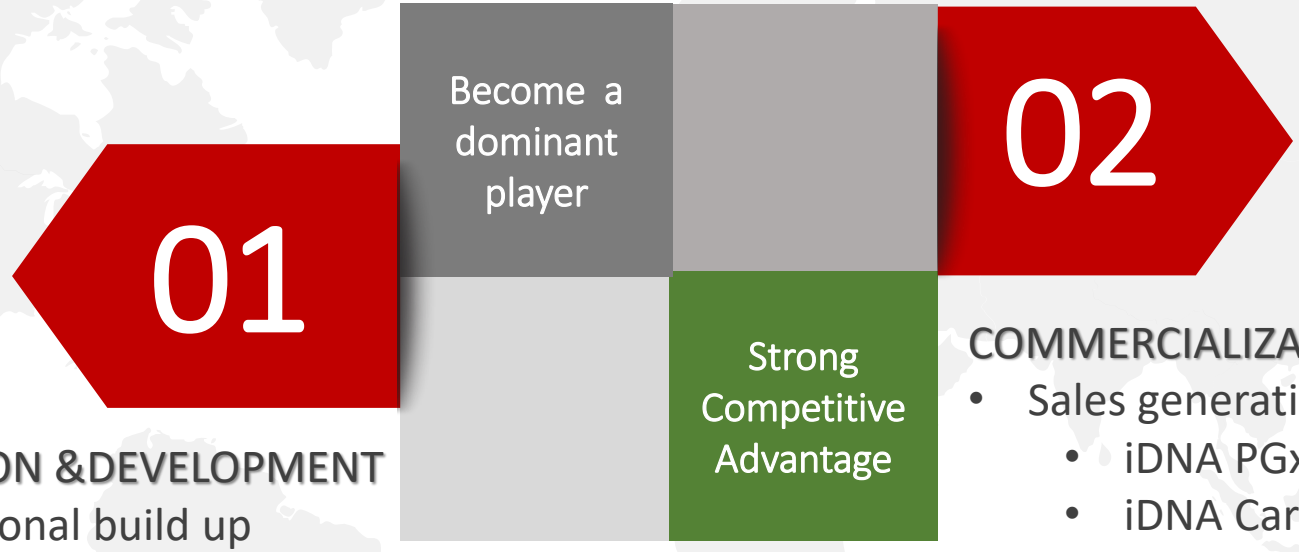
iDNA GENOMICS

- iDNA to launch the Whole portfolio of innovative genetic tests
  - Lab analysis
  - Sales promotion & demand generation
- Agreement signed
- Prosigna, for Breast Ca, will be the first launch in 2024
- Reimbursement file under adaptation for Greece to be submitted in April 2024



What is the pathway

Two phases of operational excellence



INNOVATION &DEVELOPMENT

- Operational build up
- Unique DNA tests
- Bionformatics Platform
- Certifications
- Regulatory clearance
- Proof of sales evidence

