A score to estimate the likelihood of detecting advanced colorectal neoplasia at colonoscopy

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ABSTRACT
Objective This study aimed to develop and validate a model to estimate the likelihood of detecting advanced colorectal neoplasia in Caucasian patients.

Design We performed a cross-sectional analysis of database records for 40-year-old to 66-year-old patients who entered a national primary colonoscopy-based screening programme for colorectal cancer in 73 centres in Poland in the year 2007. We used multivariate logistic regression to investigate the associations between clinical variables and the presence of advanced neoplasia in a randomly selected test set, and confirmed the associations in a validation set. We used model coefficients to develop a risk score for detection of advanced colorectal neoplasia.

Results Advanced colorectal neoplasia was detected in 2544 of the 35 918 included participants (7.1%). In the test set, a logistic-regression model showed that independent risk factors for advanced colorectal neoplasia were: age, sex, family history of colorectal cancer, cigarette smoking (p<0.001 for these four factors), and Body Mass Index (p=0.033). In the validation set, the model was well calibrated (ratio of expected to observed risk of advanced neoplasia: 1.00 (95% CI 0.95 to 1.06)) and had moderate discriminatory power (c-statistic 0.62). We developed a score that estimated the likelihood of detecting advanced neoplasia in the validation set, from 1.32% for patients scoring 0, to 19.12% for patients scoring 7–8.

Conclusions Developed and internally validated score consisting of simple clinical factors successfully estimates the likelihood of detecting advanced colorectal neoplasia in asymptomatic Caucasian patients. Once externally validated, it may be useful for counselling or designing primary prevention studies.

INTRODUCTION
The strength of evidence regarding the efficacy of colorectal cancer screening in reducing the incidence of colorectal cancer and associated mortality is increasing.1,2 Colorectal cancer screening is currently recommended in the European Union3; however, adherence to this recommendation is not sufficient.4–6 One of the most important barriers to screening is a lack of perceived risk of colorectal cancer among average-risk patients and primary care providers.7–8 The risk of colorectal cancer or advanced colorectal neoplasia varies with regard to several factors, including age,9–11 sex,10–12 family history of colorectal cancer,13–15 smoking,14–15 obesity,11–16 diabetes mellitus,17 long-term non-steroid anti-inflammatory drug use,15–18 diet15–19 and physical activity.15–16 Information about some of these factors is easy to obtain and could be used to indentify patients at high-average risk of advanced colorectal neoplasia who are likely to benefit the most from screening. This high-average risk population should be the target of most intensive participation improvement interventions and primary prevention studies.

We performed a cross-sectional analysis of data from a national colonoscopy screening programme to derive and validate a risk prediction model for detection of advanced colorectal neoplasia. The results of the model were used to develop a simple...
scoring system that estimates the likelihood of detecting advanced colorectal neoplasia in asymptomatic patients.

METHODS

Study design and oversight
We performed a cross-sectional analysis of database records for 40-year-old to 66-year-old patients who entered the national colonoscopy screening programme for colorectal cancer in Poland, from January 2007 through December 2007. The database contained demographic data, colonoscopy and histopathology results, follow-up information, and the results of an epidemiological questionnaire on potential risk factors for advanced colorectal neoplasia from 73 screening centres throughout Poland.

The research proposal was reviewed by the Research Ethical Committee at the authors’ institution and was judged to be exempt from oversight. Written informed consent was obtained from all participants entering the National Colorectal Cancer Screening Program.

Study population
Patients between the ages of 50 years and 66 years (40 years and 66 years in case of positive family history of cancer of any type) were advised by their family or general practitioners to participate in the screening. Exclusion criteria were clinical suspicion of colorectal cancer; characteristics that met the criteria for Lynch syndrome, familial adenomatous polyposis, or inflammatory bowel disease; and colonoscopy within the preceding 10 years. For this study, we excluded patients who had screening-detected polyps 10 mm or larger that were not removed (hence histology was unavailable) and patients who had not fully completed the epidemiological questionnaire.

