Using AI to improve access and accuracy of information & care in dermatology

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Google Health

Disclaimer: I am an employee of Google and own Alphabet stock

Motivation: gap in access and accuracy of dermatological care

Skin diseases are an enormous global burden and every day millions of people turn to Google to research their skin concerns



2 billion people affected with skin disease



Half the world's population faces a critical shortage of dermatologists

Q

10 billions of annual skin condition queries on Google Search

But describing what you have is really challenging!

Q

People **spend hours** searching the internet and talking to strangers on forums to find out what they have.

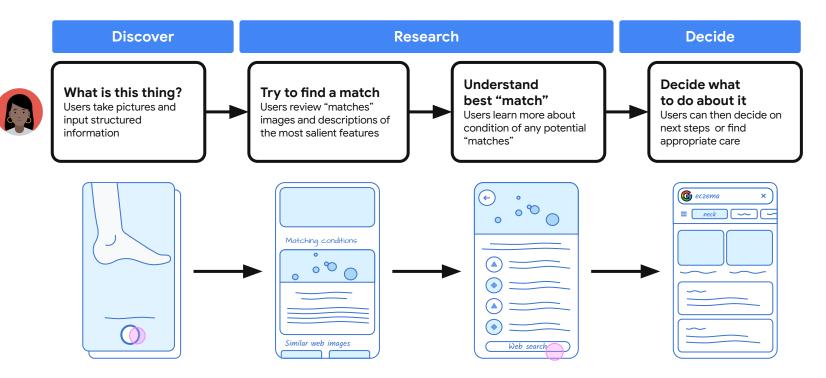


People arrive at the correct condition only 13% of the time, and nearly 3-out-4 people who needed urgent care did not realize they required it.



"I have a plant identification app. A skin app like that would be great. It would be **so much more convenient than googling.**" - Female survey participant (25 - 45yo)

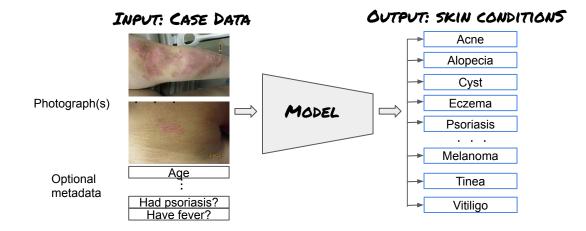
Al-powered dermatological assistive tool that helps users to research & identify their skin concerns



O2 Foundational research: the Al prototype & its clinical utility

Our overarching goal is to:

Develop an AI model to identify the most prevalent skin conditions from clinical images and metadata

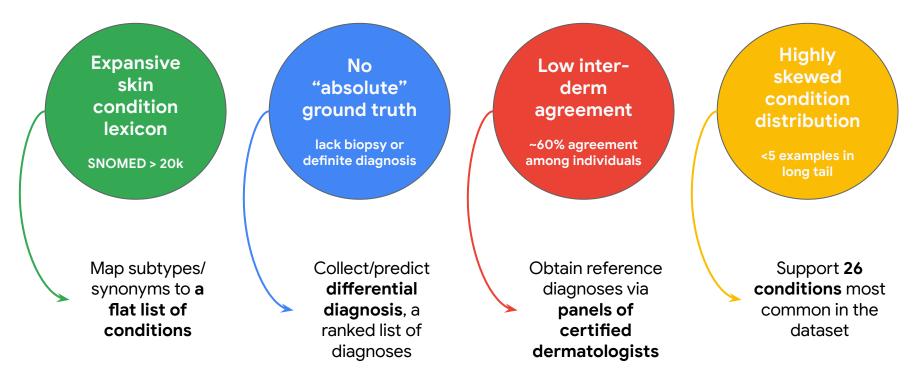


Input Data: challenges in input variation

- A teledermatology dataset
 - 20k cases, 80k images
 - 17 sites, 2 US states
- Broad condition types coverage:
 - Lesion, rash, hair loss, nail infections, etc
- Different presentations per disease:
 - Skin type
 - Body part
 - Disease subtype / severity
- Image artifacts:
 - Lighting
 - Field-of-view
 - Background
- Metadata differences:
 - Missing / inconsistent metadata



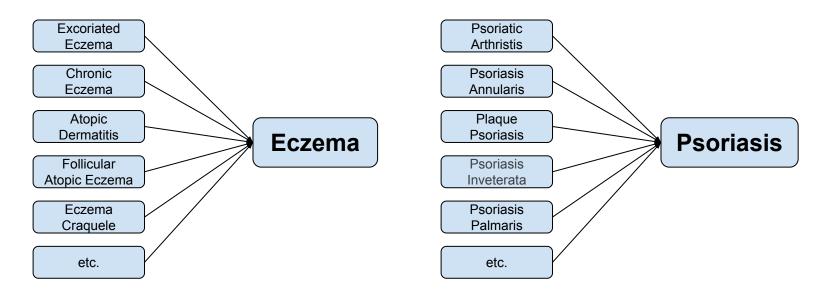
Output Labels: several challenges with labeling