COMMERCIALIZATION

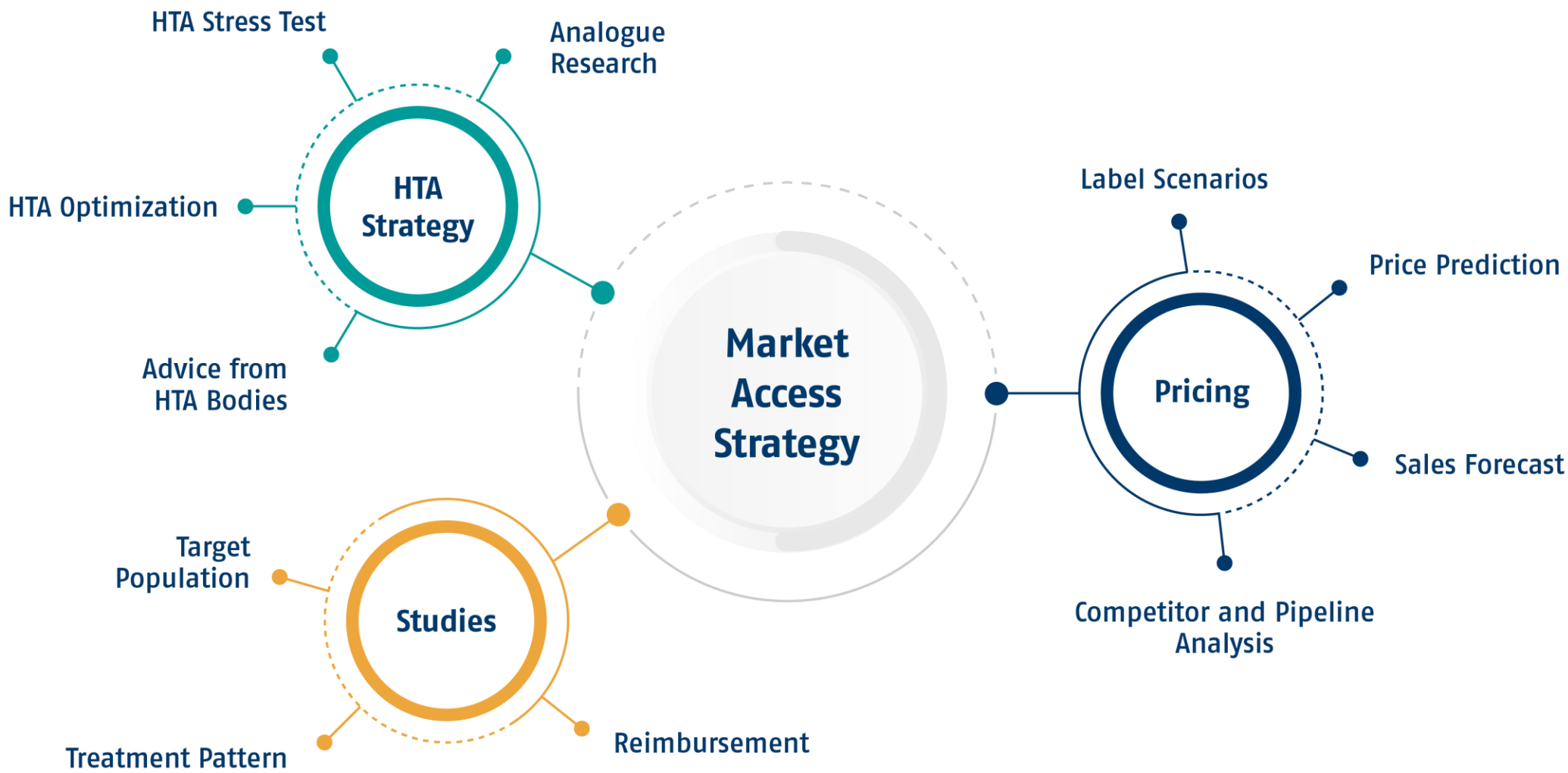
- Sales generation
  - iDNA PGx CNS : Depression
  - iDNA Cardio : CVD
  - iDNA NutriGenetix : Obesity
- Sales expansion
  - UK, Germany +
- New product development

BIANEΞ

- Ελληνική Εταιρεία
- 100 χρόνια επιχειρηματικότητας
- Εργοστάσια : 4
- Τζίρος : > 500 εκατ. Ευρώ
- Προσωπικό : >1.600 άτομα
- Προϊόντα :
  - Generics
  - Original πολυεθνικών εταιρειών
  - Food supplements φαρμακείου
- Επέκταση το εξωτερικό
- Επενδύσεις σε νέες αγορές
- Επενδύσεις σε νέα, πρωτότυπα προϊόντα στην Υγεία