Study procedures and definitions
Patients eligible for screening were asked to complete the epidemiological questionnaire regarding the following potential risk factors for advanced colorectal neoplasia: age, sex, weight and height (to calculate Body Mass Index), family history of colorectal cancer in first-degree relatives, diabetes mellitus, smoking history (number of years of smoking, number of cigarettes smoked per day, and current smoking status), and regular aspirin use (for at least 3 months at any dose). Information about physical activity, diet, other than aspirin non-steroid anti-inflammatory drug use and alcohol consumption were not collected.

Screening colonoscopy procedures have been described elsewhere. All screening colonoscopists and histopathologists participated in the quality assurance programme. Colorectal findings were categorised on the basis of the most advanced lesion identified at screening (including additional required colonoscopies to remove all polyps, when indicated). Advanced neoplasia was defined as cancer or adenoma that was at least 10 mm in diameter, had high-grade dysplasia, had villous or tubulovillous histologic characteristics, or any combination thereof. For the purpose of the analysis, traditional serrated adenomas, sessile serrated lesions, and mixed serrated polyps were categorised as tubular adenomas. Polyps <10 mm in size that were not removed or retrieved were categorised as non-neoplastic.

The following predefined categories of variables were used to analyse the risk factors for detecting advanced neoplasia: age (40–49, 50–54, 55–59, or 60–66 years), sex, family history of colorectal cancer (none, one first-degree relative ≥60 years of age with colorectal cancer, one first-degree relative <60 years of age with colorectal cancer, or two first-degree relatives with colorectal cancer), pack-years smoked (none, <10, 10–19, or ≥20 pack-years), diabetes mellitus (yes or no), Body Mass Index (<25, 25–29, or ≥30 kg/m²), and regular aspirin use (yes or no). We performed a sensitivity analysis using age as a continuous variable and compared its discriminatory power with the model using age as a categorised variable.

Statistical analysis
The original dataset was randomly partitioned in a 1:1 ratio to generate a test set and a validation set, while controlling for the distribution of the most advanced lesions. A multivariate logistic regression model was used to investigate the relation between clinical variables and the presence of advanced neoplasia in the test set. The likelihood ratio test was used to determine a significant association of a particular variable with the presence of advanced neoplasia and the interaction between variables. For statistically significant effects, the OR and 95% CI were reported for each predefined category of variables. The model was internally validated using the validation set. The Hosmer–Lemeshow test was used to check the goodness-of-fit of the models.

The calibration of the model was assessed using the validation set by comparing the expected and observed numbers of patients with advanced neoplasia, overall and for each category of variables. Homogeneous participant groups were defined by all combinations of categories of significant predictors. The expected number of patients with advanced neoplasia for each homogeneous group of study participants was calculated by summing the estimated individual absolute risk predicted by the model developed on the test set. The 95% CIs for the expected to observed ratio were calculated by using normal approximations to Poisson distributions.

The concordance statistic was used to measure models’ discrimination among patients with and without advanced neoplasia. For binary logistic regression models, the concordance statistic is equivalent to the area under the receiver-operating characteristic curve.

The results of the multivariate logistic regression model were used to develop a risk score for detecting advanced neoplasia in asymptomatic patients. Model-adjusted coefficients were rounded up to the nearest one-half integer and then multiplied by two to avoid decimals. The performance of the risk score was assessed in the validation set using the concordance statistic. A p value <0.05 was considered statistically significant. All reported p values are two-sided and not adjusted for multiple testing. The analyses were performed using Stata Statistical Software, V.10 (Stata Corporation, College Station, Texas, USA).

RESULTS

Study participants
Of the 39,265 patients who met the eligibility criteria and underwent colonoscopy in one of the 73 screening centres between January and December 2007, 3,347 (8.5%) were excluded, due to incomplete questionnaire feedback (3,242 screened participants, 8.3%) or polyps measuring ≥10 mm that were not removed (105 screened participants, 0.3%).

