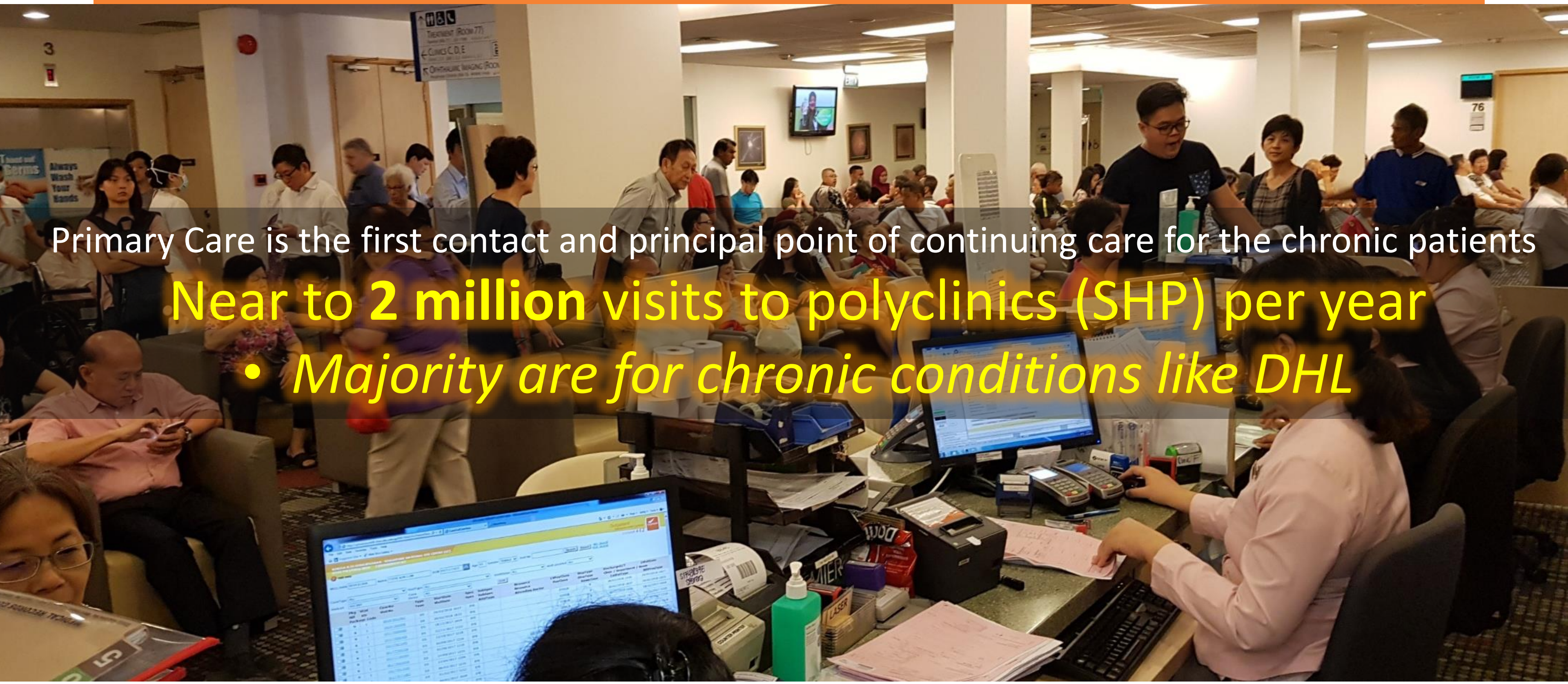
FM ACP RESEARCH GRAND ROUND

JARVIS$_{DHL}$
AI for Transforming Chronic Care

See-Kiong Ng, National University of Singapore

Growing Prevalence of DHL



Primary Care is the first contact and principal point of continuing care for the chronic patients

Near to **2 million** visits to polyclinics (SHP) per year

- *Majority are for chronic conditions like DHL*

Stroke → Handicapped

Kidney failure → Dialysis

Diabetic eye disease → blindness

Vascular disease → amputation

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AI in Health Grand Challenge

"How can Artificial Intelligence (AI) help primary care teams stop or slow disease progression and complication development in DHL patients by 20% in 5 years?"

AI SINGAPORE

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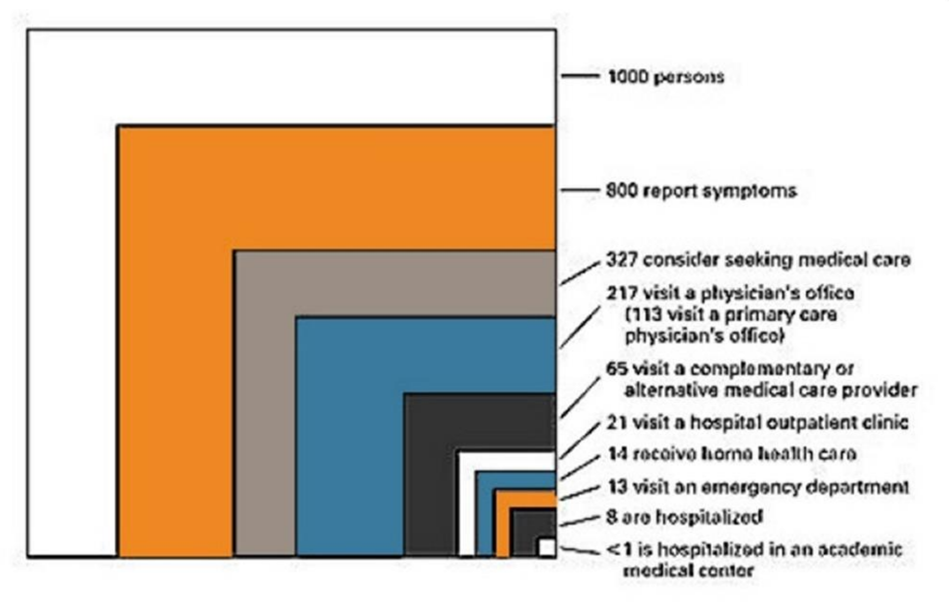
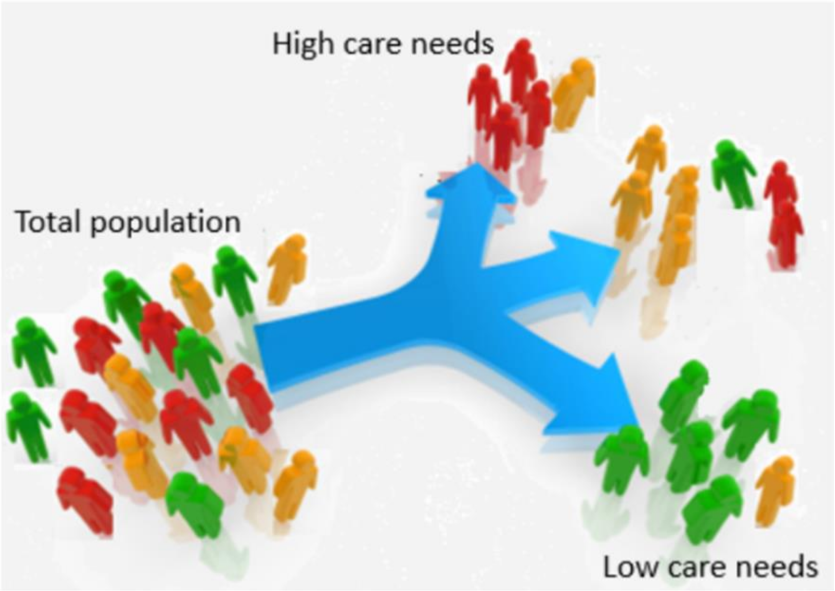
AI-enabled Chronic Care – The 3 `P's

