Artificial Intelligence and the Future of Pharmacy:

Separating Myths from Facts

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Relevant Financial Relationship Disclosures

- Scott Nelson has served on an advisory board for:
 - Merative Micromedex
 - Baxter Healthcare Corporation
- All relevant financial relationships have been mitigated.

Learning Objectives



At the completion of this activity, learners will be able to:

- 1. Describe potential uses for artificial intelligence in pharmacy practice.
- 2. Compare approaches for training machine learning models.
- 3. Assess challenges and limitations of artificial intelligence in clinical practice.



Predicting the future of healthcare





ASHP Foundation Pharmacy Forecast 2024

Health systems will embrace a "**digital-first**" approach to patient encounters (e.g., video primary care visits, telehealth, and remote patient monitoring) which will make patient access to virtual care universal.

4% 27	7%	46%		23%
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Accelerating adoption of an advanced technologies (e.g, remote patient monitoring, artificial intelligence, data integration) will **close the gap on health care disparities**.

7%	41%	42%	10%
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Health system ethics committees will have expertise that ensures the **equitable application of artificial intelligence technology when used in patient care**.



ASHP Foundation Pharmacy Forecast 2024

Integration of electronic health record data with clinical decision support algorithms will automate drug dosing adjustments (e.g., renal, weight-based, age-based dosing)

2%	12%	51%	35%
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State boards of pharmacy will develop regulations allowing the use of artificial intelligence or other technology in place of pharmacist order review and verification.

	23%		3%	31%	31%	
	Very U	Jnlikely Some	ewhat Unlikely	Somwhat Likely	Very Likely	,
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Am J Health Syst Pharm. 2024;81(2):5-36. doi: 10.1093/ajhp/zxad231. PMID: 38048298



What is "digital health"?

- An **umbrella term** for **applying** information and technology in healthcare to make a tangible difference in patient health
- Examples:
 - Wearable devices
 - Mobile health (mHealth)
 - Telehealth
 - Remote patient monitoring
 - Application of Al

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• Etc...

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DALL-E 3

Human cognitive capacity is 7 ± 2



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Psychol Rev. 1956;63(2):81-97. PMID:13310704

Al = <u>Augmented</u> Intelligence



Fundamental Theorem of Informatics

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Am. Med. Inform. Assoc. 2009;16(2):169-170. PMID:19074294

What is AI?

- Artificial intelligence describes a computer system's ability to perform a task that would normally require human cognition.
 - Perception, language processing, learning, planning, problem solving, etc.

- General vs Narrow Al
 - General AI is still a far-off reality
 - Narrow Al
 - Can do one well-defined task, but that's it



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Artificial Intelligence (AI)

The theory and development of computer systems to perform tasks that normally would require human cognition.

Machine Learning (ML)

A mathematical approach to learning the unknown rules that govern a particular phenomenon by analyzing many examples of it happening.

Neural Networks (NN)

Machine learning models inspired by nervous system architecture, in which complex mathematical rules are learned by composing many simple patterns.

Deep Learning (DL)

Neural Network models in which the composition of simple patterns occurs in greater depth, allowing for very complex rules to be learned.

Generative Al

Generative pre-trained transformers (GPT) for generating new content

Basic AI (expert systems)

RX High (1)

You are receiving this alert because you are verifying an angiotensin-converting enzyme inhibitor (ACE-I) or an angiotensin receptor neprilysin inhibitor (ARN-I) when the patient may have received an ACE-I or ARN-I within the past 36 hours.

Administration of an ACE-I or ARN-I within 36 hours of each other is contraindicated

If clinically appropriate, please hit "Cancel" and contact provider to discuss alternative therapies or re-timing of orders to allow appropriate 36 hour washout period.

ACE-I/ARN-I Medication Orders (From admission, onward)

 Start
 Ordered

 03/11/21
 sacubitril-valsartan 24-26 mg 1 tablet (ENTRESTO) 2 TIMES DAILY
 03/11/21

 0900
 0728

03/10/21 0950	Given	lisinopril 5 mg tab(s) (ZESTRIL, PRINIVIL)	5 mg

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Patient Risk/Scoring Tools

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Medication alerts

Often lack ability to consider patient specific criteria "out of the box"

Custom alerts

More likely to consider patient specific factors Example: alert for ACE-I and ARN-I overlap that accounts for administration data

Admission Med Rec Complete? PTA Medrec Sco	Admission Med Rec Complete? re (Adult)	Med List Status	
- Scor	re calculated:		
Age > 60 (1 pt) o Problem List Iter	r > 70 (3 pts) or > 80 (5 ms	5 pts)	
2 Poly-Pharmacy (2 High-risk PTA M	(10 or more meds) leds	omplete	
Inpatient status Unknown medica	tion ordered		
Med List NOT rev >50	iewed in past 12 montl	hs and age	_
Admissions in th	ne past 180 days	م	"

Refreshed 3 minutes ago 📿 Search Current Locat..

