

## Supplementary tables and figures

**Table S1: Number of tests available up to 5-year prior to index date for myeloma patients, MGUS patients and controls**

Blood test	Number tests	Myeloma Number patients	Median tests per patient	Number tests	MGUS Number patients	Median tests per patient	Number tests	Controls Number patients	Median tests per patient
Albumin	4992	409	9	4493	392	8	11967	1418	5
ALP	4177	409	7	3958	392	7	11953	1418	5
ALT	3724	408	6	3621	391	6	11179	1413	4
APTT	1174	292	2	783	220	2	4497	958	2
Basophil	4887	408	8	4675	392	8	16399	1493	5
Calcium	2134	400	3	1928	382	3	5042	960	2
Creatinine	5655	411	9	5318	393	9	18489	1488	6
CRP	2304	365	3	2112	330	3	9120	1092	4
D-Dimer	89	71	1	63	46	1	239	161	1
Derived Fibrinogen	1083	291	2	737	218	2	4075	949	2
eGFR	5390	411	9	5004	393	9	17688	1487	6
Eosinophil	4928	409	8	4707	392	8	16469	1493	5
ESR	152	96	1	226	132	1	330	199	1
Haemoglobin	5038	409	8	4783	392	8	17600	1493	5
Hypochromic	4948	409	8	4712	392	8	16498	1493	5
INR	2215	301	3	2153	236	2	8475	986	3
LDH	280	186	1	311	219	1	172	90	1
Lymphocyte	4981	409	8	4741	392	8	16665	1493	5
MCV	4940	409	8	4698	391	8	16462	1493	5
MCH	4986	409	8	4730	391	8	16638	1493	5
Monocyte	4975	409	8	4739	392	8	16653	1493	5
Neutrophil	4984	409	8	4744	392	8	16683	1493	5
PCV	4957	409	8	4705	391	8	16521	1493	5
Platelets	4998	409	8	4742	392	8	16642	1493	5
Prothrombin Time	1091	291	2	755	218	2	4188	957	2
PV	539	275	2	655	274	2	754	402	1
RDW	4973	409	8	4723	391	8	16583	1493	5
RBC	4996	409	8	4734	391	8	16668	1493	5
Urea	5577	411	9	5303	393	9	18464	1488	6
Urine Creatinine	1027	329	2	1228	365	2	1327	423	2
Vitamin D	220	131	1	316	156	1	579	293	1
WCC	5008	409	8	4754	392	8	16717	1493	5

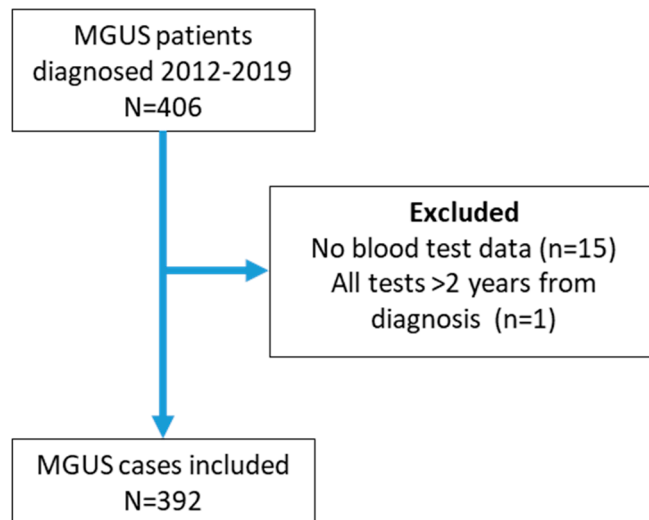
This table include all tests initially considered for this study

Abbreviations: ALP = alkaline phosphatase , ALT = alanine transaminase, APTT = activated partial thromboplastin time, CRP = C-reactive protein, eGFR = estimated glomerular filtration rate, ESR = erythrocyte sedimentation rate, INR = international normalised ratio, LDH = lactate dehydrogenase, MCV = mean cell volume, MCH = mean cell haemoglobin, PCV = packed cell volume, PV = plasma viscosity, RDW = red cell distribution width, RBC = red blood cell count, WCC = white cell count