Ground truth: complex labeling space

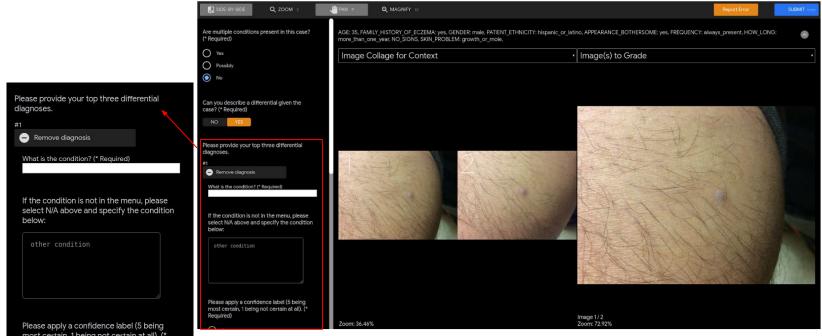
Skin condition lexicon:

- > 20k SNOMED descriptions (5k ids) + > 1k free text entries
- Manually mapped subtypes and synonyms to a flat list of conditions



Ground truth: differential diagnosis

No "absolute" ground truth: few cases have biopsy Differential diagnosis: ranked list of diagnoses to determine clinical next steps



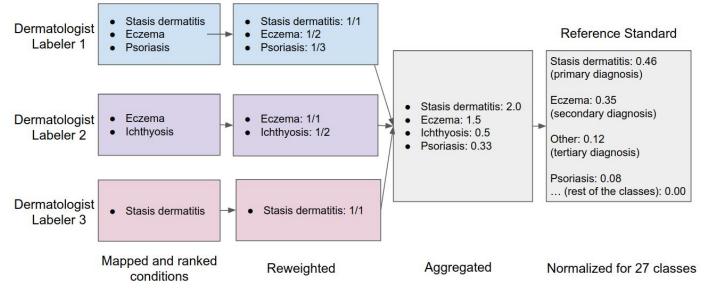
most certain, 1 being not certain at all). (* Required)

Ground truth: low inter-dermatologist agreement

Screen dermatologists via certification:

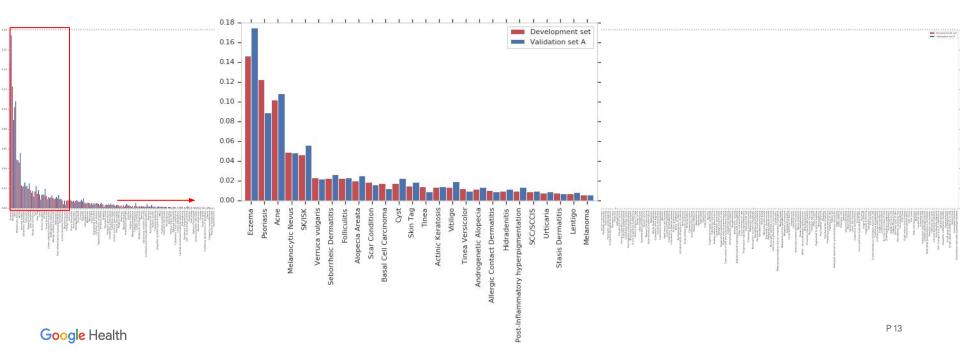
 Pass onboarding exams with score >= 0.70 top-3 agreement Establish ground truth via collective intelligence:

- "Position" weighted aggregation of individual dermatologist
- Reproducibility improves by 20%

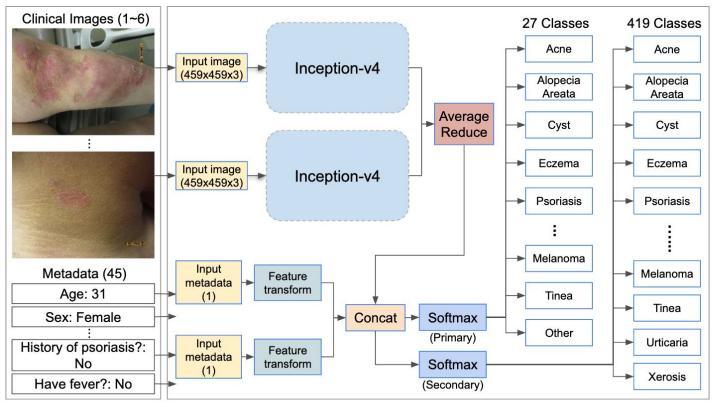


Ground truth: highly skewed distribution

Reduce from a flat list of parent conditions to 27 condition classes (26 + "Other") Still have the full flat list of conditions as a secondary prediction



Model architecture: late fusion of images + metadata



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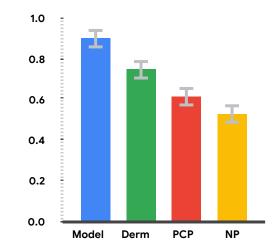
Input Data