Machine learning – Supervised

Data linked to the outcome of interest

Features = input variables Labels = the outcome to predict

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Machine learning – Supervised

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Machine learning – Supervised

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Examples

- Prediction:
 - Abnormal medication orders
 - Adverse drug events
 - Acute kidney injury
 - Readmissions
 - Sepsis early detection
 - Drug or glucose levels
 - Etc.

- Image processing:
 - Quality control and documentation
 - Pill identification
 - Highlight potential errors in verification
 - Screening for disease (diabetic retinopathy, skin cancer, etc.)

Know your labels

- External validation of a widely implemented proprietary sepsis prediction model in hospitalized patients
 - Wong A, Otles E, Donnelly JP et al. JAMA Intern Med. 2021; 181(8): 1065-70.
- Model failed to identify two-thirds of sepsis patients

VANDERBILT VUNIVERSITY MEDICAL CENTER Applied Clinical Informatics JAMA Intern Med. 2021; 181(8): 1065-70

Know your labels

- External validation of a widely implemented proprietary sepsis prediction model in hospitalized patients
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- Model failed to identify two-thirds of sepsis patients
- Vendor used ICD-9 codes for their model as the labels
 - CDC and CMS don't use billing codes for sepsis quality measures
- Also had different definitions for when a patient developed sepsis
 - Vendor used encounter-level performance, whereas the study used prediction-level performance (alerts) where the outcome = "sepsis in the next x hours"

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Machine learning – Unsupervised

No labels

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Machine learning – Unsupervised

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Examples

- Data analytics
- Natural language processing
- Auditing
- Drug diversion
- Cluster analysis
- Population identification (phenotypes)

Others

- Semi-supervised
 - Kind of a mix of supervised and unsupervised learning
 - We have some examples (labels), but not a lot
- Reinforcement learning
 - The computer makes decisions, then learns from those decisions
 - Based on action and rewards
 - Used for games. Playing against itself and learning from billions of decisions

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Examples

- Semi-supervised
 - Data analytics
 - Auditing and drug diversion

- Reinforcement
 - Identifying ideal treatment pathways
 - Mechanical ventilation
 - Reinforcement Learning from Human Feedback (RLHF) (generative AI)

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https://i.pinimg.com/474x/8a/5e/c5/8a5ec581436d07fe26ad8710f183331d.jpg

Neural Network

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Deep learning

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Examples

- Image processing
- Natural language processing

Large Language Models (LLMs) - ChatGPT

• Generative Pre-trained Transformer (GPT)

Large Language Model (LLM) overview

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Natural Language Processing with Transformers (2022) Lewis Tunstall, Leandro von Werra, and Thomas Wolf

Never gonna give you up, never gonna let you...

Prediction

#	probs	next token	ID predicted next token
0	78.85%	866	down
1	12.69%	467	go
2	0.79%	651	get
3	0.68%	510	up
4	0.57%	503	out
5	0.54%	2666	leave
6	0.37%	2121	fall
7	0.30%	307	be
8	0.25%	4656	die
9	0.23%	1011	take

https://alonsosilva-nexttokenprediction.hf.space/

How to improve the results?

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Applied Clinical Informatics Natural Language Processing with Transformers (2022) Lewis Tunstall, Leandro von Werra, and Thomas Wolf

Potential use cases

- Code generation
- Text summarization
- Text generation
- Conversational AI for patient support
- Speech recognition
- Image or text annotation
- Write clinic notes
- Writing a prior authorization letter, with supporting references
- Write notes to patients interpreting labs

pretend you are a doctor and interpret a lab result with an elevated TSH and low FT4

As a doctor, I would interpret a lab result showing an elevated TSH and low FT4 as indicating a potential thyroid dysfunction. The thyroid gland is responsible for producing hormones that regulate various bodily functions, including metabolism and energy production. TSH, or thyroid-stimulating hormone, is produced by the pituitary gland and stimulates the thyroid to produce its hormones. Elevated levels of TSH can indicate that the thyroid is not producing enough of its hormones, a condition known as hypothyroidism. Low levels of FT4, or free thyroxine, can also indicate hypothyroidism. It is important for individuals with hypothyroidism to receive proper treatment to prevent further complications.

