Supplementary Tables and Figures

Table S1: Baseline demographic, laboratory and clinical characteristics of multiple myeloma (MM) patients of MMIn and MMRF cohort

Parameters	MMIn (n = 1070)			MMRF Test Dataset (n=900)
	Training Dataset (n = 716)	Testing Dataset (n = 354)	Total (MMIn) (n = 1070)	
Age (Median, Range; in years)	57 (19 - 87)	55 (24 - 84)	56(18-87)	62 (27 - 91)
Male/ Female	471 (65·78%) 245 (34·22%)	239 (67·51%) 115 (32·49%)	710(66·36%) 360(33·64%)	NA
Hemoglobin (g/dL) <10 ≥10	404 (56·42%) 312 (43·58%)	195 (54·08%) 159 (44·92%)	599 (55·98%) 471 (44·02%)	331 (36·77%) 569 (63·23%)
Serum albumin (g/dL) <3·5 ≥3·5	309 (43·16%) 407 (56·84%)	140 (39·55%) 214 (60·45%)	449 (41·96%) 621 (58·04%)	328 (36·44%) 572 (63·56%)
Beta 2 microglobulin (mg/L) <5·5 ≥5·5	357 (49·86%) 359 (50·14%)	177 (50%) 177 (50%)	534 (49·90%) 536 (50·09%)	661 (73·44%) 239 (26·56%)
Serum LDH (IU/L) ≤280 >280	625 (87·29%) 91 (12·71%)	304 (85·88%) 50 (14·12%)	929 (86·82%) 141 (13·18%)	850 (94·44%) 50 (5·56%)
Serum creatinine (mg/dL) ≤2 >2	550 (76·82%) 166 (23·18%)	280 (79·09%) 74 (20·91%)	830 (77·57%) 240 (22·43%)	816 (90·66%) 84 (9·34%)
Serum calcium (mg/dL) ≤11 >11	631 (88.13%) 85 (11.87%)	314(88·70%) 40(11·30%)	935 (87.38%) 135 (12.62%)	831 (92·33%) 69 (7·67%)
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Table S2: Univariate analysis of Cox Proportional Hazards Model on the training dataset (n=716)

Parameter		Hazard Ratio	$p > \|z\|$	95% CI	χ^2
Age	PFS	1·41	0·017	1·06 - 1·87	5·24
(67≤, >67)	OS	1·95	3·00e-05	1·42 – 2·65	15·29
Albumin	PFS	1·18	0·08	0·97 - 1·43	2·9
(>3·6, ≤3·6)	OS	1·45	0·0029	1·13 – 1·84	9·04
β2M	PFS	1·56	6·84e-06	1·29 – 1·89	20·5
(<4·8,≥ 4·8)	OS	1·95	1·40e-07	1·52 - 2·50	28·74
Calcium	PFS	1·47	0·007	1·11 - 1·95	6·61
(<11·13, ≥ 11·13)	OS	1·46	0·03	1·03 - 2·04	4·3
eGFR	PFS	1·29	0·013	1·05 – 1·58	5·99
(>48·1, ≤48·1)	OS	1·49	0·0013	1·16 – 1·91	9·97
Hb	PFS	1·69	6·00e-04	1·25 – 2·28	13·56
(>12·3, ≤12·3)	OS	2·26	1·90e-04	1·47 - 3·47	17·52

Table S3: Evaluation of progression free survival (PFS) and overall survival (OS) in the risk categories defined by staging methods- MRS, ISS and RISS on the MMIn dataset