Deep Learning System

Al model performs comparably against tele-dermatologists

Our model has **non-inferior diagnostic accuracy to dermatologists** across the most common 26 skin conditions,

with **top-3 accuracy** of 0.90, 0.75 (dermatologists), 0.60 (PCPs/GPs), and 0.55 (NPs)





Featured on the <u>cover of Nature</u>, June 2020 issue

Liu et al, Nature Medicine 2020 https://ai.googleblog.com/2019/09/using-deep-learning-to-inform.html

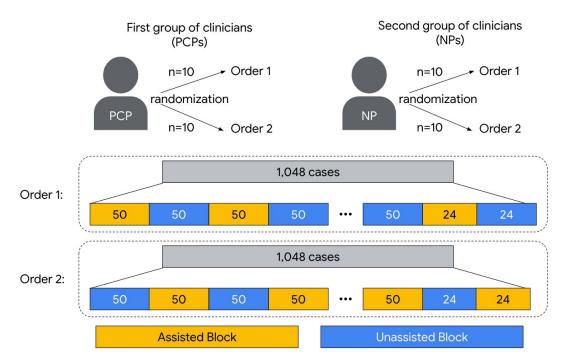
Al model can help NPs/PCPs better interpret skin cases

A multi-reader multi-case (MRMC) randomized study:

- 1,048 retrospective cases
- 120 conditions
- 40 clinicians (20 PCPs, 20 NPs)

Each case was reviewed by half the clinicians with Al assistance and half without, only once per clinician.

For each clinician, the assistance modality alternated every 50 cases.



Jain et al, JAMA Network Open 2021 <u>https://www.blog.google/technology/health/ai-assists-doctors-interpreting-skin-conditions/</u>

Al model can help NPs/PCPs better interpret skin cases

Patient's case

63 y.o. Male			
Self-reported condition	Growth or Mole	Medical history	No history of skin cancer, melanoma, eczema
Symptoms	Increasing in size, itching, burning, painful		or psoriasis
How long	Three to twelve months, always present	Family history	Skin cancer
Drugs	Treated by Rx or OTC	Drug allergies	None
ROS	No F/C, fatigue, joint pain, mouth sores, or	Medication	None
	shortness of breath	Follow-up case	Not a follow-up case





3 Matching Conditions

SCC/SCCIS, Basal Cell Carcinoma, Actinic Keratosis

SCC/SCCIS

Assistant Confidence

....

Keratinocyte malignancy, often characterized by tender, pink, scaly, bleeding nodules and plaques, often found on head, neck, dorsal hands/forearms, and legs, and comprising the second most common type of skin cancer. SCCIS, or Bowen disease, which often presents as scaly, pink-brown plaque, represents noninvasive (in situ, not penetrating dermis) stage of SCC, that may progress to invasive disease if left untreated.





Images of SCC/SCCIS similar to patient's presentation

→ View similar images

Workup

Skin biopsy (shave, punch, or excisional) performed for histologic confirmation.

Treatment

First-line treatment: Typically, surgical management. Lesions triaged into low- and high-risk categories based on clinical and histologic features. For low-risk lesions, standard surgical excision with 4-6mm clinical margin; Mohs micrographic surgery typically used for cosmetically/functionally sensitive sites; electrodessication and curettage sometimes employed for very low-risk lesions. For high-risk lesions, staging with CT, MRI, or PET; surgical excision or Mohs, often followed by adjuvant radiation therapy. Cemiplimab for locally advanced and metastatic SCC.

Pearls

Risk factors include UV exposure (sun or tanning bed), lighter skin types, increasing age, male sex, history of radiation exposure, immunosuppression (especially solid organ transplant patients), chronic inflammation (e.g., unstable scars, longstanding wounds, known as 'Mariolin ulcer'), chronic arsenic exposure, family history, and genetic syndromes (e.g., albinism). Human papillomavirus (HPV) infection can lead to SCC in predisposed patients, especially at mucosal and periungual (around nail unit) locations. SCC has 2-5% rate of metastasis (nose, ear, and lip are higher risk sites).

Commonly mistaken conditions

→ View textbook images

Actinic Keratoses	Basal Cell Carcinomas
Compared to actinic	Compared to basal cell carcinomas, SCC lesions
keratoses, SCC lesions are	usually lack superficial branching blood vessels
more commonly thicker,	('arborizing telangiectasias') and are more often
tender, and bleeding.	nodular and scaly.

Prurigo Nodularis

Compared to prurigo nodularis, SCC lesions are more commonly solitary, painful, and lack history of repeated rubbing/scratching.

