CardioVascular Precision Medicine; Hello New Era State-of-Art

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Conventional PT vs Personalized ?

Pt wt, age, gender & height

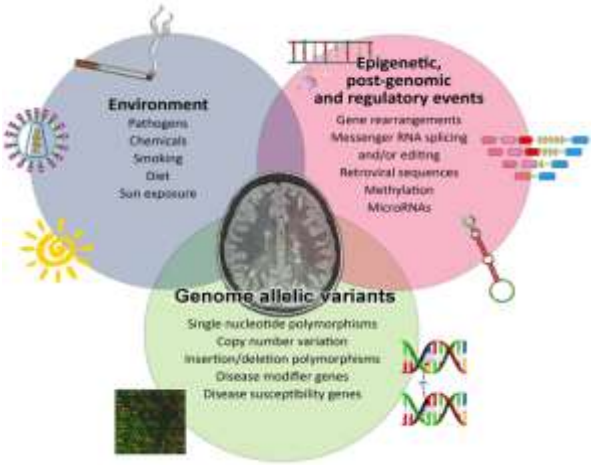
NOT "ALL People Are the SAME"

People are Different and React to Medications Differently

"Fit-For-All" treatment is Expensive

Personalized vs Precision State-of-Art ?

PGx **Precise = Exact**



(Dainis et al., 2018)

1-Trial and Error approach
2-Treatment Selection based on pt. demography, CT

www.genetests.org established, Guidelines to be issued..

Genetic Prediction In 3-4 generations

Population-Based CTs: PM

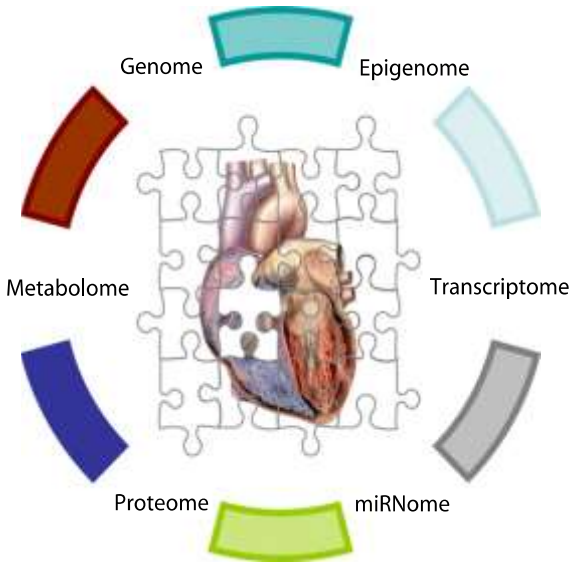
PM Catching On in Cardiology

Cardiologists focused on modifying **Environmental Factors;** smoking, obesity, lack of physical activity;

Epigenetics

Environmental modifiable risk factors identified via **large population-based registries** and achieved some reduction in CV morbidity and mortality.

Bridging CV and Genetics Clinics



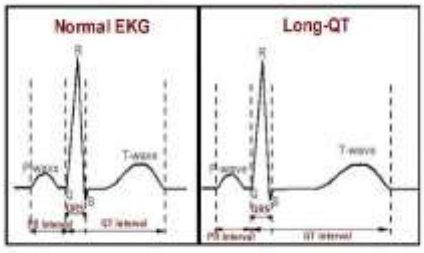
(Kassem et al., 2012)