Comparison of MRS vs ISS (n = 1070 patients)									
		MRS-1	MRS-2	MRS-3	MRS p-value	ISS-1	ISS-2	ISS-3	ISS p-value
Training data (n=716)	Median PFS in weeks	243 (n = 185)	186 (n = 332)	129 (n = 199)	**6·28 e-6**	229 (n =139)	219 (n = 216)	147 (n = 361)	1·25 e-5
	Median OS in weeks	592 (n = 185)	341 (n = 332)	219 (n = 199)	**8·15 e-10**	490 (n = 139)	489 (n = 216)	285 (n = 361)	2·03 e-5
Test data (n=354)	Median PFS in weeks	234 (n = 96)	144 (n = 179)	133 (n = 79)	0·03	234 (n = 68)	201 (n = 107)	125 (n = 179)	**1·7 e-4**
	Median OS in weeks	912 (n = 96)	301 (n = 179)	315 (n = 79)	**2·3 e-6**	912 (n = 68)	454 (n = 107)	276 (n = 179)	9·06 e-6
Comparison of MRS vs RISS (n =627 patients)									
		MRS-1	MRS-2	MRS-3	MRS p-value	RISS-1	RISS-2	RISS-3	RISS p-value
Median PFS in weeks		212 (n = 160)	178 (n = 341)	106 (n = 126)	4·09 e-5	196 (n = 47)	186 (n = 459)	107 (n = 121)	**1·59 e–6**
Median OS in weeks		478 (n = 160)	341 (n = 341)	221 (n = 126)	2·06 e-8	478 (n = 47)	440 (n = 459)	191 (n = 121)	**4·8 e-9**

Table S4: Univariate analysis of Cox Proportional Hazards Model for MMIn and MMRF dataset.

MMIn Dataset (n = 1070)					
Parameter		Hazard Ratio	$p > \|z\|$	95% CI	χ^2
Age (67≤, >67)	PFS	1·35	0·01	1·06-1·71	5·7
	OS	1·92	1·92e-06	1·46 – 2·51	19·65
Albumin (>3·6, ≤ 3·6)	PFS	1·19	0·02	1·01 – 1·39	4·8
	OS	1·50	1·20e-04	1·22 – 1·84	15·04
β2M (<4·8, ≥ 4·8)	PFS	1·64	1·34e-9	1·40 – 1·93	37·45
	OS	2·27	1·94e-13	1·82 – 2·82	57·63
Calcium (<11·13, ≥ 11·13)	PFS	1·36	0·008	1·08 – 1·72	6·44
	OS	1·45	0·012	1·08 – 1·93	5·8
eGFR (>48·1,≤48·1)	PFS	1·17	0·056	0·99 – 1·39	3·563
	OS	1·49	2·00e-04	1·2 – 1·84	13·29
Hb (>12·3, ≤ 12·3)	PFS	1·60	1·0e-4	1·26 – 2·03	17
	OS	2·54	9·60e-07	1·75 – 3·70	31·14
MMRF Dataset (n = 900)					
Parameter		Hazard Ratio	$p > \|z\|$	95% CI	χ^2
Age (67≤, >67)	PFS	1·52	3·00e-05	1·25 – 1·86	16·81
	OS	2·05	1·10e-06	1·54 – 2·75	22·85
Albumin (>3·6, ≤ 3·6)	PFS	1·39	0·001	1·14 – 1·68	10·9
	OS	2·01	1·00e-05	1·49 – 2·72	21·68
β2M (<4·8, ≥ 4·8)	PFS	2·01	1·50e-12	1·65 – 2·44	48·26
	OS	2·71	2·65e-11	2·02 – 3·63	44·78
Calcium (<11·13, ≥ 11·13)	PFS	1·48	0·05	0·99 – 2·18	3·4
	OS	2·46	1·00e-04	1·56 – 3·89	12·01
eGFR (>48·1, ≤ 48·1)	PFS	1·89	1·61e-08	1·51 – 2·36	28·54
	OS	2·51	2·90e-09	1·86 – 3·41	31·21
Hb (>12·3, ≤ 12·3)	PFS	1·5	0·0013	1·17 – 1·92	11·2
	OS	1·56	0·02	1·06 – 2·28	5·75

Table S5: Multivariate analysis of Cox Proportional Hazards Model for MMIn dataset (n=1070)