View less

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Jain et al, JAMA Network Open 2021 https://www.blog.google/technology/health/ai-assists-doctors-interpreting-skin-conditions/

Al model can help NPs/PCPs better interpret skin cases

Non-specialist clinicians can identify the correct skin disease 20% more often and feel more confident about their assessment

No increase in likelihood to recommend biopsies or referrals to dermatologists

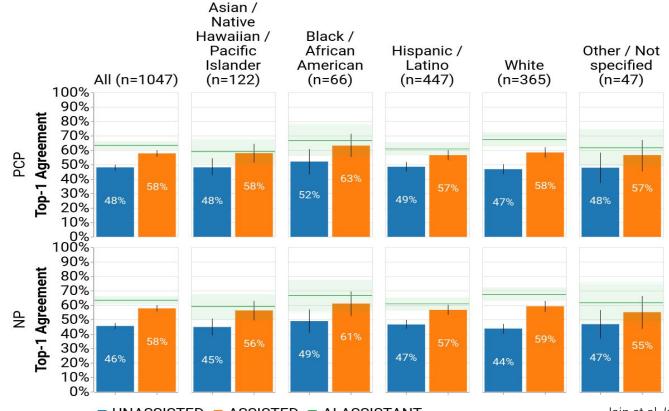
	Takeaway	Unassisted primary care clinician	Al-assisted primary care clinician
Primary analysis : diagnostic agreement with dermatologists	Significant increase with Al: p < 0.001	47%	58%
Classifying growths as benign, malignant or precancerous	Promising malignancy interpretation	62%	68%
Referrals to dermatologists	No increase	39%	36%
Desired rate of biopsy	No increase	25%	23%

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https://www.blog.google/technology/health/ai-assists-doctors-interpreting-skin-conditions/

Jain et al, JAMA Network Open 2021

This may help reduce existing disparities in dermatology

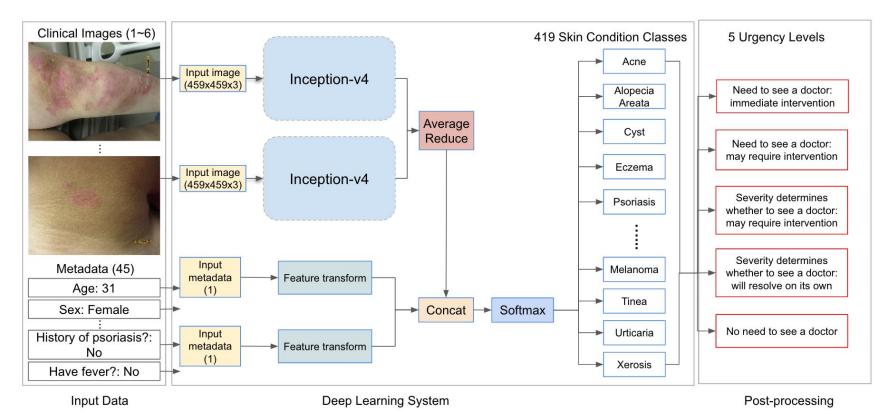


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UNASSISTED ASSISTED AI ASSISTANT

Jain et al, Iproceedings 2021

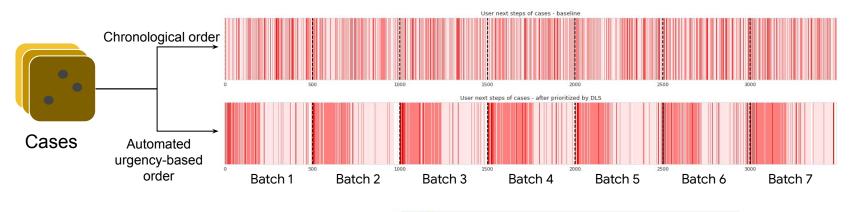
Al tools can also help triage cases in dermatology



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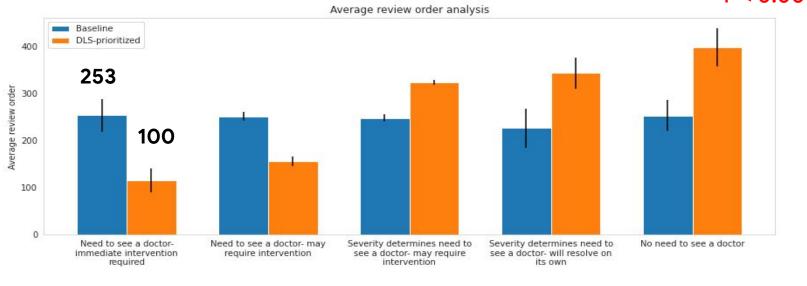
Huang et al, Skin Health and Disease 2021

Al tools can also help triage cases in dermatology



Need to see a doctor- immediate intervention required
Need to see a doctor- may require intervention
Severity determines need to see a doctor- may require intervention
Severity determines need to see a doctor- will resolve on its own
No need to see a doctor

