World Endometriosis Research Foundation Endometriosis Phenome and biobanking harmonization project: II. Clinical and covariate phenotype data collection in endometriosis research

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Received April 23, 2014; revised July 11, 2014; accepted July 24, 2014; published online September 22, 2014.

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A.F.V. has nothing to disclose. K.V. has received honoraria and travel expenses for lectures from Bayer Healthcare. N.R. has nothing to disclose. A.F. has nothing to disclose. G.M.B.L. has nothing to disclose. L.H. reports remuneration by WERF for project management. L.C.G. is an academic associate with Quest Diagnostics and is a non-remunerated Board member of WERF. P.S. has nothing to disclose. G.D.A. is CEO of Advanced Reproductive Care Inc., and has received research funds from Auxogyn, and consultancy for Bayer Healthcare, Glycotope, and Ziva, and is a non-remunerated Board member of WERF. C.M.B. has received research grants from Bayer Healthcare and consultancy fees from Roche Diagnostics. K.T.Z. is a member of scientific advisory boards for AbbVie Inc., Bayer HealthCare, and Roche Diagnostics, and has received honorarium for lectures from Bayer HealthCare. S.A.M. is a non-remunerated board member of WERF.

The other participants of the WERF EPHect Working Group make the following disclosures: C.A. is on the advisory boards of Actavis and Bayer Healthcare and the speakers bureau for Johnson & Johnson. K.C. is employed by AbbVie and holds stock in this company. T.M.D'H. has received research and travel grants from Ferring Pharmaceuticals and Merck Serono Merck, Besins, and Pharmaplex, and consultancy fees from Astellas, Bayer Healthcare, Proteomika, Roche Diagnostics, and Teva. A.F. has nothing to disclose. I.F. has nothing to disclose. T.F. is employed by Bayer Healthcare. M.G. has nothing to disclose. P.G. has nothing to disclose. S.-W.G. has nothing to disclose. T.H. has nothing to disclose. D.H. has nothing to disclose. A.W.H. has nothing to disclose. M.L.H. has nothing to disclose. M.G.I. has nothing to disclose. M.R.L. has nothing to disclose. L.K. has received speaker fees from Bayer Healthcare and consultancy fees from Roche Diagnostics. K.M. is employed by Bayer Healthcare; S.M. has nothing to disclose. G.W.M. has nothing to disclose. M.N. has nothing to disclose. A.N. has received consulting fees from Merck Serono and MSD. K.G.O. has nothing to disclose. C.A.P is a consultant for Bayer Healthcare and is a non-remunerated Board member of WERF. P.A.R. has nothing to disclose. L.R is a non-remunerated Board member of WERF. S.P.R. has received consultancy fees from Roche Diagnostics, Gedeon- Richter, and Ethicon, and honorarium for lectures from Jenapharm. J.R. is employed by Roche Diagnostics GmbH. S.R. is employed by Bayer Healthcare. A.S. has nothing to disclose. T.S. has nothing to disclose. K.L.S.-T. has nothing to disclose. E.S. has received honoraria from Ethicon and Gedeon- Richter for providing training to healthcare professionals. U.-H.W.-T. is employed by Roche Diagnostics GmbH. S.S.T. has nothing to disclose. P.V. has a consultancy for Roche Diagnostics. P.P.Y. is a consultant for Lumenis. P.Y. has nothing to disclose.

A.F.V., K.V., N.R., and A.F. should be considered similar in author order. C.M.B., K.T.Z, and S.A.M. jointly directed this work.

This work was funded by the World Endometriosis Research Foundation through grants from AbbVie, Bayer Pharma AG, and Roche Diagnostics International Ltd.; a Wellcome Trust Career Development Fellowship (grant no. WT085235/Z/08/Z, to K.T.Z.); in part by the J. Willard and Alice S. Marriott Foundation contribution to the Boston Center for Endometriosis (S.A.M. and A.F.V.), and a *Eunice Kennedy Shriver* National Institute of Child Health and Human Development Grant (grant no. HD57210, to S.A.M.); the Intramural Program of the NIH and the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (to G.M.B.L. and P.S.); an MRC grant (grant no. MR/K011480/1, to N.R.); the Oxford Partnership Comprehensive Biomedical Research Centre with funding from the Department of Health's NIHR Biomedical Research Centres Scheme (to C.M.B.); the Puerto Rico Science and Technology Trust (grant no. 2013-000032, to I.F.); a scholarship from the Ernst Schering Foundation and an Elsa Neumann Stipendium des Landes Berlin (to M.G.I.); an NIHR Academic Clinical Lecturer Award (to K.V.); grants from the Chief Scientist Office Scotland, Wellbeing of Women, and HTA (to A.W.H.); a grant from the Endometriosis Association (to K.G.O.); and the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development Specialized Cooperative Centers Program in Reproduction and Infertility Research (grant no. U54HD 055764, to L.C.G.).

