Introduction
Management of borderline breast lesions (B3 lesions) is challenging. Whilst known that they can coexist with malignancy, the magnitude of this risk varies between studies and individual lesions within this group.
Current management strategies either consider the overall risk of all lesions within the group, or rely on results from studies with relatively small sample sizes.
This systematic review was designed to calculate a more accurate estimate of the risk of coexisting malignancy of each of the lesions within the B3 group, by considering the whole body of literature available, and using pooled estimates to calculate risk of malignancy. Such robust data should allow risk stratification of individual lesions within the B3 group and guide accurate management strategies.

Methods
A systematic review was conducted to identify studies which provided data on underestimation of invasive or in situ malignancy, identified by surgical excision biopsy, following the diagnosis of a B3 breast lesion at core biopsy. A comprehensive search of the literature (MEDLINE, Embase, HNMC, Scopus and Web of Knowledge) was conducted to identify relevant studies between 1980 and 2014. The search terms used are shown in the table below.
Critical appraisal of the literature, data extraction and meta analysis were performed to calculate the rate of malignancy of the whole B3 group and individual lesion subtypes (STATA). Study heterogeneity and the association between variables and understimation rate was investigated using random effects logistic modelling.

Results
Database searches returned 2289 citations. A further 11 were identified from other sources. Removing duplicates left 1973 references, searched using title for inclusion suitability in the study. Posters and abstract only articles were excluded.
After title searching, 183 studies remained for full text review. Full text articles were only included if the initial B3 diagnosis was made on core needle biopsy, followed by diagnostic surgical excision. 54 full text articles did not meet the inclusion criteria.
Data extraction and meta analysis was performed from 129 studies. STATA was used to perform a meta-analysis to calculate the proportion of core biopsies which subsequently had malignancy identified at surgical excision biopsy for each of the individual lesions within the B3 group. Data for each individual lesion was analysed using Forrest plots, from which the estimate of malignancy risk was calculated. The rates of malignancy for subgroups of B3 lesions are shown in the table below. Sample Forrest plots are shown below.
A large amount of heterogeneity was seen within the lesion groups (as shown by the high I² values in the table), however, this could not be explained by variations in core biopsy size or year of publication. However, a significant difference in upgrade rates to malignancy was observed between the US and non-US literature. Rate of upgrade to malignancy was 11% in the US literature compared to 31% in the non-US literature (p<0.01).
Rates of malignancy varied from 6% in a radial scar with no atypia, to 32% for a papilloma with atypia. Differences in malignancy upgrade rates between atypical and non-atypical radial scars and papillomas were statistically significant (p<0.05).

Conclusions
Whilst many primary studies have assessed the risk of coexisting malignancy following the diagnosis of a borderline breast lesion, these are often small and report conflicting results. This is a comprehensive, inclusive assessment of the body of literature available concerning the malignancy risk of B3 breast lesions. Whilst some of these lesions have a high risk of malignancy, others have a much lower risk, and may be safely managed with surveillance strategies rather than surgery. Upgrade rates in the US are significantly lower than in the non-US literature, which may reflect management differences. The heterogeneous nature of the data could not be explained by technical differences between studies and are most likely due to local differences in pathology reporting thresholds for B3 lesions.

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