Al tools can also help triage cases in dermatology



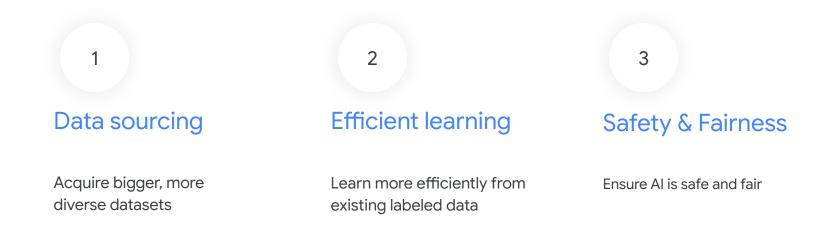
P < 0.001

More urgent

Less urgent

Real-world translation: improvements to deploy at scale

Improving AI to be more accurate, generalizable, safe, and fair



Obtain data from multiple sources

	Locations	Conditions	Demographics	Device Characteristics
A	Multiple outpatient sites throughout South America (rural and urban)	Non-urgent, common conditions treated in clinic or via telemedicine	Age mostly <=75, both male and female, diverse skin types	Clinic captured, unknown device
В	Academic outpatient & inpatient sites in Europe	Wide variety of conditions	Age mostly 25-85, both male and female, mostly lighter skin types	Clinic captured, digital camera
С	Multiple outpatient and retail sites in US (suburban, rural)	Non-urgent, common conditions referred to teledermatology	Age mostly 13-90+, both male and female, mostly lighter skin types	Assistant-captured, iPad + Canon; user-captured, various phones
D	Multiple outpatient sites throughout Australia (rural and urban)	Mostly malignancies, some benign	Age mostly 25-85, both male and female, mostly lighter skin types	Clinic captured, hand-held cameras
E	Multiple sites within US (urban)	Primarily healthy skin	Age mostly 20-50, both male and female, mostly light to brown skin types	User-captured, various phones
F	Major academic center in US (urban)	Wide variety of conditions	Age mostly 25-85, both male and female, diverse skin types	Clinic captured, unknown device (each uses their own)
G	Multiple sites within US (urban)	A wide variety of non skin images	N/A	User-captured, various phones

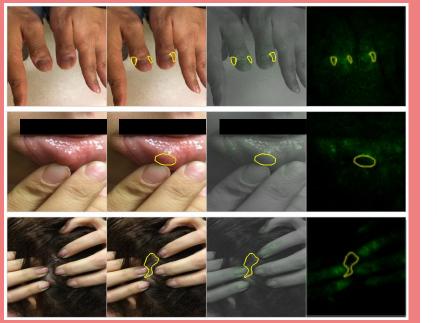
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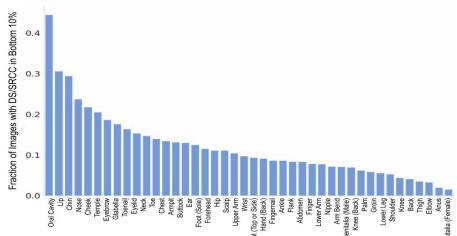
..... and more to come

1. Data sourcing

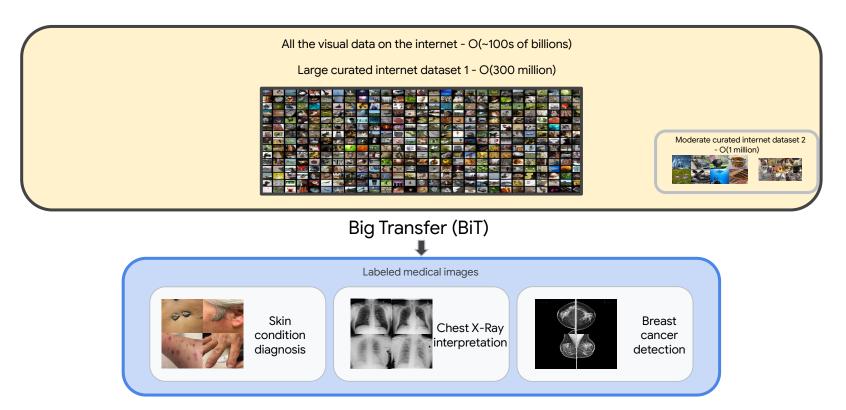
Guide data collection via saliency analysis

Low agreement: Incorrectly Classified Images



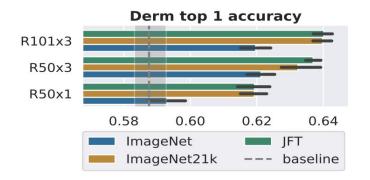


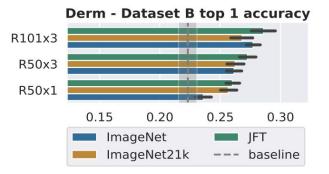
Leverage MORE NON-MEDICAL data with transfer learning