The remaining 35,918 patients, 22,164 women (61.7%) and 13,754 men (38.3%), all Caucasians, had a mean age of 53.6 ± 5.2 years. Of the 35,918 patients, 6,897 (19.2%) had a family history of colorectal cancer, 15,678 (43.7%) had history of smoking, 1,440 (4.0%) had diabetes mellitus, 7,931 (22.1%) had a Body Mass Index ≥35 kg/m², and 4,623 (12.9%) reported...
regular use of aspirin. The characteristics of the study population are summarised in table 1.

Colonoscopy results
Colonoscopy was completed to the caecum in 34 469 patients (96.0%). A total of 6909 patients (19.2%) had an adenoma or cancer. A total of 232 patients (0.6%) had polyps <10 mm in size that were not removed or retrieved, hence were categorised as non-neoplastic abnormalities. Advanced neoplasia was detected in 2544 patients (7.1%), including 336 participants (0.9%) with adenocarcinoma (table 1). Clinically significant complications requiring medical intervention occurred in 42 patients (0.1%) and included seven cases of perforation (three of which occurred after polypectomy), 21 episodes of bleeding, nine cardiovascular events, and five other events. No deaths occurred as a result of screening colonoscopy or its complications.

Model for the detection of advanced neoplasia
The test and validation sets consisted of 17 979 and 17 939 patients, respectively. We built the multivariate logistic regression model and used the test set to investigate the predictors of detecting advanced neoplasia. The results of the likelihood ratio test indicated significant association between the risk of detecting advanced neoplasia and the following variables: age, sex, family history of colorectal cancer, cigarette smoking and Body Mass Index (table 2). It also revealed significant association of the interaction between sex and Body Mass Index and the risk of detecting advanced neoplasia. The following insignificant variables were reduced from the model: diabetes and regular aspirin use (likelihood ratio test, p values equalling 0.24 and

| Table 1 Demographic and colonoscopy characteristics for the 35 918 study participants* |
|---------------------------------|---------------------------------|------------------|
| Characteristic                  | All (N=35 918)                  | Women (N=22 164) | Men (N=13 754) |
| Age, years                      |                                 |                  |
| Range                           | 40–66                           | 40–66            | 40–66          |
| Mean (SD)                       | 55.6 (5.2)                      | 55.6 (5.1)       | 55.6 (5.3)     |
| Age group, n (%)                |                                 |                  |
| 40–49                           | 3606 (10.0)                     | 2125 (9.6)       | 1481 (10.8)    |
| 50–54                           | 11 000 (30.6)                   | 6818 (30.8)      | 4182 (30.4)    |
| 55–59                           | 12 379 (34.5)                   | 7788 (35.1)      | 4591 (33.4)    |
| 60–66                           | 8933 (24.9)                     | 5433 (24.5)      | 3500 (25.4)    |
| Family history of CRC, n (%)    |                                 |                  |
| None                            | 29 021 (80.8)                   | 17 846 (80.5)    | 11 175 (81.2)  |
| One first-degree relative ≥60 years of age with CRC | 4798 (13.4) | 3000 (13.5) | 1798 (13.1) |
| One first-degree relative <60 years of age with CRC | 1809 (5.0) | 1121 (5.1) | 688 (5.0) |
| Two first-degree relatives with CRC | 290 (0.8) | 197 (0.9) | 93 (0.7) |
| Smoking history, pack-years†, n (%) |                  |                  |
| None                            | 20 240 (56.4)                   | 13 737 (62.0)    | 6503 (47.3)    |
| <10                             | 4755 (13.2)                     | 3291 (14.8)      | 1464 (10.6)    |
| 10–19                           | 4576 (12.7)                     | 2663 (12.0)      | 1913 (13.9)    |
| ≥20                             | 6347 (17.7)                     | 2473 (11.2)      | 3874 (28.2)    |
| Diabetes mellitus, n (%)        |                                 |                  |
| No                              | 34 478 (96.0)                   | 21 404 (96.6)    | 13 074 (95.1)  |
| Yes                             | 1440 (4.0)                      | 760 (3.4)        | 680 (4.9)      |
| BMI (kg/m²), n (%)              |                                 |                  |
| <25                             | 11 439 (31.9)                   | 8258 (37.3)      | 3181 (23.1)    |
| 25–29                           | 16 548 (46.1)                   | 9190 (41.5)      | 7358 (53.5)    |
| ≥30                             | 7931 (22.1)                     | 4716 (21.3)      | 3215 (23.4)    |
| Regular aspirin use, n (%)      |                                 |                  |
| No                              | 28 960 (80.6)                   | 18 110 (81.7)    | 10 850 (78.9)  |
| Yes                             | 4623 (12.9)                     | 2590 (11.7)      | 2033 (14.8)    |
| Not available                   | 2335 (6.5)                      | 1464 (6.6)       | 871 (6.3)      |
| Total colonoscopy, n (%)        | 34 469 (96.0)                   | 21 078 (95.1)    | 13 391 (97.4)  |
| Adequate bowel preparation‡, n (%) | 33 909 (94.4) | 20 942 (94.5) | 12 967 (94.3) |
| Intravenous sedation, n (%)     | 20 850 (58.1)                   | 13 565 (61.2)    | 7380 (53.7)    |
| Main colonoscopy findings, n (%) |                                 |                  |
| None                            | 14 415 (40.1)                   | 9601 (43.3)      | 4814 (35.0)    |
| Non-neoplastic abnormalities    | 14 594 (40.6)                   | 9171 (41.4)      | 5423 (39.4)    |
| Non-advanced neoplasia§         | 4365 (12.2)                     | 2207 (10.0)      | 2158 (15.7)    |
| Advanced neoplasia¶             | 2544 (7.1)                      | 1185 (5.3)       | 1359 (9.9)     |

