1.a. **Full Title**: Cardiovascular risk prediction accounting for socio-economic status: an updated and generalized ASSIGN score

**b. Abbreviated Title (Length 48 characters)**: CVD prediction in Scotland

2. **Writing Group**:
   Mark Woodward and Hugh Tunstall Pedoe

I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal

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**ARIC author** to be contacted if there are questions about the manuscript and the first author does not respond or cannot be located (this must be an ARIC investigator).

**Name**: Mark Woodward  
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3. **Timeline**:
First draft: 2 months.

4. **Rationale**:
Low socio-economic status (SES) is now a well-recognized independent predictor of cardiovascular disease (CVD), both in established market economies of Europe and north America and middle- and low-income settings. CVD risk scores are a useful clinical tool in primary prevention for deciding who should receive interventions, and the degree of intervention. However, the most popular CVD risk score, worldwide – the Framingham score – takes no account of SES. The same is true of the pan-European CVD risk score, SCORE. CVD treatment guidelines, for example in Australia, advise use of a CVD score, typically Framingham or SCORE, whilst acknowledging that extra allowance should be made for the excess residual risk amongst the most socio-economically deprived.

In 2006, we produced the first CVD risk score that included SES as one of the predictor variables – ASSIGN - using Scottish data (Woodward et al, 2006). This was followed, a few months later, by the first of the QRISK scores; following criticism of methodology, QRISK was revised a year later. One drawback of both these scores is their use of census-based neighborhood measures of SES, normalized to national data. This makes them difficult to map to each other and to apply in other settings. Although ASSIGN has been adapted for use in the US, the method used was necessarily indirect and not validated. Hence there is a clear need for a generalized version of ASSIGN that uses a universally-applicable measure of SES. Although several measures of social status have
been suggested in a vast literature, measures based on income and employment are hard to compare between countries. The degree of education received is much easier to compare, except that the ages typically covered by education levels, such as primary and secondary, vary even within the UK. Hence we decided to use years of education as our “universal” measure of SES. In Scotland, we have previously found this to be consistent, in terms of association with CVD, with alternative measures of SES based both on census-based neighborhood measurement and individual-level measurement of type of employment, housing tenure and level of education.

We propose a generalized version of ASSIGN2 – ASSIGN2G – which replaces the Scottish national measure of SES with years of education.

5. Main Hypothesis/Study Questions:
How well does ASSIGN2G predict CVD risk in the ARIC population and does it perform better than Framingham (d’Agostino et al, 2008)?

6. Design and analysis (study design, inclusion/exclusion, outcome and other variables of interest with specific reference to the time of their collection, summary of data analysis, and any anticipated methodologic limitations or challenges if present).
ASSIGN2G will be developed in a Scottish data set. The resultant risk scores, and their Framingham score equivalents, will be evaluated in ARIC using the same methods as in the CKD-PC analyses. That is, Harrell’s c-statistic for discrimination and (possibly) graphical tests and/or Hosmer-Lemeshow tests (suitable for survival data) for calibration. The variables used will be (baseline) age, sex, blood pressure, hypertensive medication use, total and HDL-cholesterol, family history of CVD, diabetes, education grade achieved plus (for exclusion purposes) history of CVD and (follow-up) incident CVD and time to occurrence/censoring. The only ARIC data that will be shown in the manuscript will be summary statistics concerning the ASSIGN2G score: e.g. c-statistics; expected and observed 10-year risk.

7.a. Will the data be used for non-CVD analysis in this manuscript? _Yes _X_ No

b. If Yes, is the author aware that the file ICTDER03 must be used to exclude persons with a value RES_OTH = “CVD Research” for non-DNA analysis, and for DNA analysis RES_DNA = “CVD Research” would be used? _Yes __ No
(This file ICTDER03 has been distributed to ARIC PIs, and contains the responses to consent updates related to stored sample use for research.)

8.a. Will the DNA data be used in this manuscript? _X_ Yes _X_ No

8.b. If yes, is the author aware that either DNA data distributed by the Coordinating Center must be used, or the file ICTDER03 must be used to exclude those with value RES_DNA = “No use/storage DNA”? _Yes _X_ No
8.c. If yes, is the author aware that the participants with RES_DNA = ‘not for profit’ restriction must be excluded if the data are used by a for profit group?  
____Yes     ____No

9. The lead author of this manuscript proposal has reviewed the list of existing ARIC Study manuscript proposals and has found no overlap between this proposal and previously approved manuscript proposals either published or still in active status. ARIC Investigators have access to the publications lists under the Study Members Area of the web site at: http://www.cscc.unc.edu/ARIC/search.php  
__X_ Yes     _______ No

10. What are the most related manuscript proposals in ARIC (authors are encouraged to contact lead authors of these proposals for comments on the new proposal or collaboration)? I am not aware of anything similar. ARIC has no CVD risk score.

11. a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data?  
__ Yes   __X__ No

11.b. If yes, is the proposal  
A. primarily the result of an ancillary study (list number* 2008.09)  
___  B. primarily based on ARIC data with ancillary data playing a minor role (usually control variables; list number(s)* __________ __________)

*ancillary studies are listed by number at http://www.cscc.unc.edu/aric/forms/

12. Manuscript preparation is expected to be completed in one to three years. If a manuscript is not submitted for ARIC review at the end of the 3-years from the date of the approval, the manuscript proposal will expire.

References