Parameter	PFS (χ^2=54·26)			OS (χ^2=95·59)		
	Hazard Ratio	$p > \|z\|$	95% CI	Hazard Ratio	$p > \|z\|$	95% CI
Age (≤67, >67)	1·31	0·02	1·03-1·66	1·83	1·00e-05	1·40-2·40
Albumin (>3·6, ≤ 3·6)	1·02	0·80	0·86-1·20	1·17	0·15	0·94-1·45
β2M (<4·8, ≥ 4·8)	1·58	3·37e-07	1·32-1·88	1·98	8.90e-09	1·57-2·5
Calcium (<11·13, ≥ 11·13)	1·28	0·04	1·00-1·62	1·23	0·15	0·92-1·66
eGFR (>48·1, ≤48·1)	0·89	0·22	0·74-1·07	1·01	0·96	0·80-1·26
Hb (>12·3, ≤12·3)	1·38	0·01	1·06-1·78	1·87	1·70e-03	1·26-2·76

Table S6: Multivariate analysis of Cox Proportional Hazards Model for MMRF dataset (n=900)

Parameter	PFS (χ^2=67·12)			OS (χ^2=82·43)		
	Hazard Ratio	$p > \|z\|$	95% CI	Hazard Ratio	$p > \|z\|$	95% CI
Age ($\leq$67, >67)	1·33	5·90e-03	1·08-1·63	1·66	8·60e-04	1·23-2·23
Albumin (>3.6, $\leq$ 3.6)	1·24	0·03	1·01-1·52	1·89	9·00e-05	1·37-2·60
β2M (<4·8, $\geq$ 4·8)	1·60	1·00e-04	1·26-2·04	1·81	1·40e-03	1·26-2·60
Calcium (<11·13, $\geq$ 11·13)	1·03	0·85	0·69-1·56	1·57	0·06	0·96-2·53
eGFR (>48·1, $\leq$48.1)	1·33	0·03	1·02-1·73	1·61	0·011	1·11-2·33
Hb (>12·3, $\leq$12·3)	1·09	0·51	0·84-1·43	0·84	0·41	0·55-1·27

Table S7: Classification accuracy obtained when J48 decision tree classifier was trained on training data (n=716) of MMIn dataset. Risk stages obtained via BIRCH clustering were used as ground truth labels. Decision tree was first trained using all the parameters and further trained consecutively excluding one of the parameters. (alb-albumin; cal-calcium; Hb-Hemoglobin)

Parameters included	**Parameter excluded**	**Accuracy (%)**
age, alb, β2M , cal, eGFR, Hb	-	**96.5**
age, alb, β2M , eGFR, Hb	Calcium	94.27
alb, β2M , cal, eGFR, Hb	Age	89.52
age, alb, β2M , cal, Hb	eGFR	86.59
age, alb, β2M , cal, eGFR	Hb	86.45
age, alb, cal, eGFR, Hb	β2M	84.77
age, β2M , cal, eGFR, Hb	Albumin	82.68

Table S8: Staging systems along with the parameters used

Staging System	ISS	RISS	MRS
Parameters	β2M Albumin	ISS CA LDH	Age Albumin β2M Calcium eGFR Haemoglobin