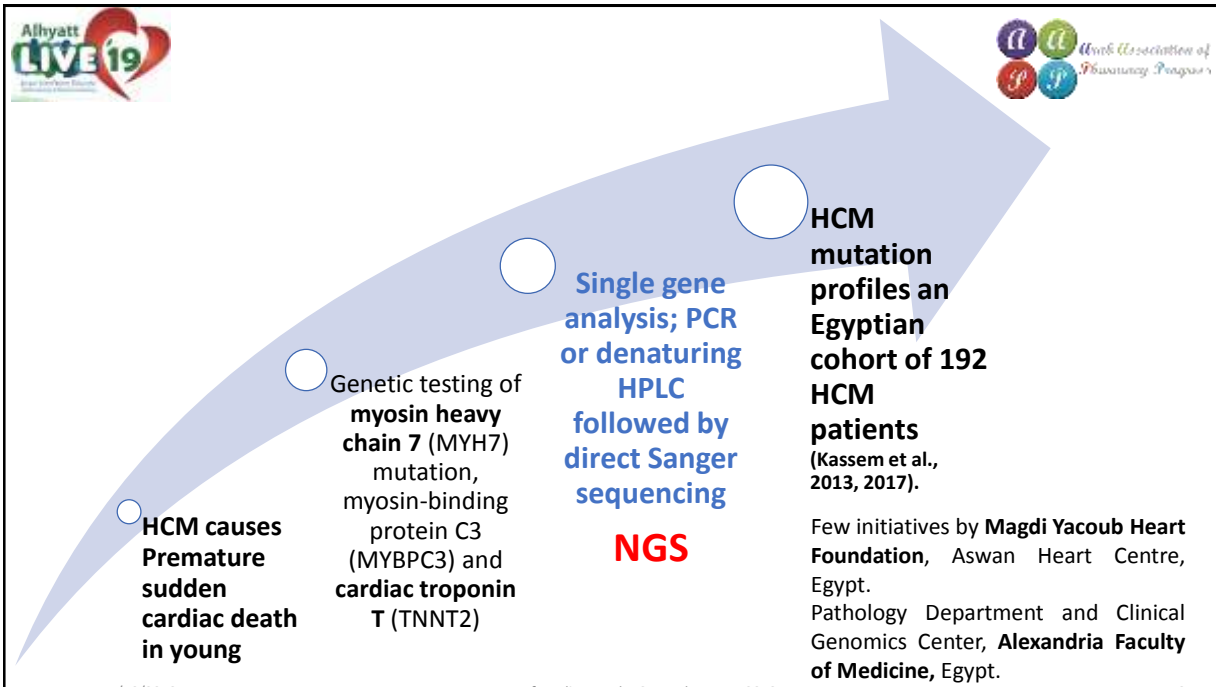
BUT..

- CVD state least to benefit from genetically guided therapy is ischemic heart disease (IHD)
- and acute coronary syndromes (ACS; MI or UA); Apolipoprotein E (apo E) plays genetic role (Mahmoud et al., 2016)
- Treatment decisions for patients with ACS must be made immediately and NO time to run a genetic test
- Individuals with angina or a previous history of AC event be genotyped so such info be utilized at the second AC event

