APPENDIX A: SEARCH STRATEGY AND SELECTION METHOD

It is not possible to identify ML devices directly from FDA databases, which function as registries of approvals.[1-3] While searchable by fields such as device name, manufacturer and product classification, there is no capability to search by the content of approvals or the algorithmic methods used by devices. Therefore, we conducted a systematic internet search to identify candidate ML devices. We then searched the FDA databases for those candidate devices and retrieved all publicly available approval documents. Each candidate was then assessed for inclusion using the approval documents.

Inclusion criteria

Medical devices that were:

1. FDA approved, evidenced by the existence of a premarket approval (PMA), premarket notification (PMN), or a De Novo classification.
2. Intended for use by clinicians or healthcare professionals.
3. Intended to be used for or assist with clinical tasks/decisions.
4. Utilised ML.

Search strategy

An internet search (www.google.com) for candidate ML devices using query combinations of "machine learning" and "FDA approved" (see Box 1) was performed in February 2020 and the resulting URLs were captured. The search was conducted using Firefox 72.0.2 (64-bit) by Mozilla Foundation utilising private browsing mode and not signed into Google or any other account that may impact search results. A virtual Private Network (VPN) allowed to search to be conducted from within the USA, that is, within the FDA's jurisdiction.

("artificial intelligence" OR "ai" OR "machine learning" OR "deep learning") AND ("FDA approved" OR "FDA approves" OR "FDA approval")

Box 1 Search query

URLs were accessed in order and any candidate devices mentioned were extracted. Extraction ceased after the 50th result having reached saturation, with the last 18 results not yielding any new candidates. We also extracted candidates from a list of 'FDA Cleared AI Algorithms' curated by the American College of Radiology's Data Science Institute [4] supplemented by additional hand searching.

Selection of ML devices

Two reviewers (D.L. and P.S) independently assessed the candidate devices against the inclusion criteria. For ML utilisation, device manufacturer marketing materials and the product website were also examined. Any claim indicative of utilisation of machine-learned algorithms, including specific mention or general descriptions of ML techniques or methods were considered.

Interrater agreement was fair to moderate (κ = .44, 95%CI .32 to .57).[5] Disagreements were independently reviewed by a third reviewer (J.C.) and resolved by consensus by all three reviewers. Seven devices had multiple approvals, with latter approvals modifying the device in a way that required a new approval. Therefore, the most recent approval for each unique device was considered. In total, our search identified 137 candidate devices for which 130 FDA approvals were retrieved. Of these, 59 approvals met the inclusion criteria covering 49 unique ML devices.

Box 2 Examples of FDA approved indications specifying responsibility for the final decision on the device task resides with the clinician.

"All automatically scored events are subject to verification by a qualified clinician." [6]

Device "is a support tool that provides relevant clinical data as a resource to the clinician and is not intended to be a source of medical advice or to determine or recommend a course of action or treatment for a patient." [7]

"Not intended for making clinical decisions regarding patient treatment or for diagnostic purposes." [8]

"not intended to diagnose, treat, or prevent diseases or conditions" [9]

"intended to provide the trained medical professional with complementary information for the evaluation and assessment of MR brain images and to aid the trained medical professional in quantitative reporting." [10 11]

"intended as an additional input to standard diagnostic pathways and is only to be used by qualified clinicians." [12]

"interpretations offered by [device] are only significant when considered in conjunction with healthcare provider over-read and including all other relevant patient data." [13]

"not intended as a sole means of diagnosis." [14]

Device "should not be used in-lieu of full patient evaluation or solely relied upon to make or confirm a diagnosis." [15]

"Clinicians should review [device] annotated images concurrently with original images before making a final determination on a case. [device] is an adjunct tool and does not replace the role of the clinician. Clinicians must not use the CAD generated output as the primary interpretation." [16]

"interpretation results are not intended to be the sole means of diagnosis for any abnormal ECG. They are offered to physicians and clinicians on an advisory basis only in conjunction with the physician's knowledge of ECG." [17]

"The clinician retains the ultimate responsibility for making the pertinent diagnosis based on their standard practices." [18]

"to aid interpreting physicians in the assessment of breast tissue composition. [device] produces adjunctive information. It is not a diagnostic aid." [19]

"Patient management decisions should not be made solely on the results of the" device. [20]

"not intended to be the sole means of diagnosis. It is offered to physicians and clinicians on an advisory basis only in conjunction with the physician's knowledge of ECG patterns, patient background, clinical history, symptoms, and other diagnostic information." [21]

Device output "may be confirmed or dismissed by the interpreting physician." [22]

"not intended for primary interpretation of digital mammography images." [23]

"provides adjunctive information and is not intended to be used without the original CT series." [24]

"Patient management decisions should not be made solely on the basis of analysis by" device. [25]

Device "does not replace clinical judgement." [26]

"Product users are responsible for image quality and diagnosis." [27]

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