1. Reactive care to Predictive care



Source: Robert Graham Center – The Contemporary Ecology of US Medical Care

Classification task
to identify at-risk patients



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AI-enabled Chronic Care – The 3 `P's

2. One-size-fits-all to Personalized care

CHRONIC CARE ALGORITHMS

DIABETES MELLITUS (DM): DM Medications *(available in SHP)*

DM DRUGS and INSULINS (Guide to prescription)

ORAL HYPOGLYCAEMIC AGENTS

Biguanides
Decreases hepatic glucose production, decrease carbohydrate absorption in the gut, and increase central and peripheral insulin sensitivity

Generic Name	*Brand Name*	*Doses (min-max)*	*Prescribing notes/ caution*
Metformin HCL	Glucophage, generic Metformin	500-3000 mg/day	• Avoid in patients with low GFR and raised creatinine • May cause metallic sensation in the mouth and reduce appetite • Useful for obese patient • Recommended as first line monotherapy in most Type 2 DM patients

Sulphonylureas
Stimulate increased insulin production

Generic Name	*Brand Name*	*Doses (min/max)*	*Prescribing notes/ caution*
Gliclazide	Diamicron	80-320mg/day	
Glimepiride	Amaryl	1-8mg/day	
Glipizide	Glucotrol	2.5-40mg/day	15 mg bd optimal for most cases
Glibenclamide	Diabeta, Glynase, Micronase	1.25-20mg/day	Long acting. Avoid in those > 60yo, CKD, Muslims (Ramadan)
Tolazamide	Tolinase	100-250mg/day	
Tolbutamide	Orinase	1000-3000mg/day	• Recommended in the elderly, less risk of hypoglycaemia

Meglitinides
Stimulate increased insulin production of short duration

Generic Name	*Brand Name*	*Doses (min/max)*	*Prescribing notes/ caution*
Replaglinide	Prandin	0.5-4mg 3x/day	• Side effects: Hypoglycemia, weight gain, hyperinsulinemia • Caution: Use with caution with chronic liver disease
Nateglinide	Starlix	60-120mg 3x/day	

Combo Orals/ Miscellaneous
Attempt to provide "convenience" of two drugs in one pill

Generic Name	*Brand Name*	*Doses (min/max)*	*Prescribing notes/ caution*
Avandia + Metformin	Avandamet	500 - 4/2000-8	
Metformin + Glyburide	Glucovance/Avandaryl	250-1.25/2000-20	
Metformin + Glipizide	Metaglip	250-2.5/2000-20	
Amylin	Symlin	15ug-120ug	
Extenatide	Byetta	5ug-10ug	

DPP-4 Inhibitors
Blocks dipeptidyl peptidase 4 enzyme which breaks down gut hormones called incretins. Results in prolonged action of latter, which stimulates insulin and inhibits glucagon in a glucose-dependent way.

Generic Name	*Brand Name*	*Doses (min/max)*	*Prescribing notes/ caution*
Sitagliptin	Januvia	100 mg OM (if creatinine clearance > 50 ml/min) 50 mg OM (Cr Cl 30-50 ml/min) 25 mg OM (Cr Cl <30 ml/min)	Costly.

Thiozolidinediones (Contraindicated when at high risk or with cardiovascular events or peripheral vascular diseases). Generally not used in SHP
Increase central and peripheral insulin sensitivity

Generic Name	*Brand Name*	*Doses (min/max)*	*Prescribing notes/ caution*
Pioglitizone	Actos	15-45mg/day	• Side effects: Weight gain, edema, CHF, bone fractures (pioglitazone, rosiglitazone) Myocardial ischemic events (rosiglitazone) • Caution: Contraindicated in severe liver disease, congestive heart failure, • Need to monitor liver enzymes • Associated with bladder cancer
Rosiglitizone	Avandia	4-8mg/day	• Contraindicated in those with previous MI

Alpha Glucosidase Inhibitors
Interferes with carbohydrate absorption in the gut

Generic Name	*Brand Name*	*Doses (min/max)*	*Prescribing notes/ caution*
Acarbose	Precose	50-100mg 3x/day	• Side-effects: GI effects (flatulence, diarrhea) • Caution: Not recommended in severe renal impairment, check serum liver enzymes
Miglitol	Glyset	25-100mg 3x/day	