100 ΧΡΟΝΙΑ
BIANEΞ Α.Ε.
ΒΙΟΜΗΧΑΝΙΑ ΦΑΡΜΑΚΩΝ
ΕΤΑΙΡΕΙΑ ΤΟΥ ΟΜΙΛΟΥ ΓΙΑΝΝΑΚΟΠΟΥΛΟΥ

iDNA GENOMICS

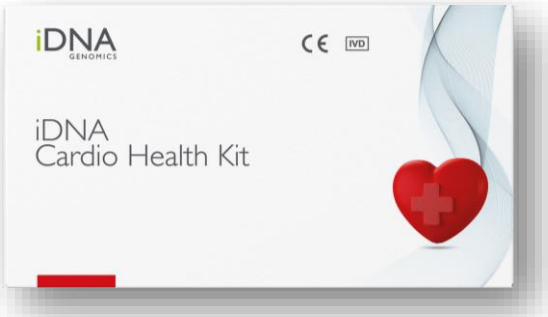

HTA Stress Test
Analogue Research
HTA Optimization
HTA Strategy
Advice from HTA Bodies
Market Access Strategy
Label Scenarios
Price Prediction
Pricing
Sales Forecast
Competitor and Pipeline Analysis
Target Population
Studies
Treatment Pattern
Reimbursement

