Appendix 1. Definition of cases with age-related macular degeneration and controls included in this study

| First Author   | Eye examination and  | Type of cases  | Type of Controls   |
|----------------|--|--|--|
| (Year)         | definition of AMD  |  |  |
| Qu<br>(2011)   | Comprehensive ophthalmologic examination, including slit-lamp biomicroscopy, funduscopy, contact lens biomicroscopic examination of the retina, fluorescein and indocyanine green fundus angiography, and OCT. | Exudative AMD.   | Age, gender, and ethnicity matched without clinical evidence of AMD and without known family history of AMD. |
| Almeida (2011) | Complete clinical ophthalmic examination, including FA and OCT. Definition of AMD were based on the Clinical Age-Related Maculopathy Staging system.   | Nonexudative and exudative AMD.  Nonexudative AMD: Grade 2 (approximately ≥10 small drusen or <15 intermediate drusen, or pigment abnormalities associated with ARM),  Grade 3 (approximately ≥15 intermediate drusen or any large drusen), and Grade 4 (GA with involvement of the macular center, or noncentral geographic atrophy ≥ 350 µm in size).  Exudative AMD: Grade 5 (exudative AMD, including nondrusenoid pigment epithelial detachments, serous or hemorrhagic retinal detachments, CNVM with subretinal or sub-RPE hemorrhages or fibrosis, or scars consistent with treatment of AMD).  Patients with >10 small drusen or <15 intermediate drusen without RPE changes were excluded. | Age and gender matched without AMD.  |
| Immonen (2010) | Visual acuity assessment, biomicroscopy of the anterior and posterior parts of the   | Exudative AMD  | Age matched without signs of AMD (absence of drusen  |

| First Author          | Eye examination and   | Type of cases  | Type of Controls  |
|-----------------------|---|--|---|
| (Year)                | definition of AMD   |  |   |
|                       | eye, and FA. Definition of AMD were based on the records and the angiograms.  |  | of more than 63 µm, major pigmentary abnormalities, eccentric geographic atrophy, or late AMD characteristics) by fundus photography. |
| Galan<br>(2010)       | Detailed ophthalmic examination, including dilated fundus examination, fundus photographs, and FA. In selected cases, indocyanine green angiography was performed. Fundus findings in each eye were classified based on a standardized set of diagnostic criteria established by the International ARM Epidemiologic Study. | Neovascular AMD and nonneovascular (small drusen, large drusen, and GA) AMD.   | Gender and ethnicity matched without detectable drusen by dilated fundus examination and fundus photography.                          |
| Janik-Papis<br>(2009) | Ophthalmic examination, including best-corrected visual acuity, intraocular pressure, slit lamp examination, fundus examination. Diagnosis of AMD was confirmed by OCT and, in some cases, by FA and indocyanin green angiography.  | Atrophic and neovascular AMD.  | Age and gender matched without AMD.   |
| Francis<br>(2009)     | Ophthalmological evaluation and photographical document. Definition of AMD were based on the Age-Related Eye Disease study (AREDS) categories.  | Atrophic and neovascular AMD: AREDS category 4 (central GA or neovascular AMD in one eye or visual loss due to AMD regardless of lesion type). | Without AMD (no drusen larger than 63 μm in diameter).  |
| Lin (2008)            | Standard examination protocol including comprehensive medical and ophthalmic  | Atrophic and neovascular AMD.  | Age and gender matched without any type of drusen,  |

| First Author      | Eye examination and                          | Type of cases  | Type of Controls              |
|-------------------|--|--|-------------------------------|
| (Year)            | definition of AMD                            |  |                               |
|                   | history review, visual acuity, intraocular   |  | geographic atrophy, CNV, or   |
|                   | pressure measurement, slit-lamp              |  | other retinal disorder in     |
|                   | biomicroscopy, dilated fundus                |  | either eye revealed by fundus |
|                   | photographs, and FA. The diagnosis of        |  | photographs and FA, without   |
|                   | AMD was established on the basis of          |  | visual impairment and family  |
|                   | clinical examination, fundus photography,    |  | history of AMD.               |
|                   | and FA. Fundus findings in each eye were     |  |                               |
|                   | classified based on a standardized set of    |  |                               |
|                   | diagnostic criteria established by the       |  |                               |
|                   | International ARM Epidemiologic Study.       |  |                               |
| Richardson (2007) | Clinical examination                         | Early (the presence of soft drusen $>125~\mu m$ , with | Ethnicity and residence       |
|                   |  | or without regions of hyperpigmentation), GA, and      | matched without AMD           |
|                   |  | neovascular AMD  |                               |
| Churchill (2006)  | Visual acuity testing, anterior segment, and | AMD, secondary to CNVMs demonstrated by                | Age matched healthy           |
|                   | fundus examination.                          | fundus FA.   |                               |

OCT optical coherence tomography; FA fluorescein angiography; ARM age-related maculopathy; GA geographic atrophy; CNVM choroidal neovascular membrane