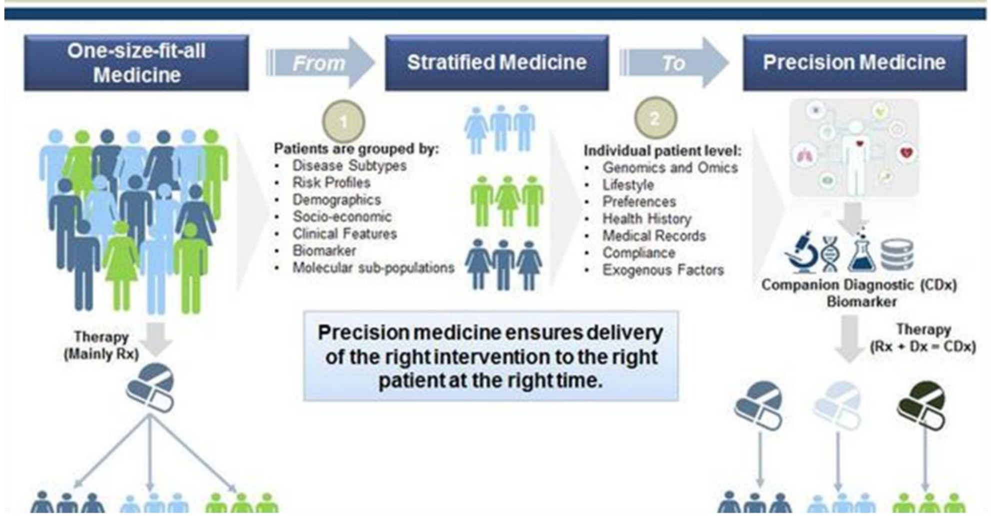
INSULIN PREPARATIONS

Insulins
Injected to replace or supplement natural insulin

	Generic Name	*Brand Name*	*Mode of action*	*Prescribing notes/ caution*
Analogs	insulin aspart	Novolog, NovoRapid	Very fast	Hypoglycemia, weight gain for all insulin
Analogs	insulin lispro	Humalog	Very fast	
Analogs	insulin glulisine	Apidra	Very fast	
Analogs	insulin glargine	Lantus	Very slow	Pen
Analogs	insulin detemir	Levemir	Very slow	Pen
Pre-mixes	Mixtard	70/30, 50/50, 75/25	fast and intermediate	Penfill or vial
Pre-mixes	Novomix	70/30	fast and intermediate	Pen
Human recombinant insulins (rDNA)	Insulin	Humulin		
Human recombinant insulins (rDNA)		Regular, Actrapid	Fast	Vial
Human recombinant insulins (rDNA)		NPH(N), Insultard	Intermediate	Vial

Optimization task

Look for best effectiveness for least chance of side effect based on each patient's profile



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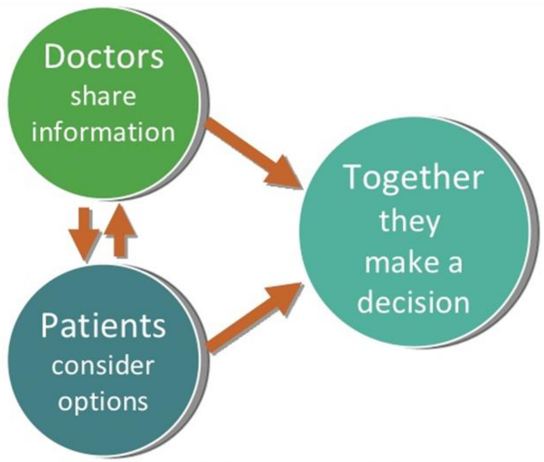
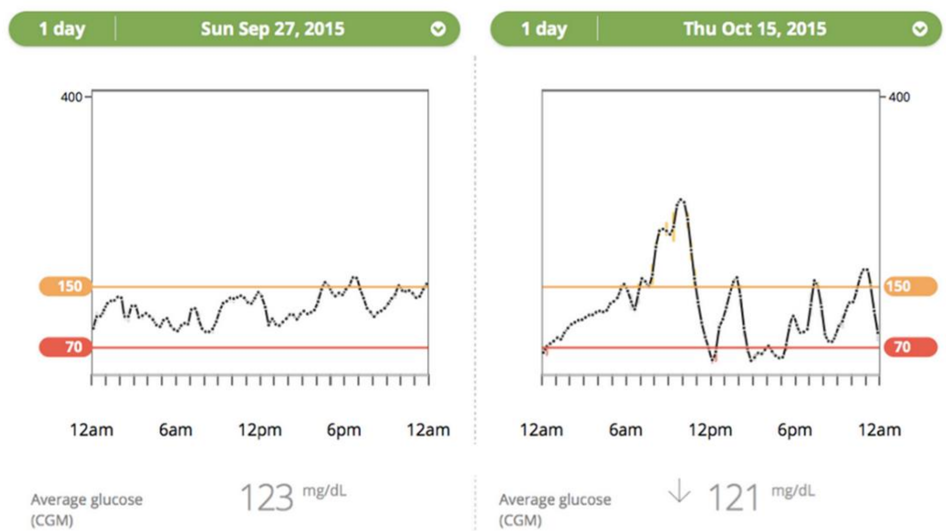
AI-enabled Chronic Care – The 3 `P’s

3. Passive to EmPowered patients



Shared-decision making
→ ownership for health decisions and own health outcomes
→ Motivation to comply with treatment



Motivation to participate in **self-monitoring and self-care** (e.g. self-monitoring of blood glucose)

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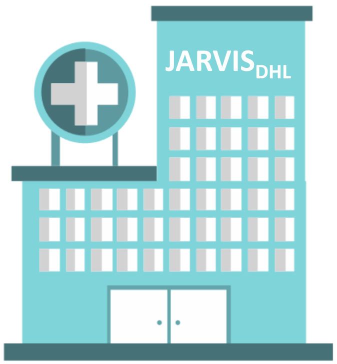
JARVIS$_{DHL}$ Objective

1.

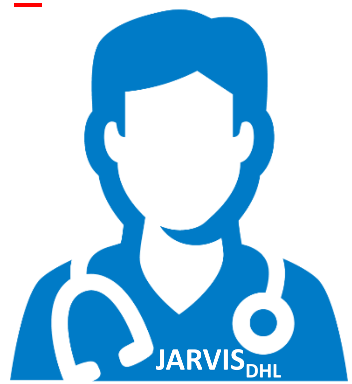
From reactive care to Predictive care



primary care delivery **efficiency**

2.

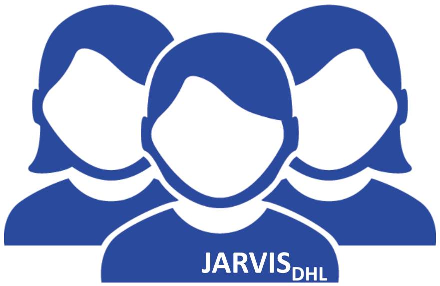
From "one-size-fit-all" to Personalized care



local-relevant treatment **effectiveness**

3.