70 Sales Reps will call 10.000 physicians

The Opportunity in Greece

Medical Genomics

- 187.000.000 €



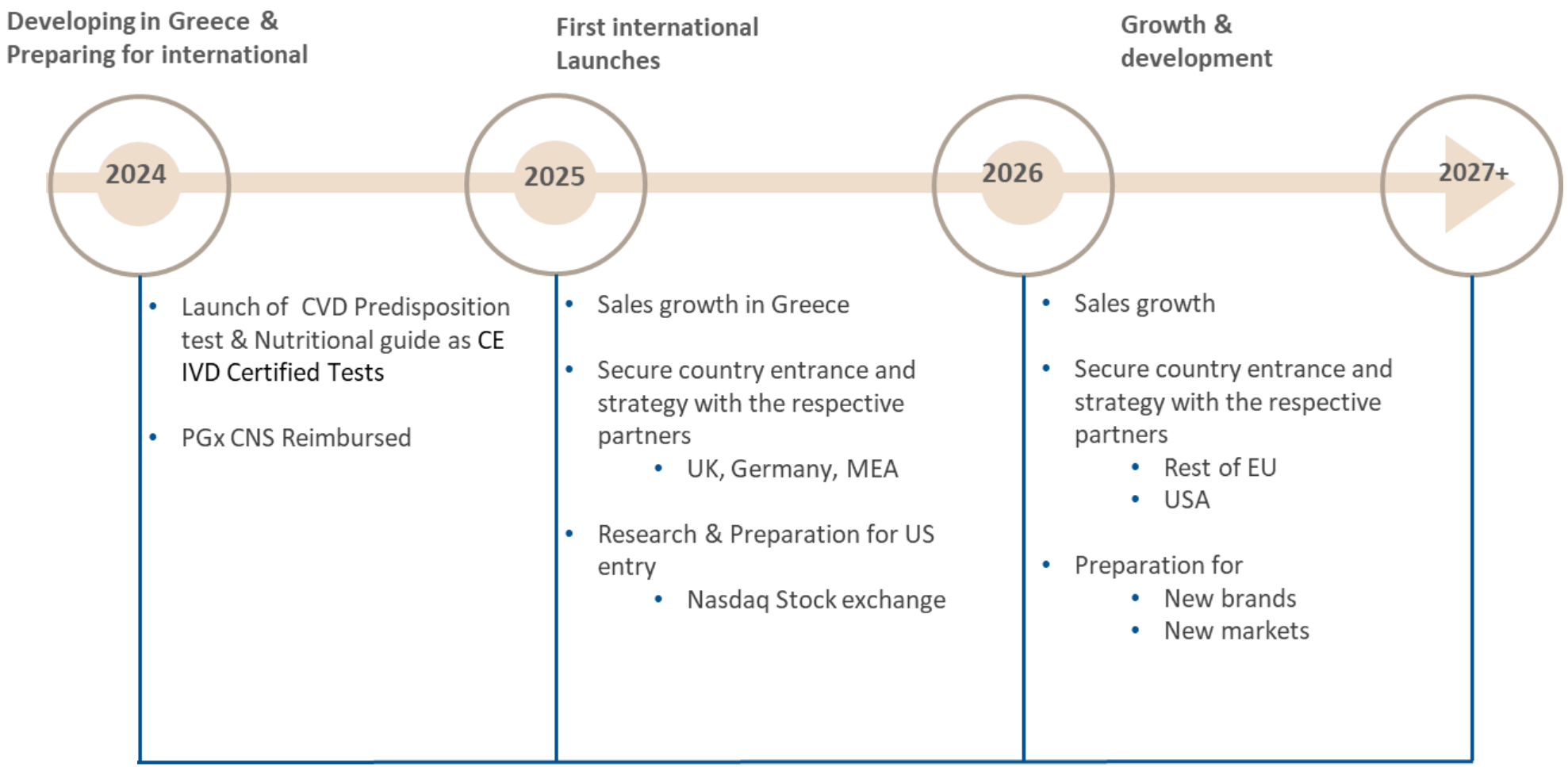
- 159.000.000 €

- 270.000.000 €

<u>> 600.000.000 €</u>

iDNA GENOMICS

Next Steps


Developing in Greece &
Preparing for international
First international
Launches
Growth &
development
2024
2025
2026
2027+
• Launch of CVD Predisposition test & Nutritional guide as CE IVD Certified Tests
• PGx CNS Reimbursed
• Sales growth in Greece
• Secure country entrance and strategy with the respective partners
• UK, Germany, MEA
• Research & Preparation for US entry
• Nasdaq Stock exchange
• Sales growth
• Secure country entrance and strategy with the respective partners
• Rest of EU
• USA
• Preparation for
• New brands
• New markets

Development and Manufacturing Costs	Low end (US Dolars)	High end (US Dolars)
Technology acquisition and protection	0.6	4
QSR and FDA compliance	1	3
GMP manufacturing	0.5	5
Platform development (buy in or make)	3	20
R&D (based on 1-3 years of FTEs at 200k/yr loaded spend)	3	8
Clinical utility trials retrospective versus prospective	1	10
Admin and financing	3	5
Subtotal costs to launch	12.1	55
Sales and Marketing Costs (US market only)		
Direct sales team (assuming required for 3 years)	3	12
Health technology assessment and payer negotiations	1	4
Clinical education (guidelines – KOL endorsement multi-stakeholder education)	2	25
Marketing (launch meetings, representative detail aids, online marketing)	2	10
Subtotal costs to drive adoption	8	51
Total costs to commercialize	20.1 M	106.0 M

The cost to bring an IVD into the market
zimmerpeacocktech.com

iDNA : Financials

	2020	2021	2022
TOTAL NTS	160.989	1.410.856	1.523.352
COGS	21.101	333.783	477.386
OTHER COSTS	11.430	17.674	46.252
TOTAL COGS	**32.531**	**351.457**	**523.638**
% COGS	**20,2%**	**24,9%**	**34,4%**
TOTAL GP	**128.457**	**1.059.399**	**999.714**
% GP	**79,8%**	**75,1%**	**65,6%**
TOTAL OVERHEAD	339.638	860.972	530.634
A&P	371.652	312.968	85.435
OPERATIONAL EXPENSES	543.924	322.942	288.387
IT SUPPORT SERVICES		268.044	229.790
R&D			
TOTAL OPEX	**1.255.214**	**1.764.925**	**1.134.246**
% OPEX	**779,7%**	**125,1%**	**74,5%**
OPERATIONAL PROFIT	**-1.126.757**	**-705.527**	**-134.532**
% OP	**-699,9%**	**-50,0%**	**-8,8%**
FINANCIAL EXPENSES	7.915	56.660	48.243
DEPRECIATION			
EBITA	**-1.134.672**	**-762.186**	**-182.774**
% EBITA	**-704,8%**	**-54,0%**	**-12,0%**

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Thank you

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