**Table S2: Candidate predictors variables included in model development**

<b>Predictor variable</b>	<b>Units</b>	<b>Variable Type</b>
Age at diagnosis/index date	Year	Continuous
Sex		Factor (Male, Female)
Albumin	g/L	Continuous
ALP	iu/L	Continuous
ALT	iu/L	Continuous
Basophils	10 <sup>9</sup> /L	Continuous
Calcium	mmol/L	Continuous
Creatinine	Umol/L	Continuous
CRP	mg/L	Continuous
Eosinophils	10 <sup>9</sup> /L	Continuous
Haemoglobin	g/L	Continuous
Lymphocytes	10 <sup>9</sup> /L	Continuous
MCV	fL	Continuous
Monocytes	10 <sup>9</sup> /L	Continuous
Neutrophils	10 <sup>9</sup> /L	Continuous
Platelets	10 <sup>9</sup> /L	Continuous
WCC	10 <sup>9</sup> /L	Continuous

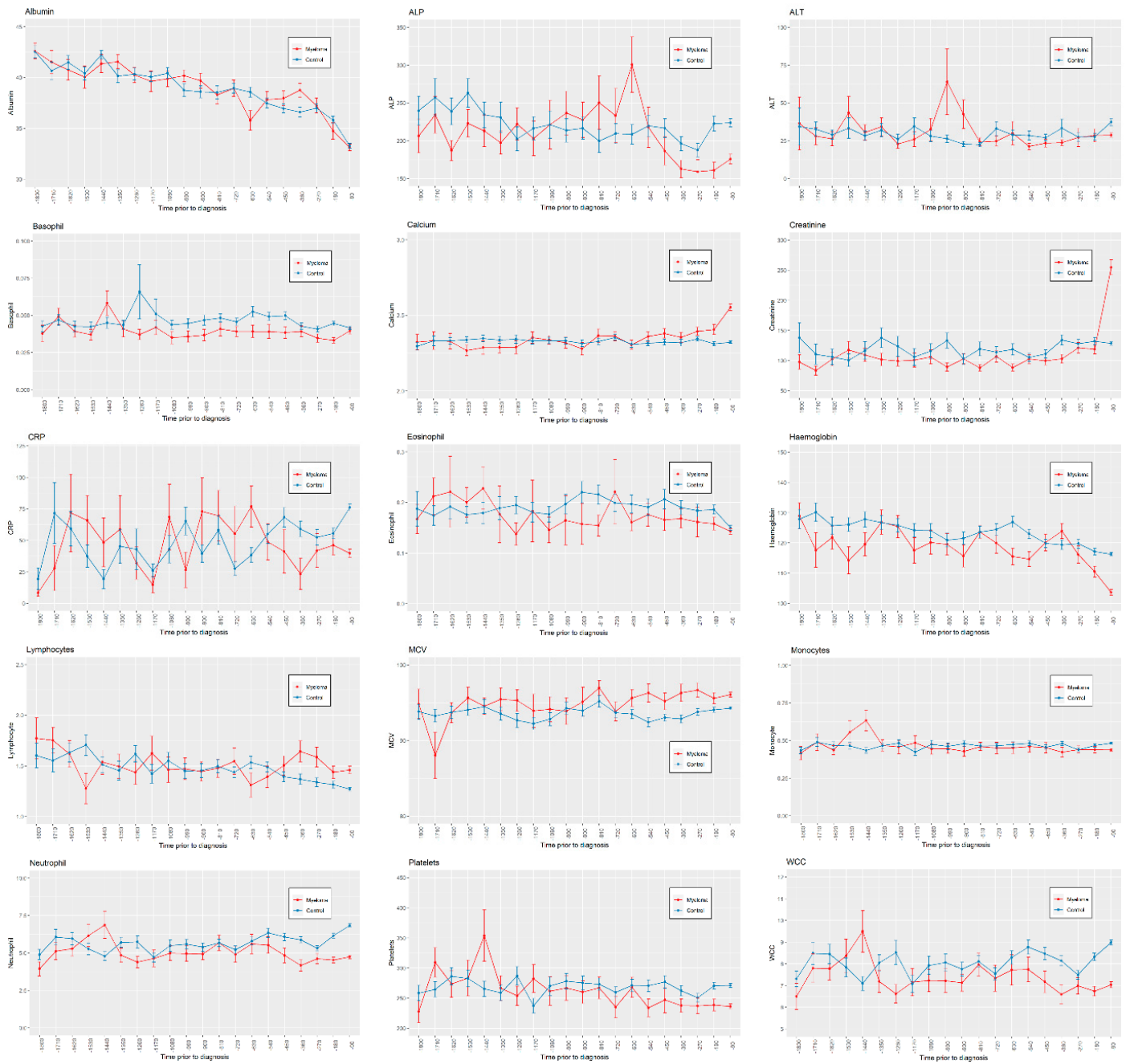
**Figure S1: Flow chart of MGUS cohort**