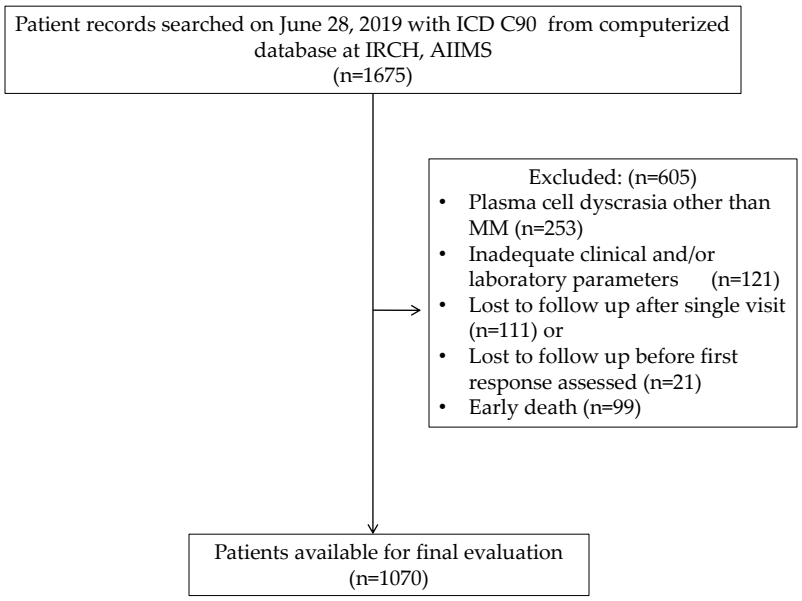

Figure S1: Flowchart of Study Population

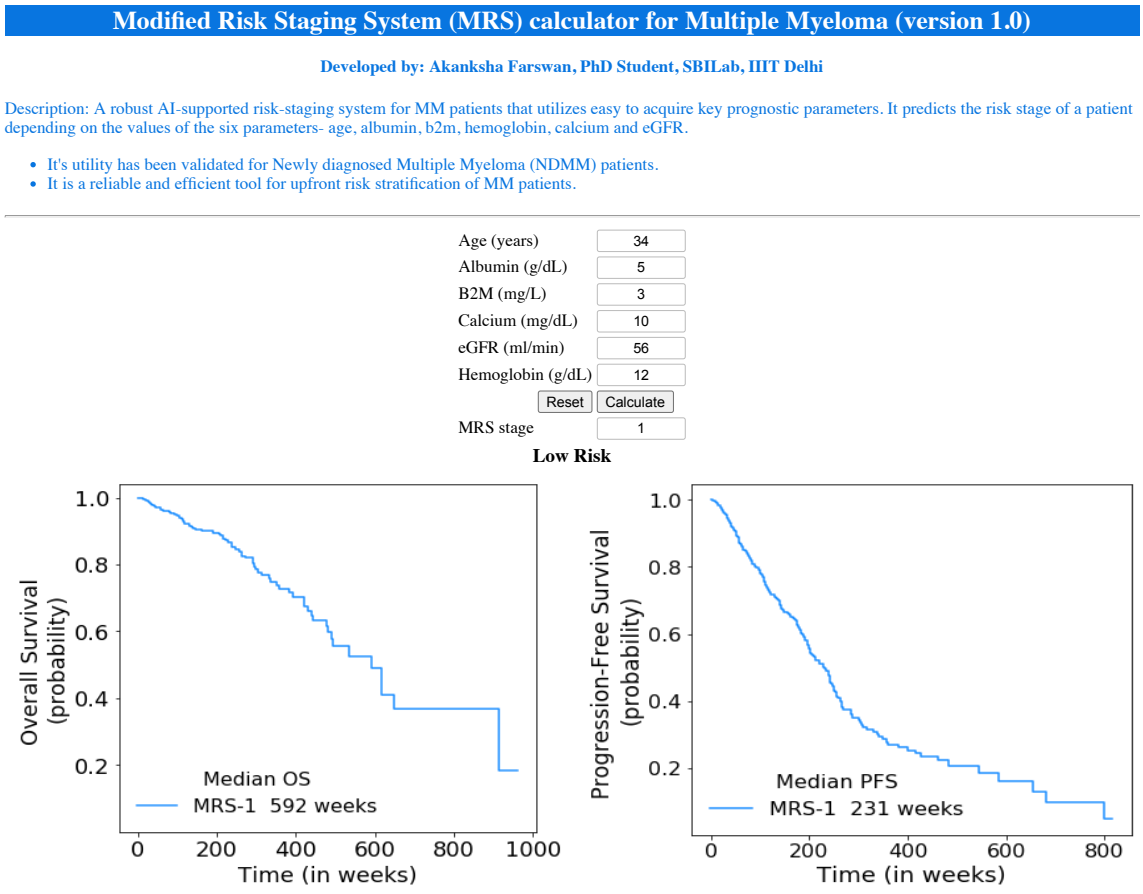

Figure S2: Online version of MRS calculator