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Fertility and Sterility® Vol. 102, No. 5, November 2014 0015-0282/$36.00

http://dx.doi.org/10.1016/j.fertnstert.2014.07.1244

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Objective: To harmonize the collection of nonsurgical clinical and epidemiologic data relevant to endometriosis research, allowing large-scale collaboration.
Design: An international collaboration involving 34 clinical/academic centers and three industry collaborators from 16 countries on five continents.
Setting: In 2013, two workshops followed by global consultation, bringing together 54 leaders in endometriosis research.
Patients: None.
Intervention(s): Development of a self-administered endometriosis patient questionnaire (EPQ), based on [1] systematic comparison of questionnaires from eight centers that collect data from endometriosis cases (and controls/comparison women) on a medium to large scale (publication on >100 cases); [2] literature evidence; and [3] several global consultation rounds.
Main Outcome Measure(s): *Standard recommended* and *minimum required* questionnaires to capture detailed clinical and covariate data.
Result(s): The *standard recommended* (EPHect EPQ-S) and *minimum required* (EPHect EPQ-M) questionnaires contain questions on pelvic pain, subfertility and menstrual/reproductive history, hormone/medication use, medical history, and personal information.
Conclusion(s): The EPQ captures the basic set of patient characteristics and exposures considered by the WERF EPHect Working Group to be most critical for the advancement of endometriosis research, but is also relevant to other female conditions with similar risk factors and/or symptomatology. The instruments will be reviewed based on feedback from investigators, and—after a first review after 1 year—triannually through systematic follow-up surveys. Updated versions will be made available through http://endometriosisfoundation.org/ephect. (Fertil Steril® 2014;102:1223–32. ©2014 by American Society for Reproductive Medicine.)

Key Words: Endometriosis, EPHect EPQ, pelvic pain, questionnaire, standardization, symptoms

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It is generally accepted that endometriosis is a heterogeneous disease with respect to its natural history, disease burden, extent of inflammation, state of progression, and phenotypic presentation of lesions and symptoms. The variability of patient "types" included in endometriosis research studies is not solely determined by the surgical characterization of the (extent of) disease during laparoscopy (1). There are important nonsurgical aspects that characterize patient (sub)populations, including symptomatology (onset, duration, extent and severity of symptoms, comorbidity) and other nonsymptomatic phenotypes such as anthropometric characteristics, ethnicity, and reproductive and demographic factors. These are important to consider in any endometriosis research study, and it may be that the inclusion of different patient populations in studies, which cannot be adequately defined or recognized as they have been poorly characterized, has led to conflicting results between studies of different populations (2).

To study phenotypic variation in endometriosis successfully, studies need to include sufficient numbers of patients to allow for the detection of differences between subphenotype groups with adequate statistical power. Collaboration and pooling of individual participant data across research centers can enable much larger sample sizes, can afford subgroup analyses, and is more effective than meta-analyses (3). However, data are often not collected in a manner that allows them to be prospectively or retrospectively compared. For example, in a study attempting to retrospectively pool epidemiologic data from 53 large population-based studies of >10,000 individuals, part of the P3G collaborative network (www.p3gobservatory.org), 47% of the variables studied were impossible to match (4). Given the variation in quality and complexity of the data collected across disparate centers, data pooling may not always be feasible, which can impede scientific progress. Moreover, standardization and harmonization of phenotypic data and biologic sample collection methods are crucial to allow meaningful comparison between different patient populations and (ethnic) groups in endometriosis research, and will aid the scientific inquiry into the etiology and pathogenesis of the disease. Indeed, successful, field-altering risk-factor and subphenotype investigations among many centers have been demonstrated by large consortia across an array of health outcomes (5–11).

The mission of the World Endometriosis Research Foundation (WERF) Endometriosis Phenome and Biobanking Harmonisation Project (EPHect) is to develop a consensus