From passive to emPowered patients



patient **engagement**

JARVIS$_{DHL}$

1.
Predictive stratification for right-siting of at-risk individuals.

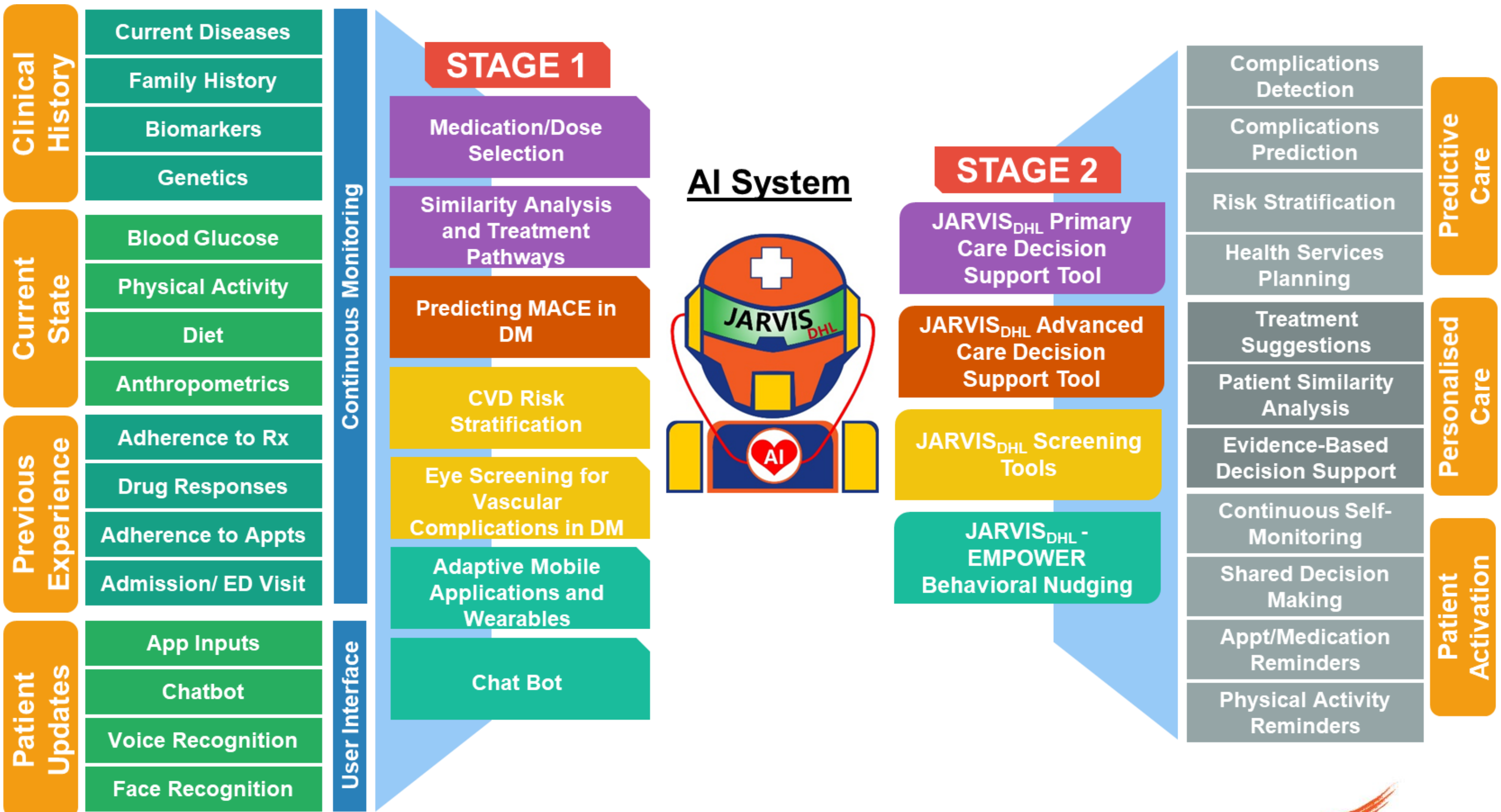
JARVIS$_{DHL}$

2.
Individually tailored **treatment options** for <u>local</u> patients.

JARVIS$_{DHL}$

3.
360◦ knowledge about patient with **clinical + patient reported data**.

JARVIS$_{DHL}$ (“Just” A Rather Very Intelligent System)



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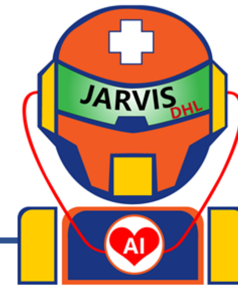
Data-driven AI

- **Continuously learn from local primary care DATA** to provide <u>individualized evidence-based decision support</u> to physicians to facilitate <u>shared-decision making (SDM)</u> with patients

- **Harvest next-generation healthcare and lifestyle tracking DATA** to include behavior and lifestyle data for <u>360-degree 24/7 view</u> of the patient



AI algorithms that are efficient, robust, and explainable to

- ***quantify*** benefits of treatment and risk of complications
- ***adapt*** customized treatment regimen according to lifestyle
- ***alleviate*** patient anxiety over perceived side effects
- ***support*** robust clinical decision-making
- ***recommend*** evidence-based treatment options

AI for Chronic Care: Considerations

1. Efficiency

- Deep neural architecture with small footprint and high accuracy

2. Robustness

- Robust learning with self-regularization and non-linear kernels

3. Complexity

- Multi-objective learners for understanding complex interactions

4. Explainability

- Automatic generation of explanations based on machine learning and database techniques

5. Causality

- Inference of models from clinical and lifelog data

Stage 1: Research Findings

Predicting high risk pts for DM complications	• Developed RNN-Survival based on Temporal Point Process Model to identify diabetes patients who are at-risk of MACE complications in 1, 2, 5 years. • Measure the risk of both new and repeated MACE events and predict the next event time. • Validated on Singhealth Diabetes Registry (SDR) Data. • Out-performs state-of-the-art model in terms of c-index for MACE complications in SDR and MIMIC-III dataset. • Dashboard for prediction of diabetes complication is done and demonstrated. • Next: Extend prediction to Kidney, eye and foot complications
Patient similarity analytics for shared decision making	• Designed and developed machine learning method to infer the distance metric for the identification of similar patients for shared decision making. • Initial results have shown a substantial agreement of 0.707 between the learned distance metric and 2 physicians
Personalized treatment effectiveness for local population	Local data on statin treatment effectiveness based on real-world data varies from what is known from trial-based studies mostly conducted on Caucasian populations. (e.g. trial-based = statin initiation lowers LDL by 30-60%- ours was 20-30%, trial-based = doubling statin dose lowers LDL by about 6%, we found that uptitration lowered LDL by 12-24%) Next: To work on diabetic and hypertension medications.
Predicting CVD risk	Low cost CVD screening tool reduce unnecessary clinical tests and cardiac stress imaging for CVD risk stratification. [(questionnaire surveys variables, 24hours vitals monitoring, clinical blood investigation and data from wearable device)]
Diabetic screening using SIVA-DLS for automated measurement of retinal vessel calibers from retinal images	High agreement of between 082 to 0.95. SIVA-DLS found to have association with CVD risk factors, incident CVD and with mortality. Next: Linking of SIVA-DLS data with Diabetes main registry to prediction of macro and micro vascular complications

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JARVIS$_{DHL}$ Timeline

01 — **2021**

Fine-tuning of models and pilot interfaces for deployment

- Models/algorithms validated and improved
- Design of interventions finalized based on each tool
- Study protocols finalized for each theme

02 — **2022-24**

Multi-site, adaptive, multi-modality, real-world, hybrid, implementation trial

- Deployment of tools in implementation trial
- Refinement of models, tools, platform etc.