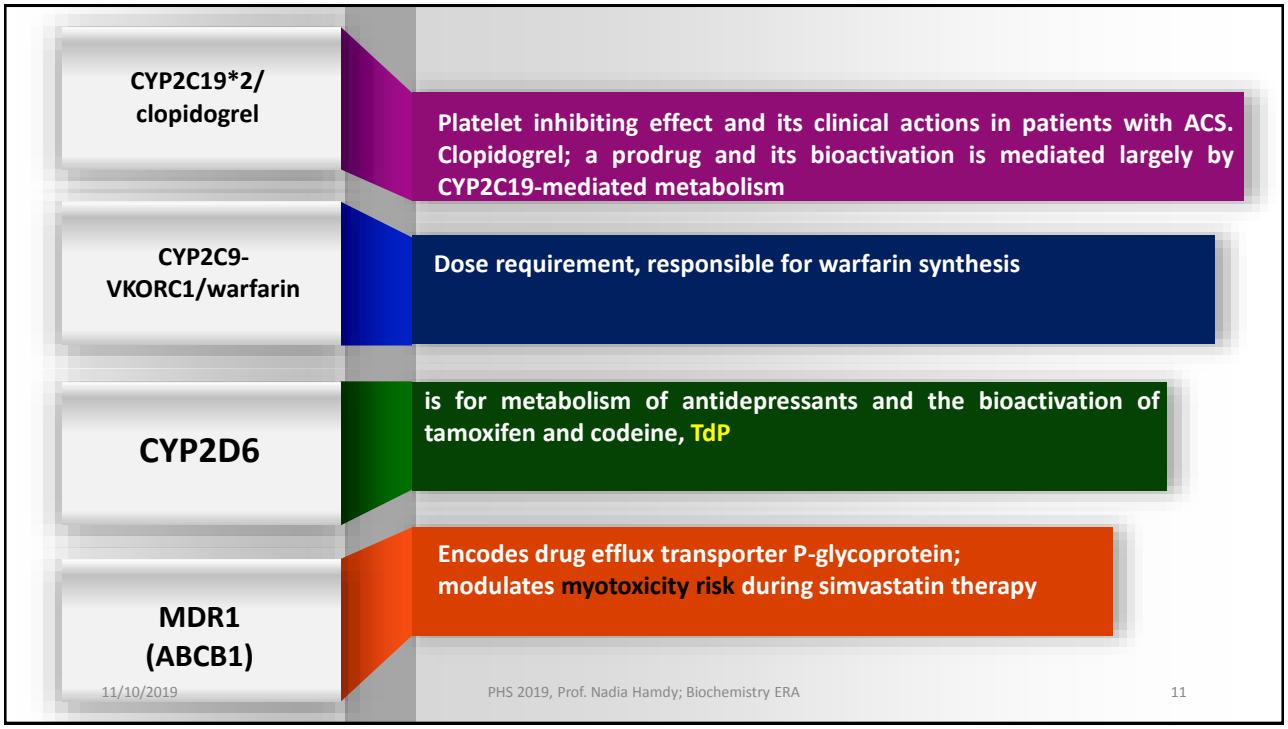
Genetic CVD

- Hypertrophic, restrictive, and dilated cardiomyopathies (HCM, RCM, DCM),
- Inherited heart rhythm disorders; LongQTs and Brugada syndromes (BrS is a heart rhythm disorder), familial hyperlipidemia
- Vascular disease in Marfan's syndrome (MFS; CT affection)





- The genetic basis for **drug-induced** **(antiarrhythmics, and quinidine, non-sedating antihistamines, macrolides antibiotics, antifungals, antimalarials, tricyclic antidepressants, neuroleptics, and prokinetics)** **Torsades de Pointes (TdP)** sudden death; a serious adverse effect of many antiarrhythmic drugs and numerous other non-CV drugs.



- Genetic test to predict those at risk for **impaired warfarin metabolism** **(reduced enzyme activity; increased bleeding risk (early in therapy), need for reduced doses of warfarin and prolonged time to a therapeutic INR or stable dose),**

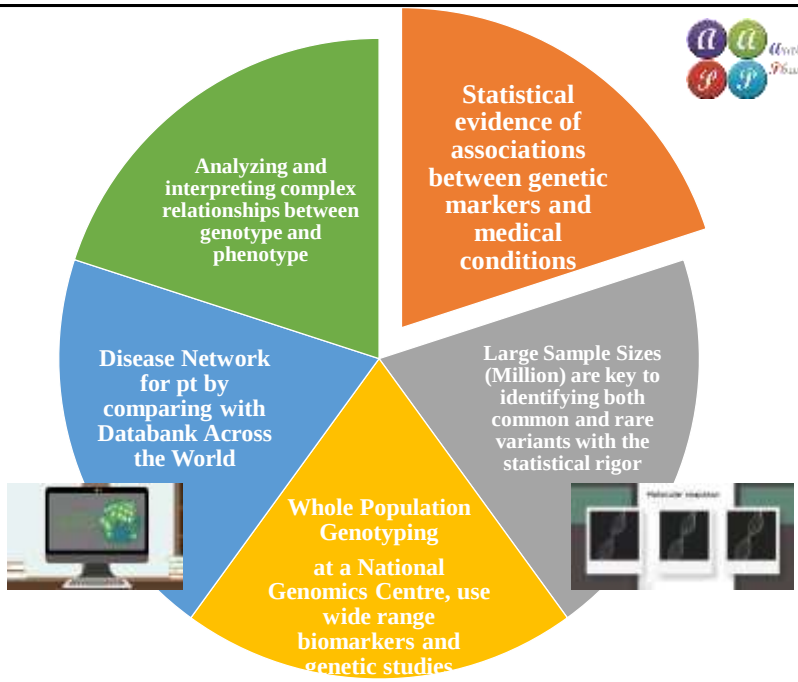
then warfarin dosing might be individualized from the outset of therapy,

as opposed to the current practice, where most patients are started on the same dose (e.g. 5 mg), with adjustments made based on the patient's INR.

