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Introduction

Melanoma incidence rates are rising worldwide, predominantly in countries with fair-skinned populations [1]. Among other factors, having many melanocytic naevi on the skin is a risk factor for melanoma [2]. However, the generalizability of standardized nevus counting is limited by a lack of reliable counting methodology, despite the 1990 International Agency for Research on Cancer's (IARC) protocol [3-4]. Significant variations are still present across individual studies due to differences in the naevus size, anatomic site, and types of naevi considered for analysis [4-5]. This systematic review evaluated variations in nevus counting and reporting methods, adherence and deviations from the IARC's protocol, and the reproducibility of previous nevus counting.

Discussion

This systematic review evaluated variations in naevus counting and reporting methods in studies published during the past 22 years and assessed reproducibility and comparability of results. Given the previously observed significant heterogeneity in naevus counting methods [4], we limited our review to studies using skilled examiners for naevi counting, including naevi at least 2 mm in diameter on the total body in adults sampled from the general population. Only eight studies were eligible for evaluation, and even among them there was a considerable variation in counting methods. Overall, included studies did not often follow a standard counting protocol and differed in their handling of inter- and intra-observer variation.

Conclusions

Given the importance of nevus counts for accurate melanoma risk prediction, these results demonstrate a necessity for an easily accessible and feasible updated protocol for identifying, counting, and reporting nevi. Using total body medical imaging technologies and automated nevus counts in nevus studies should be discussed in such updated protocols, as should the role of artificial intelligence-based algorithms in assisting clinicians' dermatological decision-making.

Results

Eight eligible studies (n=375,464 participants; four case-control studies and four cross-sectional studies) were identified from 4,638 articles. Considerable variation in nevus counting methods existed across studies, illustrated by none reporting adherence to IARC protocol or a well-defined criterion for nevus identification. Amongst the eight studies reviewed, there was little to no agreement in naevus counting and reporting procedures, and most studies did not report their procedures adequately. Total nevus counts varied in terms of nevus size, types, anatomical areas considered, and observer expertise. These studies' reproducibility exhibits inter- and intra-observer variation, noting that intra-observer reliability increases with training and experience. Further, their methodology for obtaining reliable and valid exposure measurements and nevus outcome measures could be improved.

Table 1. Naevus related outcomes reported.