03 — **2023-24**

Evaluation of process, clinical and patient reported outcomes

- Evaluate outcomes
- Prepare for manuscripts
- Prepare for wider deployment and implementation at a health systems level.

JARVIS$_{DHL}$ AI Tools

JARVIS$_{DHL}$ Primary Care Decision Support Tool

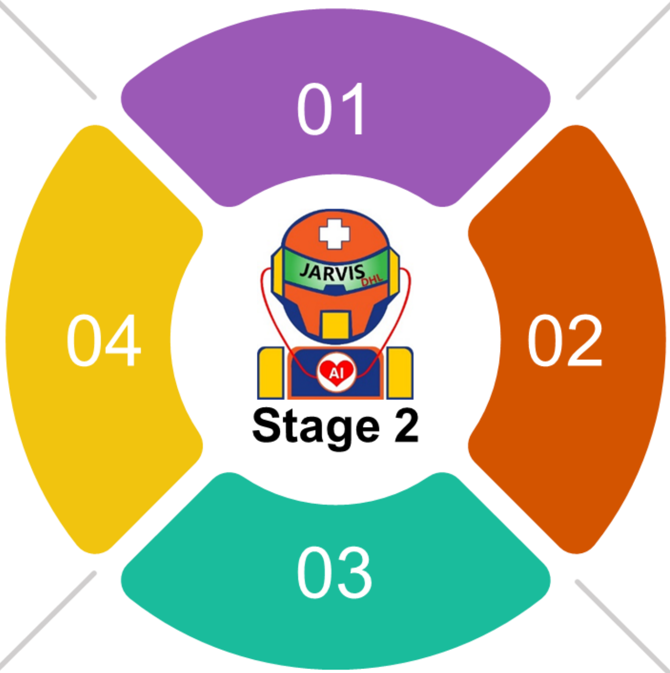
Shared decision tool on Medication Effectiveness and DHL prognostication for low risk patient

- Medication/Dose Selection
- Similarity Analysis and Treatment Pathways

JARVIS$_{DHL}$ Advanced Care Decision Support Tool

Shared decision tool on developing MACE in 5 years for high risk patient

- Predicting MACE in DM



JARVIS$_{DHL}$ Screening Tools

Self-administrating CVD Stratification Tool and Predicting vascular complications and coronary artery calcium score (retina-CAC) from retinal images.

- CVD Risk Stratification
- Eye Screening for Vascular Complications in DM

JARVIS$_{DHL}$-EMPOWER Behavioral Nudging

Semi-automated Shared decision tool that decides and delivers personalized behavioral cues and nudges based on patients' risk profiles and tracked wearables

- Adaptive Mobile Applications and Wearables
- Chat Bot

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TO SAVE SOME TIME
LET'S JUST ASSUME
I'M ALWAYS RIGHT

DATA


MULTIVARIATE
BIOSTATISTICS
DATA
LARGE
WATCH
MEDICINE
SUPPLY
CROSS
INTIMATE
TRIALS
REGISTER
ALGEBRA
MODELS
MATHEMATICAL
MONTE
LOGIN
CARLO
TIME
LINEAR
ANALYSIS
LOGIC
FIFTY
QUALITY
MODERN
CRITICAL
RD
STATISTICS
APRIL
PANEL
GUIDE
DESIGN
FUNDAMENTALS
APPLICATIONS
RISK
GOULD
SYSTEMS
TESTING
TOOLS
HEALTH
ADVANCES
SOCIETY
PROBABILISTIC
METHODS
PEARL
MIXED
RESEARCH
CLINICAL
INDUSTRIAL
ASSESSMENTS
DYNAMICS
REVIEW
EVALUATION
PRODUCTION
EVENTS
SCIENCE
REGRESSION
SIMULATION
AI
Machine Learning
SOCIAL
EXPLORATIONS
ISSUES
RANDOM
BUSINESS
CAUSALITY
UNDERSTANDING
ANALYTICS
THEORY
NETWORKS
SERIES
MINING
PROCESSES
PHARMACEUTICAL
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ALGORITHMS
ENGINEERING
COMPUTATIONAL
MANAGEMENT
GRAPHS
DIFFERENCE EPIDEMIOLOGY