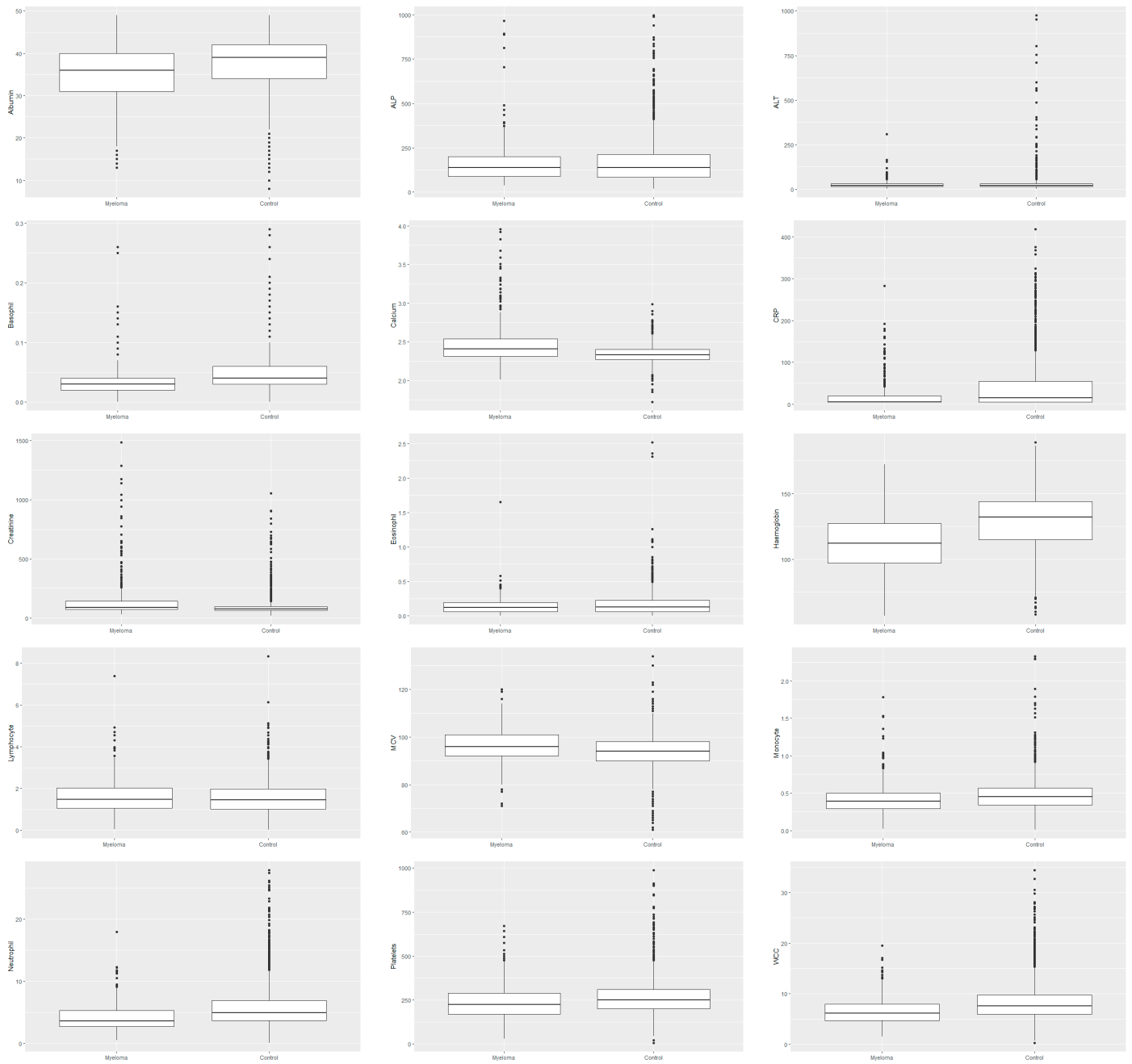
**Table S3: Baseline characteristics of MGUS cohort**