- Genetic test reduce the risk of over-anticoagulation and bleeding early in the course of therapy and rapid attainment of a stable warfarin dose.

PM

IoT, Computer Algorithms & AI decrease time for translation from "Big Data" to "Clinical Setting"



6Ps PM

Pharmacogenetic

Statistical evidence of the associations between genetic markers and medical conditions

Profile

Large sample sizes are key to identifying both common and rare variants with the statistical rigor

Predictive

Enable advancements in research and clinical and direct-to-consumer applications

Predisposition

Analyzing and interpreting complex relationships between genotype and phenotype

Prognostic

1.Evidence-Based Studies
2.for reporting "Variants" and guiding treatment from CT

Whole population Genotyping at a National Genomics Centre, use wide range biomarkers and genetic studies;

Pharmacotherapeutic

IoT and AI will decrease the time required for the testing and TTT decision.

Challenges ..

1. “Role of genetic variants” in complex diseases and traits.
2. Multiple common variants throughout the genome role to rare single-gene mutations.
3. A single trait may be affected by thousands of variants.
4. Patients cannot afford to wait weeks or months to receive a treatment plan based on analysis of that data—it is critical to accelerate the genomics analytics process to produce results in less than a day.

Challenges ..

5. Affordable approach ‘It is a poor man’s sequence of the genome,’ Metspalu says. ‘It means that in Estonia, for each person who provides a sample to the biobank, we can extract their DNA and genotype it using an SNP array – all for just EUR 50. This low cost allows a large part of the population to be covered – a prerequisite for providing health benefits at the population scale.’

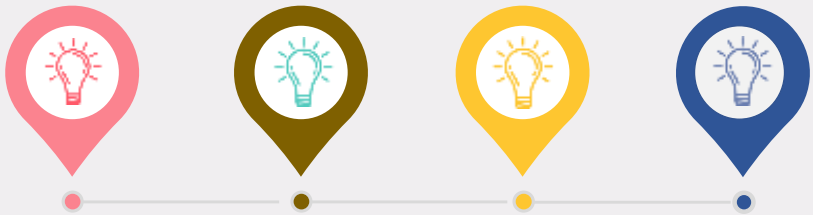
So, Where are We in 2020 ?

"The Book of You"

- Dive into your DNA; DNA microarray, SNP & NGS,
- Revile any disease, carrier state, genetic abnormality and family planning;

1. Bookinghealth.com
2. https://www.hassanhealth.com/diseases
3. https://dnacenter.com/egypt/
4. https://www.nsa-lab.com/
   - Pharmacogenomics Knowledgebase (PharmGKB) markers,
   - Genotyping Biobanks,
   - thermoFisher.com Scientific,
   - TissueGnostics.com
   - Applied Biosystems™ Axiom™ arrays.

What is The Plan?



Genotyping data & personal risk scores stored in biobank database

Guidelines to be issued..

PM program "the All of Us" Research Program 1 million Egyptians Considering diversity in race/ethnicity

Clinical CV genetics = Cardiologists + Geneticists + Genetic Counsellors expedite the 'bench-side-to-bed-side' translation

What's Next?

Personalized Prevention; Preventive Precision

- Create **gene maps** of individuals in order to calculate their **genetic risk** of developing conditions such as heart disease, diabetes or cancer.

- The approach, which can be scaled affordably to the population level, will enable people to **adopt lifestyle changes** and take preventive action to protect their health.

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Thank You!