ACTION

Laypersons' Assumptions

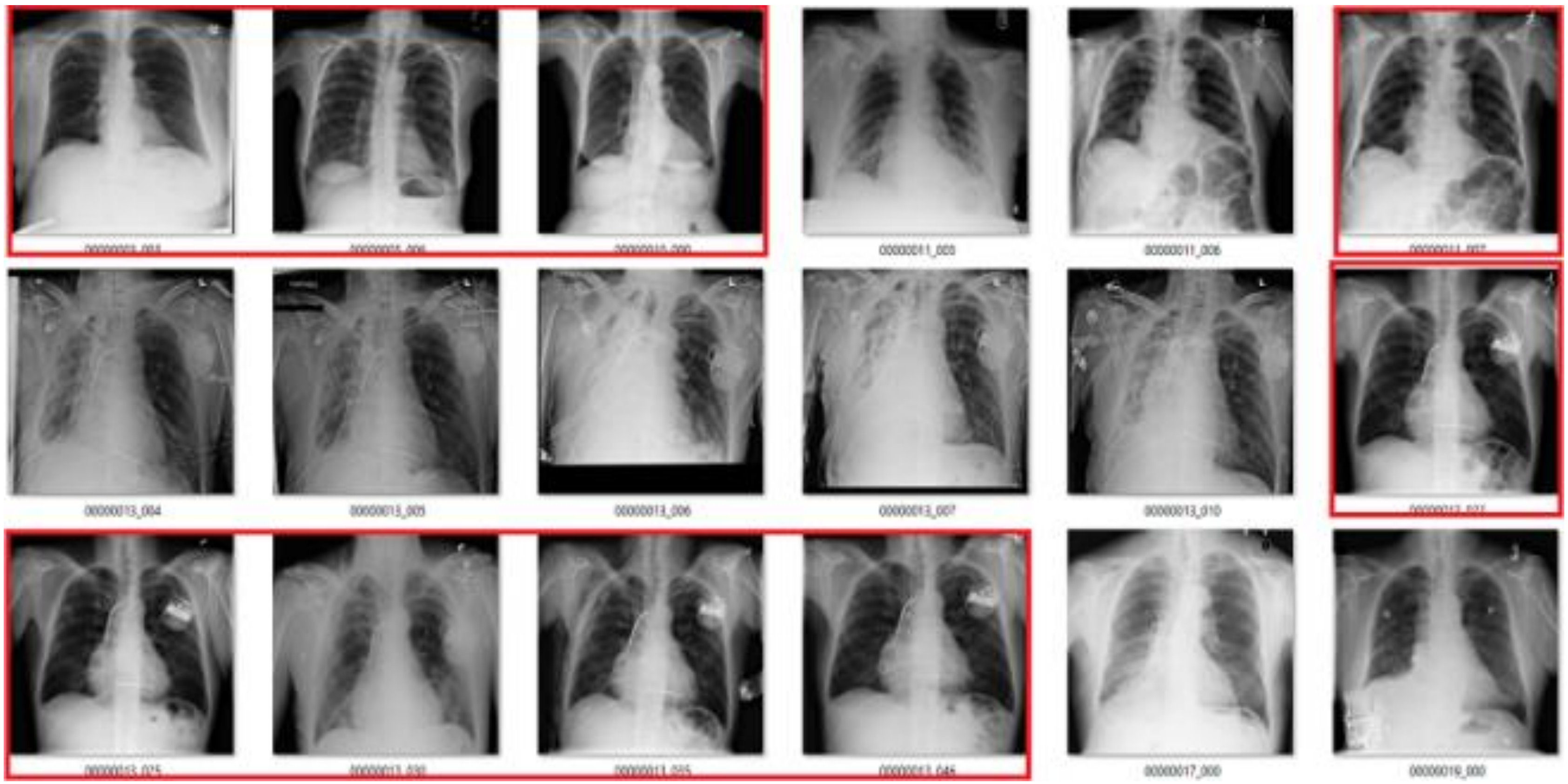
The Data is Always Right

The Computer is Always Right

↓

The Action is Always Right

AI Accuracy: *What You Teach is What You Get*



“Exploring the ChestXRay14 Dataset: Problems”