Variable	MGUS cohort N=392	
	Median (IQR) or n(%)	
<b>Age</b>	75	(66, 82)
<b>Sex</b>		
Male	224	57.1%
Female	168	42.9%
<b>Ethnicity</b>		
White British	342	87.2%
Black	19	4.9%
South Asian	14	3.6%
Other and missing	17	4.3%
<b>Total number of comorbidities</b>		
0	266	67.9%
1	86	21.9%
2	34	8.7%
3+	6	1.5%
<b>Blood tests</b>		
Albumin	40.0	(37.0, 42.0)
ALP	121.5	(82.0, 202.0)
ALT	19.0	(14.0, 26.0)
Basophils	0.04	(0.03, 0.05)
Calcium	2.39	(2.31, 2.45)
Creatinine	80.0	(63.0, 100.3)
CRP	5.00	(5.0, 11.58)
Eosinophils	0.13	(0.08, 0.22)
Haemoglobin	131.0	(118.0, 141.5)
Lymphocytes	1.51	(1.12, 1.96)
MCV	94	(90, 98)
Monocytes	0.38	(0.30, 0.50)
Neutrophils	4.16	(3.25, 5.40)
Platelets	242.0	(189.5, 300.0)
WCC	6.55	(5.42, 8.14)

**Figure S2: Trend plots for blood test for cases and controls, mean values (and 95% CIs) within 90 day periods**



**Figure S3: Box plot of distribution of blood tests for cases and controls for test results included in the model**



**Table S4: Most frequent requesting departments for blood test results used in model development**

<b>Cases</b>		<b>Controls</b>	
<b>Requesting department</b>	<b>% of tests</b>	<b>Requesting department</b>	<b>% of tests</b>
Primary Care	36%	Primary Care	34%
Medicine	19%	Medicine	15%
Haematology Outpatients	9%	Accident and emergency	9%
Elderly care	7%	Cardiology	8%
Renal	6%	Elderly care	4%
Respiratory	5%	Respiratory	4%
Accident and emergency	5%	Spinal surgery	4%
Haematology inpatients	3%	General surgery	3%
Orthopaedics	2%	Orthopaedics	3%
General surgery	2%	Renal	2%

Each component of the FBC is counted as a separate test

**Table S5: Number and percentage with missing data for blood tests in cases and controls.**

<b>Test</b>	<b>Overall</b>		<b>Cases</b>		<b>Controls</b>	
	<b>n</b>	<b>%</b>	<b>n</b>	<b>%</b>	<b>n</b>	<b>%</b>
Albumin	98	5.3	8	2.2	90	6.0
ALP	98	5.3	8	2.2	90	6.0
ALT	110	5.9	15	4.1	95	6.4
Basophil	18	1.0	12	3.3	6	0.4
Calcium	656	35.4	60	16.3	596	40.0
Creatinine	11	0.6	3	0.8	8	0.5
CRP	510	27.5	89	24.3	421	28.3
Eosinophil	16	0.9	11	3.0	5	0.3
Haemoglobin	15	0.8	11	3.0	4	0.3
Lymphocyte	15	0.8	11	3.0	4	0.3
MCV	16	0.9	12	3.3	4	0.3
Monocyte	15	0.8	11	3.0	4	0.3
Neutrophil	15	0.8	11	3.0	4	0.3
Platelets	15	0.8	11	3.0	4	0.3
WCC	15	0.8	11	3.0	4	0.3