Curtesy Yaa Kuma-Crystal

now write a message to your patient communicating those labs results

Dear patient,

ፊ 🖓

I am writing to inform you that your recent lab results indicate a potential thyroid dysfunction. Specifically, your TSH levels are elevated and your FT4 levels are low. This can be indicative of a condition called hypothyroidism, in which the thyroid gland is not producing enough of its hormones.

It is important to note that these results do not necessarily confirm a diagnosis of hypothyroidism. Further testing and evaluation will be needed to determine a proper diagnosis and course of treatment. In the meantime, it is important to monitor your symptoms and contact me immediately if you experience any concerning changes.

Curtesy Yaa Kuma-Crystal

Considerations In healthcare

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AI models will solve all our problems!

https://xkcd.com/1831/ Creative commons

Truth

- Health care is incredibly complex
- "All models are wrong, but some are useful"

– George Box

- The ultimate decisions are in the hands of the patients and caregivers
 - They have the additional context that is required and making these sometimes difficult decisions

More than just a score...

- What are the next steps someone should take?
- What is the expected outcome or workflow?
- What factors went into producing the score?
- Models must be trained/calibrated on local data
 - External validation

People – Process – Technology!

Model drift

- The performance of a model degrades over time as the environment changes
 - Relationships between variables change over time
 - The underlying data could change
 - Clinical practice changes
- The model must be recalibrated
- Have a long-term maintenance plan
 - Consider when to remove/retire the model

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AI hallucinations

skier_adv.png

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Al Has a Hallucination Problem That's Proving Tough to Fix | WIRED

AI hallucinations

Dall-E 2. Image source: OpenAl

Large Language Models (LLMs) - ChatGPT

- AI hallucination
 - A confident response by AI that is not true
 - Cannot be grounded on any data ever accessed or trained on
 - Generates false information
 - Predictive text

Al-generated suggestion for identifying immunocompromised patients: "add biologic agents, such as adalimumab, **etanerfigut**, and golimumab, which are used to treat autoimmune disorders."

VANDERBILT VUNIVERSITY MEDICAL CENTER Applied Clinical Informatics J Am Med Inform Assoc. 2023. PMID:37087108

Myth or fact??

Write a clinic note about a patient with diabetes that in not compliant

>

\$

Patient is a 50-year-old female with a history of type 2 diabetes mellitus. She has been non-compliant with her diabetes management, including not taking her prescribed medications and not following a proper diabetic diet. She has also not been regularly monitoring her blood sugar levels. As a result, she has experienced increased glucose levels and symptoms of uncontrolled diabetes, such as frequent urination and fatigue. It is important for the patient to improve her compliance with her diabetes management in order to prevent potential complications and improve her overall health.

ு பாtesy Yaa Kuma-Crystal

More data => better Al! AI BE LIKE "MORE DATA!" MORE

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Kylo Ren MORE Meme Generator - Imgflip

Truth

• Al is only as good as the data it trains on or ingests

- Labeling large amounts of data is very difficult
- Beware of model bias (fairness metrics)

Shortcuts in the training data

• Researchers developed a model to identify if cows were in the picture or not

VANDERBILT VUNIVERSITY MEDICAL CENTER Applied Clinical Informatics Recognition in terra incognita. In *Proceedings of the European conference on computer vision (ECCV)* 2018. pp. 456-473

In healthcare – AI for COVID-19 in CXR

High performance at one hospital Failed at another health system

Saliency maps showed that laterality markers were important features

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Normal chest radiograph (male) | Radiology Case | Radiopaedia.org Creative Commons Nature Machine Intelligence. 2021;3(7):610-619.

Model Bias

- Background
 - Researchers discovered significant disparities in diagnostic accuracy for skin conditions across skin tones
 - Less accuracy when diagnosing conditions in **darker skin tones**
 - Researchers developed a deep learning model to provide decision support and enhance accuracy, particularly for darker skin tones
 - The model was tested with dermatologist and primary care providers (PCPs)

VANDERBILT VUNIVERSITY MEDICAL CENTER Applied Clinical Informatics Nat Med. 2024;30(2):573-583. PMID:38317019

Model Bias

- The model successfully <u>improved accuracy</u> for both dermatologists and PCPs
 - Dermatologists saw a **33% improvement** in diagnostic accuracy
 - PCPs experienced an **impressive 69%** improvement
- Impact on disparities
 - Disparities **persisted** among dermatologists across skin tones
 - Surprisingly, disparities across skin tones increased by 5% for PCPs