* Because of rounding, percentages may not total 100.
† Regardless of current smoking status.
‡ Bowel preparation was assessed by endoscopists.
§ Includes 232 patients with polyps <10 mm in size that were not removed or retrieved.
¶ Advanced neoplasia was defined as a cancer or adenoma that was ≥10 mm in diameter, had high-grade dysplasia, had a villous component, or any combination thereof.
BMI, Body Mass Index; CRC, colorectal cancer.
of the model (0.64, 95% CI 0.63 to 0.66; continuous variable showed comparable concordance statistics. A sensitivity analysis performed in a test set, with age as
and 0.62 for the validation set, indicating moderate discrimin-
concordance statistics of the model were 0.64 for the test set
(95% CI 0.91 to 1.06) in men, indicating good calibration. The
observed risk of advanced neoplasia was 1.00 (95% CI 0.95 to

Table 2  Associations between individual characteristics and advanced colorectal neoplasia in a multivariable analysis and development of the
score (test set, N=17 979)

| Covariates| LR test*| Adjusted OR (95% CI) p Value Adjusted β coefficient† Risk score‡ |
|---|---|---|---|---|---|
| Age group, years| <0.001| | | | |
| 40–49| 1| 0.002| 0| 0| |
| 50–54| 1.53 (1.16 to 2.02) <0.001| 0.43| 1| |
| 55–59| 2.29 (1.75 to 3.00) <0.001| 0.83| 2| |
| 60–66| 3.14 (2.40 to 4.12) <0.001| 1.15| 3| |
| Family history of CRC| <0.001| | | | |
| None| 1| <0.001| 0| 0| |
| One first-degree relative with CRC, aged ≥60 years| 1.40 (1.17 to 1.67) <0.001| 0.34| 1| |
| One first-degree relative with CRC, aged <60 years| 1.66 (1.28 to 2.17) 0.008| 0.51| 2| |
| Two first-degree relatives with CRC| 2.11 (1.22 to 3.66) 0.75| 2| |
| Sex| <0.001| | | | |
| Female| 1| <0.001| 0| 0| |
| Male| 2.14 (1.71–2.67) 0.76| 2| |
| Smoking history, pack-years§| <0.001| | | | |
| None| 1| 0.654| 0| 0| |
| <10| 1.05 (0.86 to 1.27) 0.001| 0| 0| |
| 10–19| 1.34 (1.12 to 1.59) <0.001| 0.30| 1| |
| ≥20| 1.60 (1.39 to 1.85) 0.47| 1| |
| BMI (kg/m²) 0.033| | | | | |
| <25| 1| 0.192| 0| 0| |
| 25–29| 1.14 (0.94 to 1.38) 0.008| 0| 0| |
| ≥30| 1.34 (1.08 to 1.67) 0.081| 0.30| 1| |
| Interaction with male sex**| | | | | |
| 25–29| 0.78 (0.59 to 1.03) 0.031| 0| |
| ≥30| 0.70 (0.51 to 0.97) <0.001| −0.35| |