https://lukeoakdenrayner.wordpress.com/2017/12/18/the-chestxray14-dataset-problems

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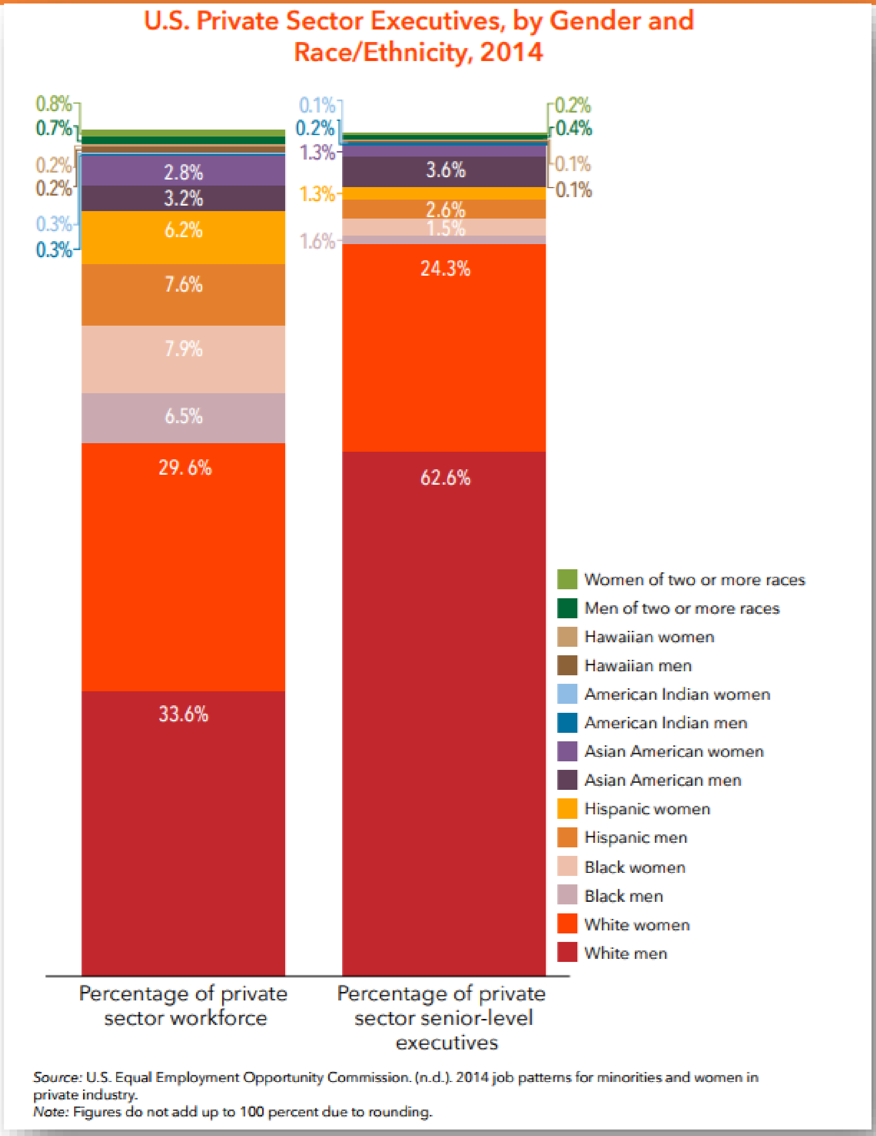
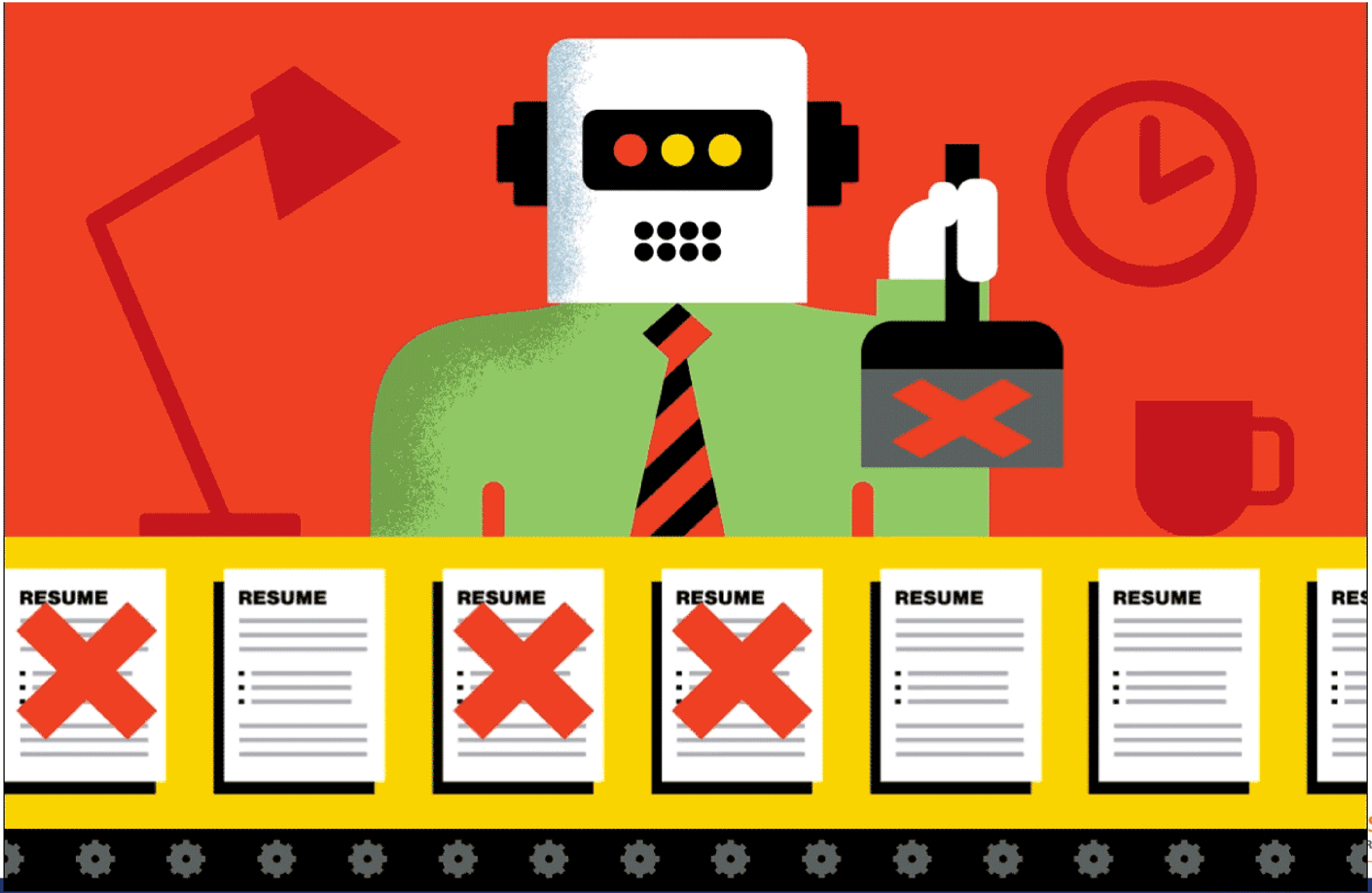
AI Ethics: *Bias begets Bias (algorithmically!)*