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Al Recognition of Patient Race in Imaging

- Deep learning models detecting race from medical images
 - X-ray, CT, and mammography from various body sites
 - Chest, spine, breasts, lungs, and hand
- Model predicted self-reported race with AUC 0.90
 - Attempted to control for BMI, disease distribution, breast density, etc.
 - Then corrupted, cropped, and noised the images

• Model could still detect race in images when experts couldn't

ANDERBILT WUNIVERSITY MEDICAL CENTER Applied Clinical Informatics Lancet Digit Health. 2022;4(6):e406-e414. PMID:35568690

Healthcare Data is Biased

- Researchers used a commercially available model to identify patients with the greatest care needs for referral to care management programs
- At the same risk score, Black patients had:
 - 26% more chronic illnesses
 - More uncontrolled hypertension and higher SBP
 - Higher HbA1c values
 - Higher serum creatinine levels
 - Higher LDL levels

VANDERBILT VUNIVERSITY MEDICAL CENTER Applied Clinical Informatics Science. 2019;366(6464):447-453. PMID:31649194

Healthcare Data is Biased

- Sex and gender bias
 - Differences in physiological markers and disease prevalence
 - Cardiovascular disorders, cancer, autoimmunity, diabetes, etc.
 - Men and women respond differently to treatments
 - i.e. statins, ACE inhibitors, beta-blockers, etc.
 - Differences in data representation
 - i.e. coronary heart disease is the leading cause of death in women, but the majority (67%) of patients in clinical trials are men.

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Will AI will take over my job?

This Photo by Unknown Author is licensed under CC BY-NC-ND

Truth: AI = "Augmented Intelligence"

- Pharmacists excel at:
 - <u>Common sense</u>
 - <u>Compassion</u>
 - <u>Context</u>
 - Dilemmas
 - Morals

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- Imagination
- Abstraction
- Generalization

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• Al systems excel at:

- Pattern identification
- Endless capacity
- Natural language processing
- Locating knowledge
- Machine learning
- Minimizing bias

"The rise of machines has to be accompanied by heightened humaneness — **with more time together, passion and tenderness** — to make the 'care' in healthcare real" — Eric Topol

Deep Medicine: How Artificial Intelligence Can Make Healthcare Human Again (2019)

Weird Ai Generations

Everyone: AI art will make designers obsolete

Al accepting the job:

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Balancing excitement and safety

• Some AI models have shown improvements in mortality and patient outcomes

• Many have not, and most fail to make it to clinical practice

- Some AI models have even increased mortality!
 - Model for predicting AKI

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BMJ. 2021;372:m4786. PMID:33461986

Analogy to medications

Phase 0 – Needs assessment

Phase 1 – Algorithm training

Phase 2 – Evaluation by end users

Phase 3 – Clinical trial

Phase 4 – Post-deployment

surveillance

DALL-E 3

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Regulations

- FDA Software as a Medical Device (SaMD)
 - "Software intended to be used for one or more medical purposes that perform these purposes without being part of a hardware medical device."
- Good Machine Learning Practice (GMLP)
 - Jointly by USA FDA, Health Canada, and the United Kingdom's Medicines and Healthcare products Regulatory Agency (MHRA)
 - 10 guiding principles

VANDERBILT VUNIVERSITY MEDICAL CENTER Applied Clinical Informatics Software as a Medical Device (SaMD). Updated December 4, 2018. https://www.fda.gov/medical-devices/digital-health-center-excellence/software-medical-device-samd

The best way to predict the future is to build it!

Building the future: Key considerations

- How does the use of ML/AI affect pharmacy practice?
 - Examine Board of Pharmacy rules
 - Are there things that can be safely delegated to ML/AI models?
- Humanize care and address burnout
 - Al to bring joy to healthcare work, not do more complicated tasks
 - Assure that "normal" is still in the human workflow
- Focus on the human-AI team
 - "Augmented intelligence"

Building the future: Key considerations

- Project identification and prioritization
 - Where should resources focus?
 - Pharmacists understand the workflows
- Assure AI in healthcare is safe, efficacious, and equitable
 - Support equity and fairness metrics
- ML/AI (and healthcare) are rapidly evolving!
 - Consider maintenance and updating policies

Key Takeaways

1. Al describes a computer system's ability to perform a task that would normally require human cognition.

Example: perception, learning, vision, etc. Very powerful tool, but also has limitations

2. Humans + machines

Focus on the power of the combination!