*LR test, the likelihood ratio test for models with and without the specified covariate.
†Non-significant covariates were assigned β coefficient=0.
‡Model-adjusted coefficients were rounded up to the nearest one-half integer and then multiplied by two to avoid decimals.
§Regardless of current smoking status.
¶1 point for female sex and 0 point for male sex.
**Significant interaction was shown only between male sex and BMI.
BMI, Body Mass Index; CRC, colorectal cancer; LR, likelihood ratio test.

0.95, respectively). Table 2 depicts the ORs and 95% CI for
each category of a significant variable. Tests for goodness-of-fit
of the models in the test and validation datasets permitted
acceptance of the fit (p values equalling 0.74 and 0.16,
respectively).

The results of the model calibration performed in the valid-
ation dataset are shown in table 3. The ratio of expected to
observed risk of advanced neoplasia was 1.00 (95% CI 0.95 to
1.06) overall, 1.03 (95% CI 0.97 to 1.12) in women, and 0.98
(95% CI 0.91 to 1.06) in men, indicating good calibration. The
concordance statistics of the model were 0.64 for the test set
and 0.62 for the validation set, indicating moderate discrimina-
tion. A sensitivity analysis performed in a test set, with age as
continuous variable showed comparable concordance statistics
of the model (0.64, 95% CI 0.63 to 0.66; χ² p value=0.82).

The score to predict detection of advanced colorectal neoplasia

The adjusted β coefficients of the logistic regression model fitted
on the test set were used to develop the risk score by estimating
the likelihood of detecting advanced neoplasia for each category
of significant factors (see table 2). The scores for Body Mass
Index ≥30 kg/m² for different sexes were adjusted according to
the interaction coefficient. The score calculated for each person
from the validation set estimated the likelihood of detecting
advanced neoplasia from 1.32% for patients with a score of 0 to
19.12% for patients with scores of seven and eight (figure 1). The
performance characteristics of the score in the validation set
are shown in table 4. The concordance statistic for the simpli-
fied score in the validation set was 0.62 (95% CI 0.60 to 0.64); the
course of the receiver operating characteristics curve is shown in
online supplementary figure S1. Online supplementary table S1
depicts the ratio of expected to observed risk for advanced colo-
rectal neoplasia in the validation set by simplified score.

DISCUSSION

Our previous study found that male sex, age of 50 years or
more and family history of colorectal cancer were independent
risk factors for detecting advanced colorectal neoplasia.10 In the
ensuing discussion, it has been suggested that the observed dis-
parity of advanced neoplasia risk between men and women
might have merely reflected sex-based differences in smoking
patterns.23 In the present study, we used a new dataset to derive
and validate a model for the detection of advanced colorectal
neoplasia that included smoking status and other potential con-
founders, such as age, sex, family history of colorectal cancer,
and Body Mass Index. We confirmed previously identified asso-
ciations, and also found that smoking ≥10 pack-years, and Body
Mass Index ≥30 kg/m² were independent risk factors for detect-
ing advanced colorectal neoplasia. Our study corroborated pre-
viously identified risk factors for advanced colorectal neoplasia;10–16 it also, for the first time, combined all five

Kaminski MF, et al. Gut 2014;63:1112–1119. doi:10.1136/gutjnl-2013-304965 1115
important factors and their categories in a multivariate analysis and confirmed obtained results in a validation set.

