



## No Difference in Colorectal Cancer Incidence or Stage at Detection by Colonoscopy Among 3 Countries With Different Lynch Syndrome Surveillance Policies

Christoph Engel,<sup>1,\*</sup> Hans F. Vasen,<sup>2,\*</sup> Toni Seppälä,<sup>3,\*</sup> Stefan Aretz,<sup>4,5</sup> Marloes Bigirwamungu-Bargeman,<sup>6</sup> Sybrand Y. de Boer,<sup>7</sup> Karolin Bucksch,<sup>1</sup> Reinhard Büttner,<sup>8</sup> Elke Holinski-Feder,<sup>9,10</sup> Stefanie Holzapfel,<sup>4,5</sup> Robert Hüneburg,<sup>5,11</sup> Maarten A. J. M. Jacobs,<sup>12</sup> Heikki Järvinen,<sup>3</sup> Matthias Kloor,<sup>13,14</sup> Magnus von Knebel Doeberitz,<sup>13,14</sup> Jan J. Koornstra,<sup>15</sup> Mariette van Kouwen,<sup>16</sup> Alexandra M. Langers,<sup>17</sup> Paul C. van de Meeberg,<sup>7</sup> Monika Morak,<sup>9,10</sup> Gabriela Möslein,<sup>18</sup> Fokko M. Nagengast,<sup>16</sup> Kirsi Pylvänäinen,<sup>19</sup> Nils Rahner,<sup>20</sup> Laura Renkonen-Sinisalo,<sup>3</sup> Silvia Sanduleanu,<sup>21</sup> Hans K. Schackert,<sup>22</sup> Wolff Schmiegel,<sup>23</sup> Karsten Schulmann,<sup>24</sup> Verena Steinke-Lange,<sup>9,10</sup> Christian P. Strassburg,<sup>5,11</sup> Juda Vecht,<sup>25</sup> Marie-Louise Verhulst,<sup>26</sup> Wouter de Vos tot Nederveen Cappel,<sup>25</sup> Silke Zachariae,<sup>1</sup> Jukka-Pekka Mecklin,<sup>27,28,§</sup> and Markus Loeffler,<sup>1,§</sup> on behalf of the German HNPCC Consortium, the Dutch Lynch Syndrome Collaborative Group, and the Finnish Lynch Syndrome Registry

<sup>1</sup>Institute for Medical Informatics, Statistics and Epidemiology, University of Leipzig, Leipzig, Germany; <sup>2</sup>Department of Gastroenterology and Hepatology, Leiden University Medical Centre, Leiden, The Netherlands; <sup>3</sup>Department of Abdominal Surgery, Helsinki University Hospital, Helsinki, Finland; <sup>4</sup>Institute of Human Genetics, University of Bonn, Bonn, Germany; <sup>5</sup>Center for Hereditary Tumor Syndromes, University Hospital Bonn, Bonn, Germany; <sup>6</sup>Department of Gastroenterology and Hepatology, Medisch Spectrum Hospital, Enschede, The Netherlands; <sup>7</sup>Department of Gastroenterology and Hepatology, Slingeland Hospital, Doetinchem, The Netherlands; <sup>8</sup>Institute of Pathology, University of Cologne, Cologne, Germany; <sup>9</sup>Medizinische Klinik und Poliklinik IV, Campus Innenstadt, Klinikum der Universität München, Munich, Germany; <sup>10</sup>Center of Medical Genetics, Munich, Germany; <sup>11</sup>Department of Internal Medicine I, University Hospital Bonn, Bonn, Germany; <sup>12</sup>Department of Gastroenterology and Hepatology, Free University Medical Centre, Amsterdam, The Netherlands; <sup>13</sup>Department of Applied Tumour Biology, Institute of Pathology, University Hospital Heidelberg, Heidelberg, Germany; <sup>14</sup>Cooperation Unit Applied Tumour Biology, German Cancer Research Center (DKFZ), Heidelberg, Germany; <sup>15</sup>Department of Gastroenterology and Hepatology, University Medical Centre Groningen, University of Groningen, Groningen, The Netherlands; <sup>16</sup>Department of Gastroenterology and Hepatology, Radboud University Medical Centre, Nijmegen, The Netherlands; <sup>17</sup>Department of Gastroenterology and Hepatology, Leiden University Medical Centre, Leiden, The Netherlands; <sup>18</sup>Center for Hereditary Tumors, HELIOS Klinikum Wuppertal, University Witten-Herdecke, Wuppertal, Germany; <sup>19</sup>Department of Education and Research, Jyväskylä Central Hospital, Jyväskylä, Finland; <sup>20</sup>Institute of Human Genetics, Medical Faculty, Heinrich-Heine-University, Düsseldorf, Germany; <sup>21</sup>Department of Gastroenterology and Hepatology, University Medical Centre Maastricht, Maastricht, The Netherlands; <sup>22</sup>Department of Surgical Research, Technische Universität Dresden, Dresden, Germany; <sup>23</sup>Department of Medicine, Knappschaftskrankenhaus, Ruhr-University Bochum, Bochum, Germany; <sup>24</sup>Department of Internal Medicine, Hematology and Oncology, Klinikum Arnsberg, Arnsberg, Germany; <sup>25</sup>Department of Gastroenterology and Hepatology, Isala Clinics, Zwolle, The Netherlands; <sup>26</sup>Department of Gastroenterology and Hepatology, Maxima Medical Centre, Eindhoven, The Netherlands; <sup>27</sup>Departments of Education and Research and Surgery, Jyväskylä Central Hospital, Jyväskylä, Finland; and <sup>28</sup>Sports and Health Sciences, Jyväskylä University, Jyväskylä, Finland

**BACKGROUND & AIMS:** Patients with Lynch syndrome are at high risk for developing colorectal cancer (CRC). Regular colonoscopic surveillance is recommended, but there is no international consensus on the appropriate interval. We investigated whether shorter intervals are associated with lower CRC incidence and detection at earlier stages by comparing the surveillance policies in Germany, which evaluates patients by colonoscopy annually, in the Netherlands (patients evaluated at 1–2-year intervals), and Finland (patients evaluated at 2–3-year intervals). **METHODS:** We collected data from 16,327 colonoscopic examinations (conducted from 1984 through 2015) of 2747 patients with Lynch syndrome (pathogenic variants in the *MLH1*, *MSH2*, or *MSH6* genes) from the German HNPCC Consortium, the Dutch Lynch Syndrome Registry, and the Finnish Lynch Syndrome Registry. Our analysis included

23,309 person-years of cumulative observation time. Time from the index colonoscopy to incident CRC or adenoma was analyzed using the Kaplan-Meier method; groups were compared using the log-rank test. We performed multivariable Cox regression analyses to identify factors associated with CRC risk (diagnosis of CRC before the index colonoscopy, sex, mutation, age, and presence of adenoma at the index colonoscopy). **RESULTS:** The 10-year cumulative CRC incidence ranged from 4.1% to 18.4% in patients with low- and high-risk profiles, respectively, and varied with age, sex, mutation, and prior detection of CRC or adenoma. Observed colonoscopy intervals were largely in accordance with the country-specific recommendations. We found no significant differences in cumulative CRC incidence or CRC stage at detection among countries. There was no significant association between CRC stage and