Leverage MORE NON-MEDICAL data with transfer learning

Simple to use, drop in replacement for existing feature extraction backbones

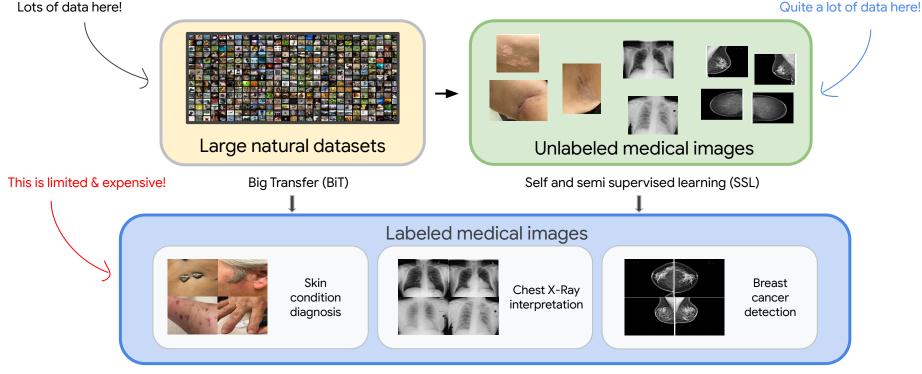




Significant improvement in task performance

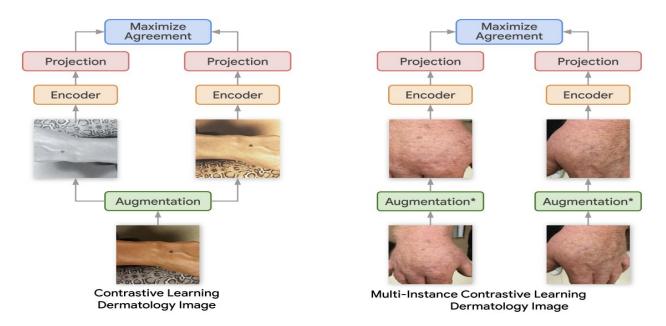
BiT Models significantly more robust to distribution shifts!

Leverage UNLABELED data with self-supervised learning



Leverage UNLABELED data with self-supervised learning

Maximizes agreement between augmented views of the same image, or images of the same case

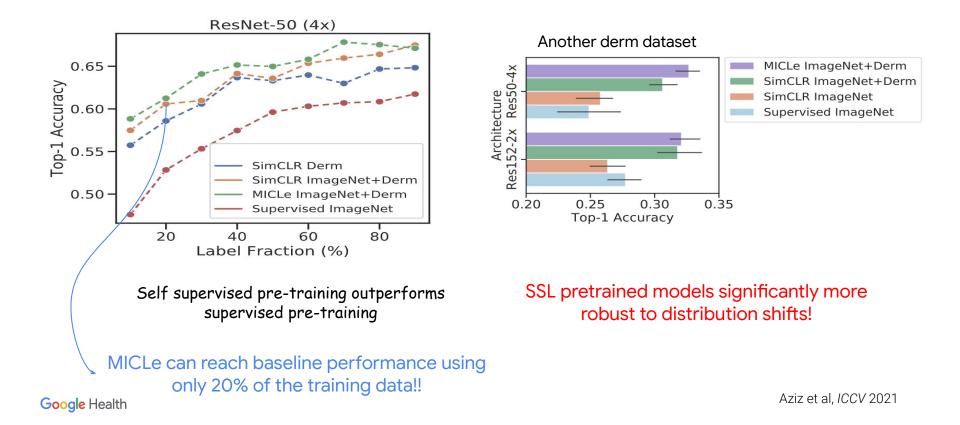


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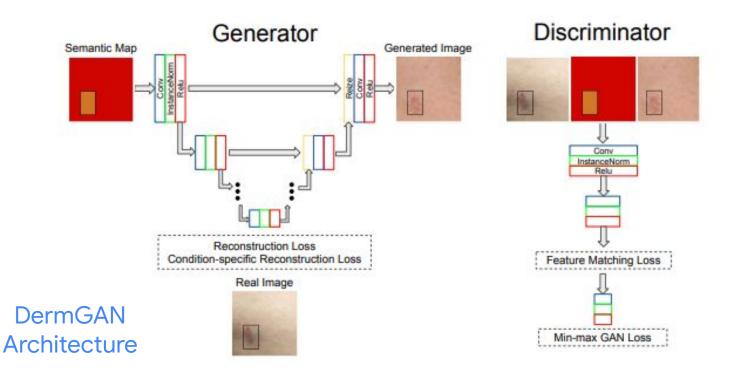
SimCLR and MICLe (multi-instance contrastive learning)

Aziz et al, ICCV 2021

Leverage UNLABELED data with self-supervised learning

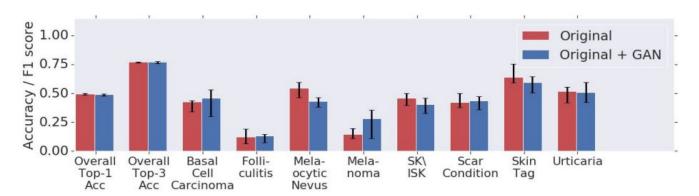


Synthesize dermatology images using generative learning



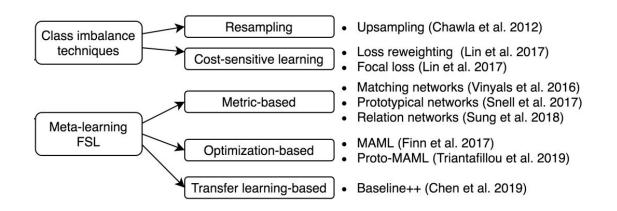
Synthesize dermatology images using generative learning