The present model was well calibrated overall, as well as in men and women, as verified in the validation set, which means that the observed risk of advanced colorectal neoplasia well fitted the expected risk. Therefore, we used the model to develop a simple score for the detection of advanced colorectal neoplasia in asymptomatic patients. The score, based on age, sex, family history of colorectal cancer, smoking status and Body Mass Index, estimated the likelihood of detecting advanced colorectal neoplasia in the validation set from 1.32% to 19.12% in patients with 0 to 7–8 points, respectively. The estimation of individual risk of detecting advanced colorectal neoplasia may help asymptomatic patients and healthcare providers to make informed decisions about screening.26 For example, the likelihood of detecting advanced colorectal neoplasia in a 53-year-old, overweight, never-smoking woman, with one first-degree relative 60 years of age or older with colorectal cancer, is difficult to compare with that of a 56-year-old man who smoked for 20 pack-years, but has healthy weight and no family history of colorectal cancer. However, based on the results of the present model, the respective likelihood of detecting advanced neoplasia for two such patients are 4.65% and 12.46% (or 4.57% and 11.27%, respectively, using simplified scoring). Such results do not mean that one should discourage the woman from participation in an existing screening programme in a given country aiming at average risk group; rather they indicate that the man should be especially encouraged to be screened, because the likelihood of detecting advanced neoplasia in his colorectum is almost twice that of the average screening population. For ease of clinical application, the present model could be transformed into an online calculator of the likelihood of detecting advanced colorectal neoplasia and used in mobile easy access media. Although lack of symptoms and low perceived risk of colorectal cancer are considered major barriers to screening,7 it is unknown, whether providing the

| Variables                  | Observed risk | Expected risk | Expected to observed ratio (95% CI) |
|----------------------------|---------------|---------------|------------------------------------|
| Overall                    | 1270          | 1275.3        | 1.00                               |
| Sex                        |               |               |                                    |
| Female                     | 582           | 601.5         | 1.03                               |
| Male                       | 688           | 673.8         | 0.98                               |
| Age group, years           |               |               |                                    |
| 40–49                      | 83            | 76.2          | 0.92                               |
| 50–54                      | 331           | 280.1         | 0.85                               |
| 55–59                      | 443           | 468.6         | 1.06                               |
| 60–66                      | 413           | 450.4         | 1.09                               |
| Family history of CRC      |               |               |                                    |
| None                       | 1028          | 1010.2        | 0.98                               |
| One first-degree relatives |               |               |                                    |
| with CRC, aged ≥60 years   | 170           | 176.9         | 1.04                               |
| One first-degree relatives |               |               |                                    |
| with CRC, aged <60 years   | 57            | 69.6          | 1.22                               |
| Two first-degree relatives |               |               |                                    |
| with CRC                   | 15            | 18.6          | 1.24                               |
| Smoking history, pack-years* |             |               |                                    |
| None                       | 582           | 609.5         | 1.05                               |
| <10                        | 164           | 141.9         | 0.87                               |
| 10–19                      | 200           | 185.7         | 0.93                               |
| ≥20                        | 324           | 338.2         | 1.04                               |
| Women BMI, kg/m²            |               |               |                                    |
| <25                        | 219           | 193.3         | 0.88                               |
| 25–29                      | 234           | 256.5         | 1.10                               |
| ≥30                        | 129           | 151.6         | 1.18                               |
| Men BMI, kg/m²              |               |               |                                    |
| <25                        | 161           | 158.7         | 0.99                               |
| 25–29                      | 331           | 344.1         | 1.04                               |
| ≥30                        | 196           | 171.0         | 0.87                               |

*Regardless of current smoking status.