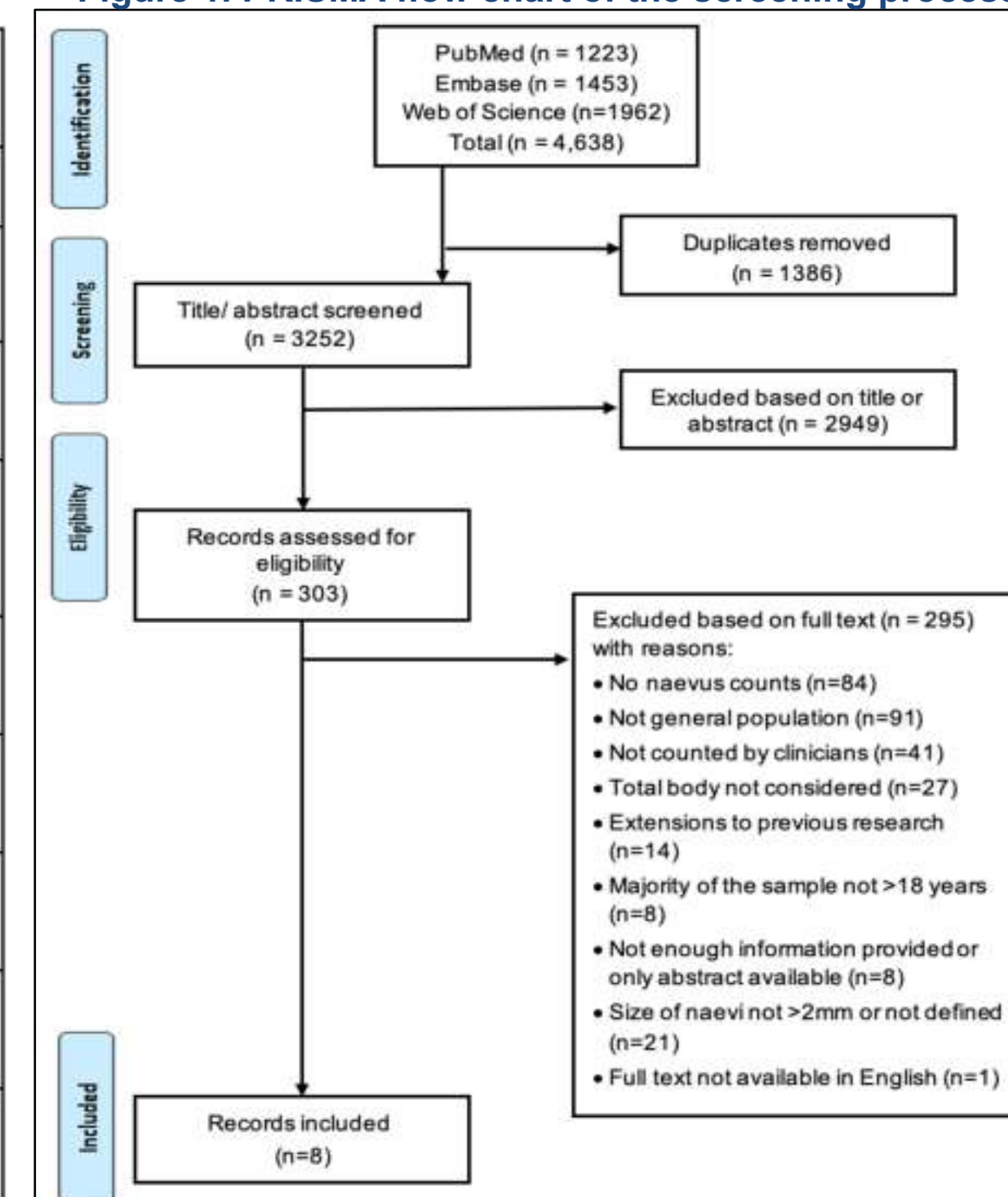
First author (Year) & Country	Included Studies' Characteristics Type of Study	Outcome Reported		Naevus Prevalence	
		Naevus count reported	Categorized naevus count	Average/Proportion	Dispersion
Karlsson (2000), Sweden	Cross-sectional	Yes	Yes	Median=15	Range=0-332
Silva (2009), UK	Cross-sectional	Yes	Yes	Median=45, Mean=57.6	Range=0-355
Newton-Bishop (2010), UK	Case-control	Yes	No	Median *	Interquartile range *
Bataille (2000), UK	Cross-sectional	Yes	Yes	Mean=35, Median=22	Range=0-324
Breitbart (2012), Germany	Cross-sectional	No	No	>=40 naevi=56.2%	NR
Landi (2001), Italy	Case-control	No	Yes	0-12 (21.2%), 13-20 (18.8%), 21-34 (17.7%), 35-51 (22.4%), 52-190 (20%)	NR
Nagore (2010), Spain	Case-control	No	Yes	< 20 (89%), 20-50 (8.8%), >50 (2.2%)	NR
Naldi (2000), Italy	Case-control	No	Yes	0-5 (48.7%), 6-15 (27.9%), 16-30 (14.3%), 31-45 (5.8%), >= 46 (3.3%)	NR

* Reported separately for 11 sun exposure characteristics and 3 nevus genotypes
Abbreviations: NR – Not reported

Methods

This systematic review followed PRISMA guidelines, was registered with PROSPERO, and searched Embase, PubMed, and Web of Science. Studies conducted between 2000 – 2022, utilized skilled examiners, and reported total body melanocytic nevus counts of >2mm in diameter of the general adult population were eligible. Studies recruiting from dermatology clinics, self-performed nevus counts, and studies on atypical nevus syndrome or specific types of nevi were excluded. Three independent reviewers engaged in screening and quality assessment.

Figure 1. PRISMA flow chart of the screening process.



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