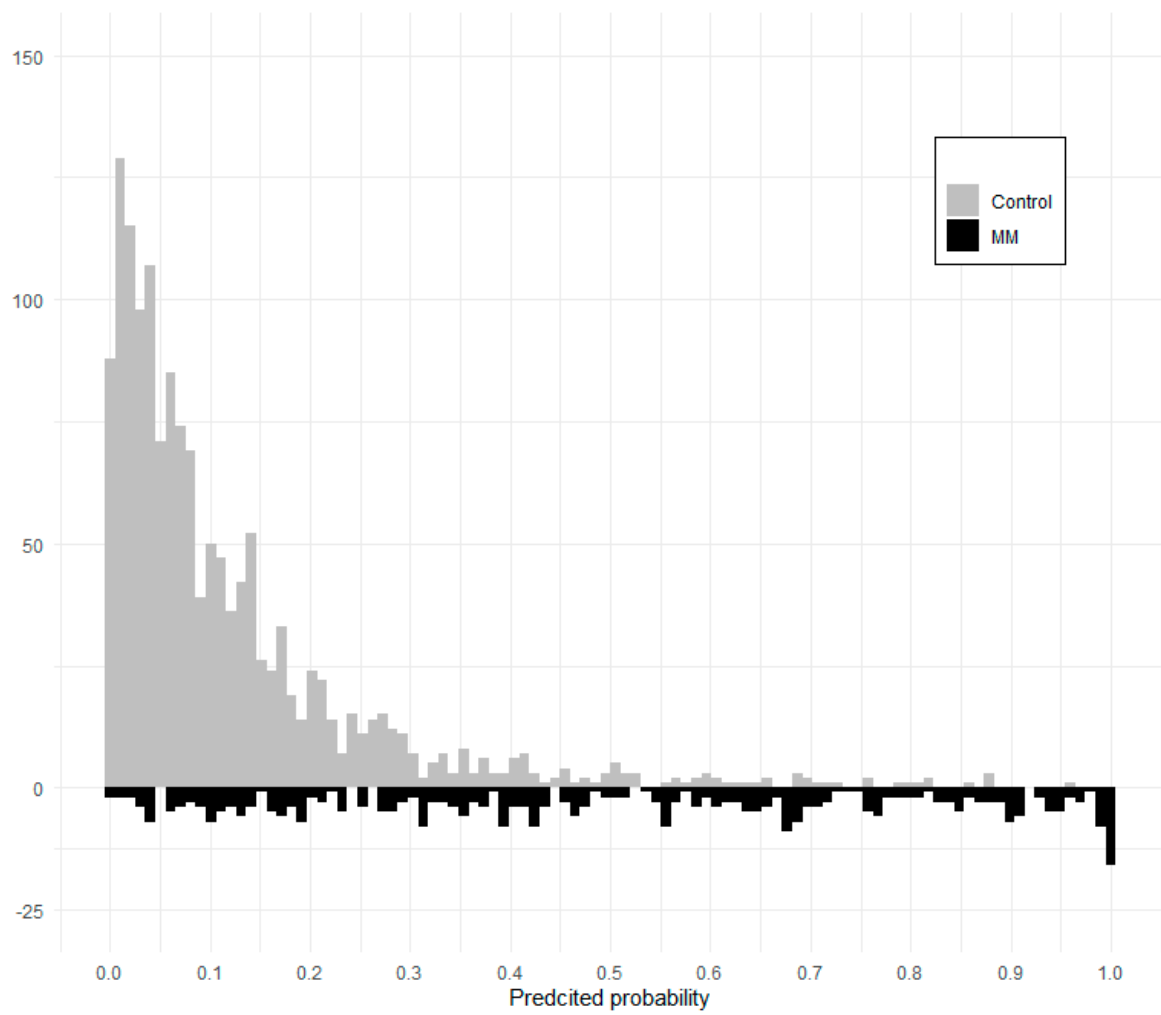
**Table S6: Model coefficients for final model based**

<b>Variable</b>	<b>Coefficient (log(OR))</b>	<b>Standard error</b>
Intercept	-10.617	4.401
Sex	-0.255	0.177
Age	0.006	0.014
Age spline 1	-0.017	0.016
Albumin	-0.019	0.023
Albumin spline 1	-0.006	0.026
ALP	0.007	0.002
ALP spine 1	-0.009	0.003
ALT	0.014	0.015
ALT spline 1	-0.023	0.021
Basophil	-27.403	8.695
Basophil spline 1	21.675	11.557
Calcium	1.922	1.549
Calcium spline 1	3.372	1.744
Creatinine	0.018	0.006
Creatinine spline 1	-0.024	0.009
CRP	-0.029	0.008
CRP spline 1	0.050	0.022
Eosinophil	-0.841	2.204
Eosinophil spline 1	-0.733	2.700
Haemoglobin	-0.023	0.008
Haemoglobin spline 1	-0.029	0.010
Lymphocytes	1.740	0.420
Lymphocytes spline 1	-1.109	0.377
MCV	0.071	0.025
MCV spline 1	-0.058	0.030
Monocytes	1.185	1.259
Monocytes spline 1	0.747	1.446
Neutrophil	0.150	0.282
Neutrophil spline 1	-0.271	0.289
Platelets	0.003	0.002
Platelets spine 1	-0.003	0.002
WCC	-0.535	0.271
WCC spline 1	0.457	0.235