BMI, Body Mass Index; CRC, colorectal cancer.

Figure 1 The prevalence of advanced colorectal neoplasia or cancer in the complete dataset (N=35 918) by simplified score. Advanced neoplasia includes advanced adenomas and cancers. Due to small sample sizes, risk scores 7 and 8 are presented together.
estimate of individual risk could facilitate the informed decision to undergo endoscopy screening in a similar way as it worked for prostate cancer screening. It is particularly unknown, what kind of effect on participation in screening, would have the lower than average estimate of likelihood of detecting advanced colorectal neoplasia.

Another potential application of a model for the detection of advanced colorectal neoplasia is to guide practical recommendations for mass screening; however, this application would require a model with high discriminatory power. The present model had only moderate concordance statistic value, comparable to that of previously published models for the detection of advanced colorectal neoplasia in Western populations, even though the present model included more risk factors than previous models did. Three issues may explain this observation. First, the model of Betes et al lacked validation, which may have led to overestimation of its discriminatory power. Second, the models of Betes et al and Lin et al were derived from populations with a broader age range, which may have increased their discriminatory power, because age is the most powerful clinical risk factor for advanced colorectal neoplasia. Third, additional independent risk factors included in the present model were too weak to significantly change its discriminatory power. The models for the detection of advanced colorectal neoplasia in East Asian populations demonstrated variable discriminatory power. The model by Yeoh et al demonstrated discriminatory power comparable to that achieved in Western populations, while the model by Cai et al demonstrated better discrimination. The latter model missed family history of colorectal cancer but included various dietary factors, which (in contrast to previous studies) showed strong association with the risk of advanced colorectal neoplasia; however, these factors are prone to recall bias. Therefore, it is rather unlikely that a model based on simple, reliable clinical factors alone would ever have sufficient discriminatory power to limit the target population for screening. It is corroborated by the results of a very recent study by Tao et al. The model that included risk factors missing in the present study (alcohol consumption, red meat consumption, ever regular use of non-steroidal anti-inflammatory drugs, previous colonoscopy and previous detection of polyps), also demonstrated moderate discriminatory value. On the other hand, indirect comparison suggests that the present model’s sensitivity and specificity for advanced colorectal neoplasia may be comparable with a single round guaiac faecal occult blood test (mostly due to poor diagnostic performance of guaiac faecal occult blood test for detection of advanced adenomas). Although the model has considerably lower discriminatory power for advanced colorectal neoplasia compared to the one reported for faecal immunochemical tests, it has been shown that combining clinical risk factors with faecal immunochemical test outcome results in improved discrimination. Therefore, it is likely that in the future the clinical factors identified in the model will be combined with results of faecal immunochemical test and/or blood-based biomarkers to select a target population for colonoscopy.

Our study has certain notable features. Despite a large sample size, we have not identified any statistically significant association between diabetes mellitus or aspirin use and the risk of advanced colorectal neoplasia. Although diabetes mellitus is a known risk factor for colorectal cancer, its association with advanced colorectal neoplasia is less certain. The observed lack of association may also be due to the lower-than-expected prevalence of diabetes mellitus in the study cohort, which likely reflects recall bias or self-selection to opportunistic screening.

The lack of a statistically significant association between aspirin use and the risk of advanced colorectal neoplasia in our study may be due to recall bias or missing data regarding the dose and regularity of aspirin use. Moreover, we have not collected the data on other non-steroid anti-inflammatory drugs, which in some studies were analysed together with aspirin. Advanced neoplasia, not just cancer, was chosen for analysis because it has been suggested as the most appropriate target for endoscopy screening. Although some previous risk prediction models were developed for cancer alone, cancers and advanced neoplasia are surrogate endpoints of primary cancer screening endpoint, which is colorectal cancer mortality. Early detection and treatment of colorectal cancer is associated with a reduction in colorectal cancer mortality, but a detection and removal of adenomas, especially advanced ones, is associated with additional reduction in colorectal cancer incidence and mortality. Therefore, it is uncertain, whether cancer alone or advanced neoplasia is a better endpoint for risk prediction models, but the latter may be particularly suited for use in endoscopy screening.