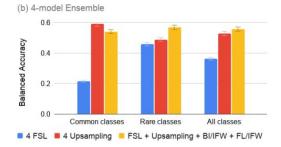




Improve long-tail recognition with few-shot learning

Use an ensemble of few shot learning and conventional supervised learning models





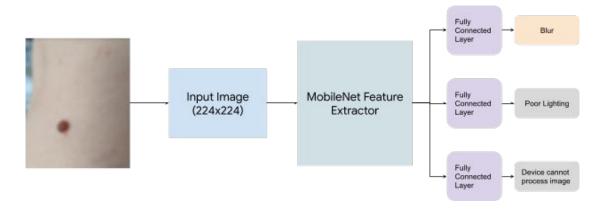
Weng et al, NeurIPS ML4H 2020

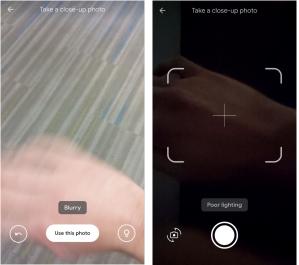
Guide intake to ensure sufficient input quality

In teledermatology, up to <u>10%</u> of images submitted by everyday users are so suboptimal that dermatologists cannot render a confident interpretation:

- Common quality reasons: blurry and bad lighting
- Real world adversarial use case: "non-skin"

Goal is to filter out **far out-of-distribution (OOD)** examples

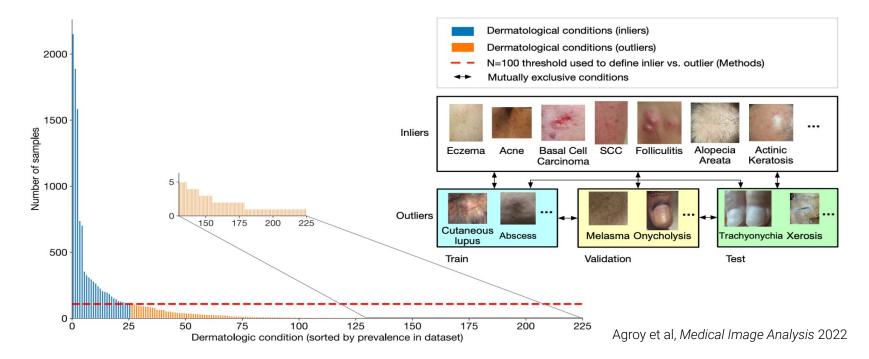




3. Safety & fairness

Teach AI to know when it doesn't know

Near OOD: many conditions in the long tail which AI hasn't encountered in training Need to abstain from making predictions when encountering them in the wild

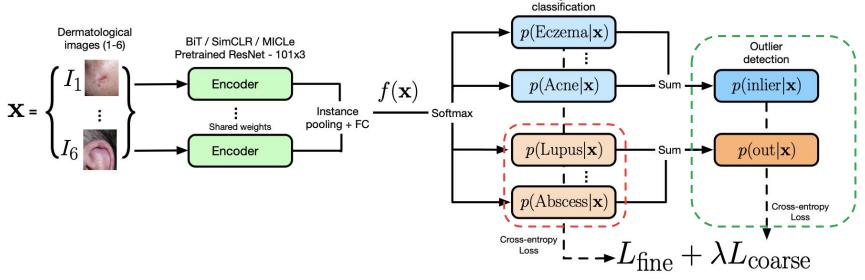


3. Safety & fairness

Teach AI to know when it doesn't know

Hierarchical Outlier Detection (HOD) Loss:

- Multiple Abstention classes (Expanded fine-grained training outlier classes)
- High-level coarse inlier vs. outlier loss
- p(out|x) is used as the OOD score



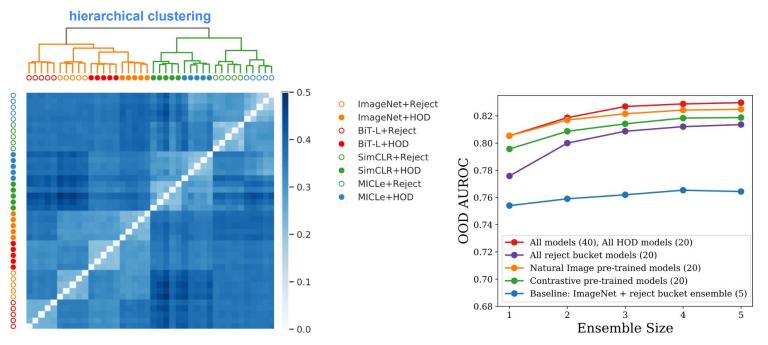
Fine-grained

Agroy et al, Medical Image Analysis 2022

3. Safety & fairness

Teach AI to know when it doesn't know

Complementarity in learnt representations -> more diverse ensembles -> better predictive uncertainty quantification



Evaluate fairness under distribution shift

Fairness considerations need to be built into the entire process: problem definition, data collection, algorithm development, and post-deployment evaluation

A largely fair model may exhibit disparities in performance when deployed in the real world

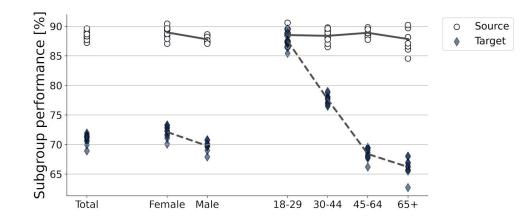


Fig. 4. Model performance in dermatology, as estimated via Top-3 accuracy (in %). The plot displays the total performance, as well as performance stratified by sex and by age on the source (circles with plain line) and target (diamonds with dashed line) data. Each marker represents one replicate of the model.