"Barriers and Bias:
The Status of Women in Leadership"
(2016)

Automated Propagation

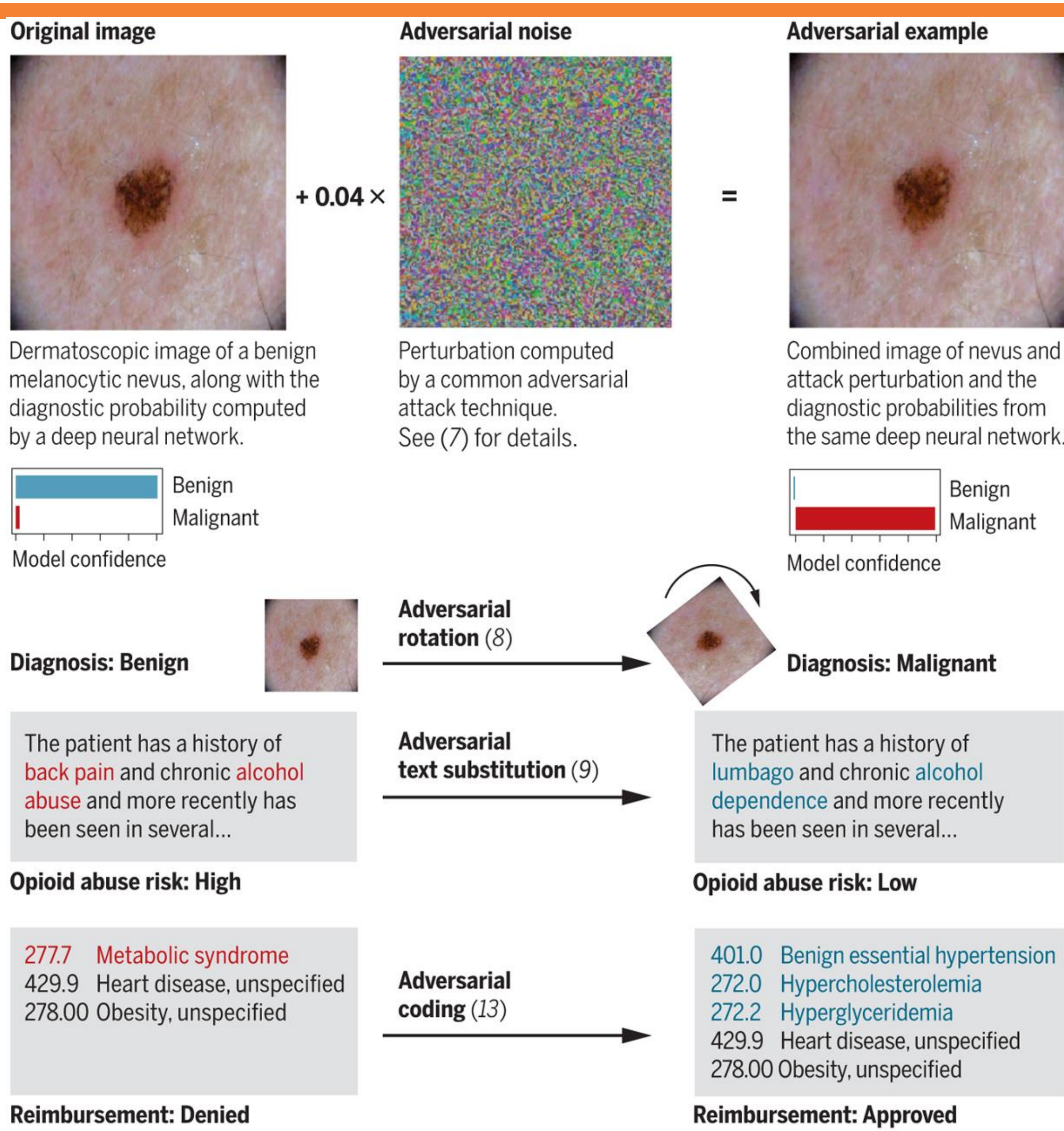


AI Security: *It's not as smart as you'd think!*

Camouflage graffiti and art stickers cause a neural network to misclassify stop signs as speed limit 45 signs or yield signs

"Robust Physical-World Attacks on Deep Learning Models" Evtimov et al (2017)

AI Security: *It's not as smart as you'd think!*



Adversarial attacks on medical machine learning

BY SAMUEL G. FINLAYSON, JOHN D. BOWERS, JOICHI ITO, JONATHAN L. ZITTRAIN, ANDREW L. BEAM, ISAAC S. KOHANE

*SCIENCE*22 MAR 2019 : 1287-128

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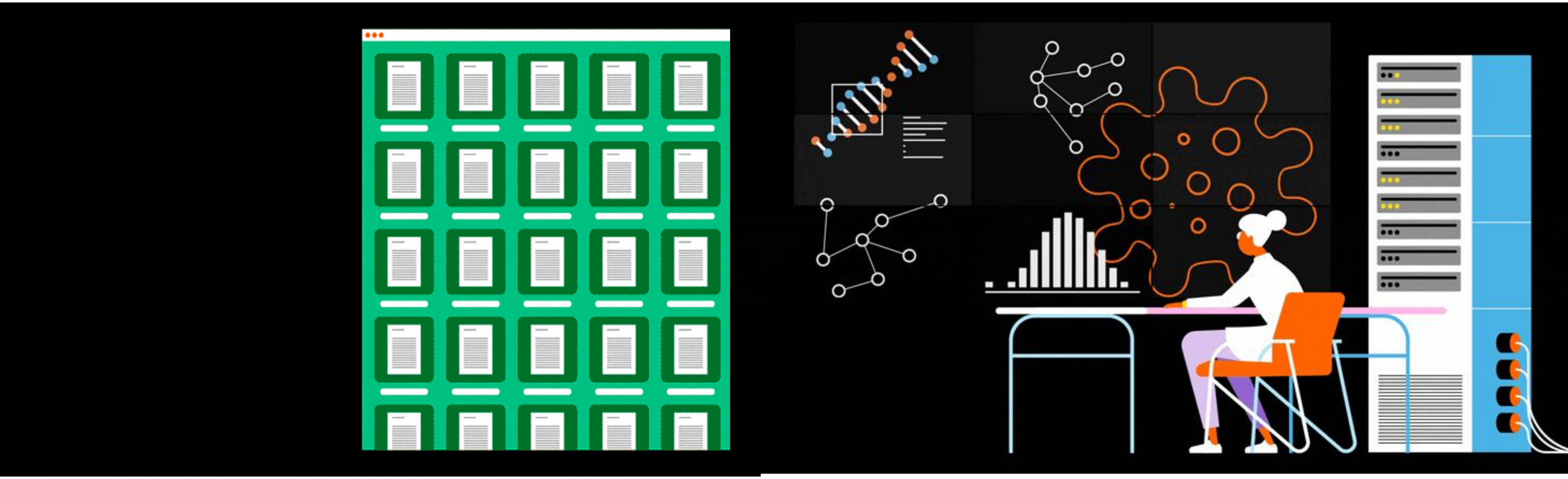
SUCCESS

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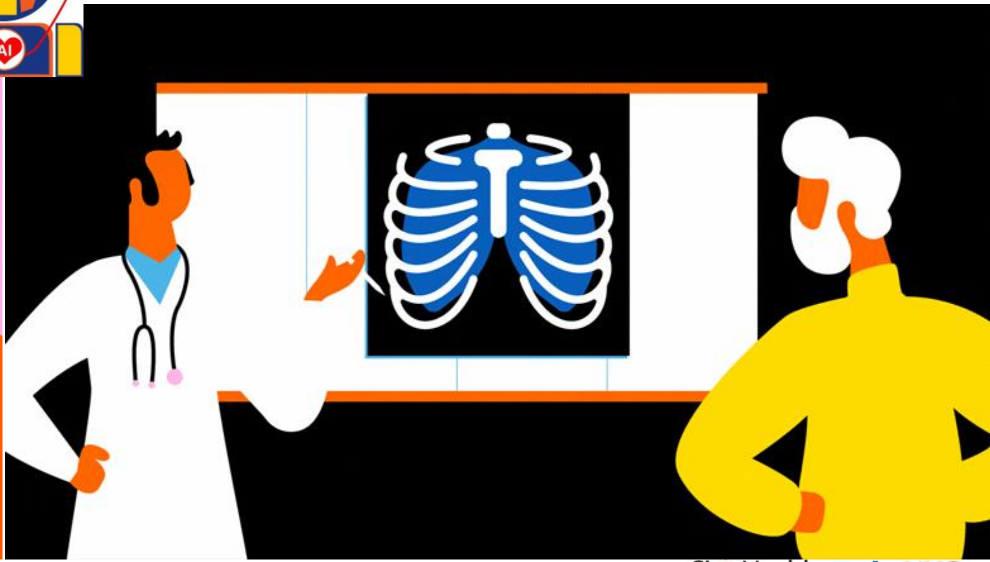


JARVIS$_{DHL}$ Team

Collaboration between:

NUS National University of Singapore — Institute of Data Science

NUS National University of Singapore — School of Computing

SingHealth

DukeNUS Medical School

NUS


Wynne Hsu (Main PI)


See-Kiong Ng


Mong Li Lee


Chee Yong Chan


Hock Hai Teo

SingHealth

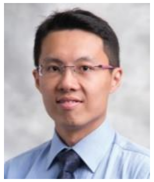

Marcus Ong


Ngiap Chuan Tan


Tien-Yin Wong


Amanda Lam


Khung Keong Yeo


Lian Leng Low

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THANK YOU