The primary endpoint of our model was advanced neoplasia located anywhere in the colorectum, therefore, the risk score is not optimised for sigmoidoscopy screening. Nevertheless, we built an additional model to investigate risk factors for detecting distal advanced neoplasia, using sigmoid-descending colon junction as an artificial boundary between distal and proximal colon. The model for the detection of distal advanced neoplasia

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**Table 4** Performance characteristics of the score in the validation set (N=17 939)

| Risk score | Persons, n | N | Per cent | Sensitivity, % | Specificity, % | Positive predictive value, % | Negative predictive value, % |
|------------|------------|---|----------|---------------|--------------|----------------------------|----------------------------|
| 0          | 152        | 2 | 1.32     | 100.00        | 0.00         | 7.08                       | –                         |
| 1          | 2259       | 95| 4.21     | 99.84         | 0.90         | 7.13                       | 98.68                     |
| 2          | 3608       | 165| 4.57     | 92.36         | 13.88        | 7.55                       | 95.98                     |
| 3          | 4626       | 284| 6.14     | 79.37         | 34.54        | 8.46                       | 95.65                     |
| 4          | 3745       | 290| 7.74     | 57.01         | 60.59        | 9.93                       | 94.87                     |
| 5          | 2432       | 274| 11.27    | 34.17         | 81.31        | 12.23                      | 94.19                     |
| 6          | 981        | 134| 13.66    | 12.60         | 94.26        | 14.32                      | 93.40                     |
| 7 and 8†  | 136        | 26 | 19.12    | 2.05          | 99.34        | 19.12                      | 93.01                     |
| Total      | 17 939     | 1270| 7.08     |               |              |                           |                           |

*Advanced neoplasia includes advanced adenomas and cancers.
†Due to small sample risk scores 7 and 8 are presented in one row.
identified the same risk factors and showed comparable discriminatory power (data not shown).

The limitations of our study require comment. First, the validation process was limited because it was performed in a dataset that was randomly selected from a population recruited in the same setting. The model’s performance has not been tested outside Poland or in non-Caucasians. Nonetheless, the National Colorectal Cancer Screening Program recruited participants in 73 centres located in all administrative and geographic regions of Poland, and was open free of charge to all eligible Polish citizens, providing our study with sociodemographic diversity. Moreover, the prevalence of advanced colorectal neoplasia identified in our study was 7.1%, which is within the range of values reported in studies performed in the USA 13 29 and Europe. 5 10 11 Additionally, the adjusted ORs for detecting advanced colorectal neoplasia in various categories of risk factors in our study are similar to that reported in previously published large studies. 10 31 32 47 48 Notably, in our previous study, 19 performed several years before and in different endoscopy centres, we used the same key to categorise age, family history of colorectal cancer and gender and yielded virtually the same adjusted ORs for each category of variables.

Second, our cohort does not fully cover the recommended age range for screening (people aged 67–73 years were not included) what may limit the applicability of the results for the entire population eligible for screening. 49 On the other hand, by including people at the lower age range for screening (people aged 40–49 years with family history of cancer), this model may help to identify and encourage younger people at considerable risk to undergo screening.

Third, given the cross-sectional design of the study, our risk score is suitable only to predict the detection of advanced neoplasia at the present time, and not the future risk of developing advanced colorectal neoplasia or dying from colorectal cancer.

In summary, we derived and internally validated a model that predicts the likelihood of detecting advanced colorectal neoplasia in asymptomatic Caucasian patients based on age, sex, smoking habits, Body Mass Index, and family history of colorectal cancer. The results of the model were used to develop a simple score that estimates the likelihood of detecting advanced colorectal neoplasia. Once externally validated, the score may be useful for counselling or designing primary prevention studies.

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Competing interests None.

Patient consent Obtained.

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