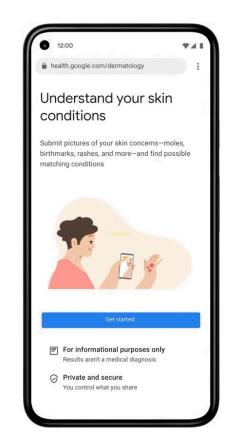
DermAssist and beyond

We have developed DermAssist, an AI-powered, dermatology assistive tool, with the AI model covering up to **288 conditions** by training the model on millions more images and using advanced AI technologies.

This informational tool has obtained **CE Mark** as a **Class I** medical device in the EU.*

We continue to learn how best we can leverage AI to improve the world's access to accurate dermatological information and care.

*This product has not been evaluated by the U.S. FDA for safety or efficacy.



A list of publications

Journals:

- Huang, S., et al., Machine learning for clinical operations improvement via case triaging. Skin Health and Disease (2021).
- Guha Roy, A., et al., Does your dermatology classifier know what it doesn't know? Detecting the long-tail of unseen conditions. Med. Image Analysis (2021).
- Jain, A., et al., <u>Development and Assessment of an Artificial Intelligence–Based Tool for Skin Condition Diagnosis by Primary Care Physicians and Nurse Practitioners in Teledermatology Practices</u>. JAMA Netw Open (2021).
- Liu, Y., et al., A deep learning system for differential diagnosis of skin diseases. Nat. Med. (2020).
- D'Amour, A., et al., <u>Underspecification Presents Challenges for Credibility in Modern Machine Learning</u>. JMLR. arXiv [cs.LG] (2020).
- Eng, C., Liu, Y. & Bhatnagar, R. Measuring clinician-machine agreement in differential diagnoses for dermatology. Br. J. Dermatol. (2019).

Conferences:

- Schrouff, J., et al., <u>Maintaining fairness across distribution shift: do we have viable solutions for real-world applications?</u>. NeurIPS. arXiv [cs.LG] (2022).
- Jain, A., et al., <u>Race- and Ethnicity-Stratified Analysis of an Artificial Intelligence-Based Tool for Skin Condition Diagnosis by Primary Care Physicians and Nurse Practitioners</u>. *Iproceedings* (2022).
- Azizi, S., et al., <u>Big Self-Supervised Models Advance Medical Image Classification</u>. ICCV (2021).
- Mustafa, B., et al., <u>Supervised Transfer Learning at Scale for Medical Imaging</u>. arXiv [cs.CV] (2021).
- Weng, W.-H., et al., Addressing the Real-world Class Imbalance Problem in Dermatology. Machine Learning for Health NeurIPS Workshop (ML4H) (2020).
- Singh, N., et al., <u>Agreement Between Saliency Maps and Human-Labeled Regions of Interest: Applications to Skin Disease Classification</u>. Skin Image Analysis CVPR Workshop (ISIC) (2020).
- Ghorbani, A., et al., DermGAN: Synthetic Generation of Clinical Skin Images with Pathology. Machine Learning for Health NeurIPS Workshop (ML4H), (2019).

Blog posts:

- "Ask a Techspert: What does AI do when it doesn't know?" by Iz Conroy | Google Keyword Blog | 08-Feb-2022
- "Does Your Medical Image Classifier Know What It Doesn't Know?" by Abhijit Guha Roy & Jie Ren | Google Al Blog | 27-Jan-2022
- "How Underspecification Presents Challenges for Machine Learning" by Alex D'Amour and Katherine Heller | Google Al Blog | 18-Oct-2021
- "Self-Supervised Learning Advances Medical Image Classification" by Shekoofeh Azizi | Google Al Blog | 13-Oct-2021
- "How DermAssist uses TensorFlow.js for on-device image quality checks" by Miles Hutson & Aaron Loh | TensorFlow Blog | 11-Oct-2021
- "Using AI to help find answers to common skin conditions" by Peggy Bui & Yuan Liu | Google Keyword Blog | 18-May-2021
- "Al assists doctors in interpreting skin conditions" by Ayush Jain & Peggy Bui | Google Keyword Blog | 28-Apr-2021
- "Generating Diverse Synthetic Medical Image Data for Training Machine Learning Models" by Timo Kohlberger & Yuan Liu | Google Al Blog | 19-Feb-2020
- "Using Deep Learning to Inform Differential Diagnoses of Skin Diseases" by Yuan Liu & Peggy Bui | Google Al Blog | 12-Sep-2019

Thank you

For more, please reach out to: <u>yuanliu@google.com</u> or <u>dermatology-research@google.com</u>