Restricted cubic spline knot positions:

Age: 52, 70, 84, Albumin: 28, 38, 44, ALP: 64,137, 302, ALT: 12, 21, 48, Basophil: 0.02, 0.04, 0.08, Calcium: 2.21, 2.34, 2.51, Creatinine: 54, 78, 170, CRP: 5.1, 30, 155, Eosinophil, 0.02, 0.13, 0.33, Haemoglobin: 96, 129, 153, Lymphocytes: 0.74, 1.48, 2.63, MCV: 87, 94, 103, Monocytes: 0.26, 0.43, 0.73, Neutrophil: 2.55, 4.75, 9.52, Platelets: 152, 244, 377, WCC: 4.53, 7.32, 12.35

**Figure S4: Predicted probabilities cases and controls (over imputed models)**



**Table S7: Estimated prevalence based on published studies and national cancer data**

Author, year	Study population	Estimated prevalence/incidence
Koshiaris et al, 2021 (1)	CRPD >40 years, registered GP for >1 year,	737 cases Total population 1,281,926
	Two FBCs within 1 year between 2000 and 2014 with 2 years follow-up	57 cases per 100,000 (paper used 60 cases per 100,00 pop for diagnostic performance statistics)
Seesaghur et al, 2021 (2)	CRPD, aged 18+, registered GP for >2 years,	2646 cases Total population 17,756,119
	Newly diagnosed MM between 2006 and 2016	15 cases per 100,000
NHS Digital, 2022 (3)	England cancer registrations 2019	Age standardised incidence rate Males 12.9 per 100,000
	All ages	Females 8.2 per 100,000

## References

1. Koshiaris C, Van den Bruel A, Nicholson BD, Lay-Flurrie S, Hobbs FR, Oke JL. Clinical prediction tools to identify patients at highest risk of myeloma in primary care: a retrospective open cohort study. Br J Gen Pract. 2021;71(706):e347-e55.
2. Seesaghur A, Petruski-Ivleva N, Banks VL, Wang JR, Abbasi A, Neasham D, et al. Clinical features and diagnosis of multiple myeloma: a population-based cohort study in primary care. BMJ Open. 2021;11(10):e052759.
3. National Disease Registration Service NHS Digital. CancerData. Cancer Incidence 2019. [https://www.cancerdata.nhs.uk/incidence\\_and\\_mortality](https://www.cancerdata.nhs.uk/incidence_and_mortality) 2022

**Table S8: Total number to additionally test at different prevalence estimates and probability thresholds for each model**

Model	Threshold	Prevalence per 100,000		
		10	15	60
Full model	0.1	39805	39808	39830
	0.2	17706	17709	17736
	0.4	5205	5208	5232
Calcium removed	0.1	44404	44407	44427
	0.2	21506	21508	21534
	0.4	5805	5807	5830
Over 60s only	0.1	38405	38408	38432
	0.2	19406	19409	19337
	0.4	5706	5709	5736
MGUS as controls	0.1	36105	36107	36129
	0.2	14006	14009	14136
	0.4	4004	4006	4026
MGUS as controls and calcium removed	0.1	40604	40607	40627
	0.2	17205	17208	17233
	0.4	4304	4306	4324
Over 60s only, MGUS as controls, all predictors	0.1	36005	36008	36031
	0.2	15406	15409	15436
	0.4	5104	5107	5126
Over 60s only, MGUS as controls, calcium removed	0.1	39305	39307	39329
	0.2	18506	18508	18634
	0.4	5404	5406	5426

**Figure S5: Number needed to additionally test to diagnose 1 case at different prevalence estimates and probability thresholds for each model**

