

SUPPLEMENTARY DATA

Principal investigators

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Supplementary Table S1. Prevalence of anxiety and depression 5-years after surgery among our three trajectory-groups, according to the HAD anxiety score, the HAD depression score, and the BDI depression score. Chi-square test was used to asses between remission status differences.

	5y-DR	5y-Relapse	5y-NDR	P-value
HAD anxiety scores (3)				
<i>Number of participants</i>	45	14	27	-
No anxiety (score ≤ 7) – n (%)	27 (60.0)	7 (50.0)	17 (63.0)	0.92
Doubt ($8 \leq$ score ≤ 10) – n (%)	7 (15.6)	5 (35.7)	5 (18.5)	0.43
Overt anxiety (score ≥ 11) – n (%)	11 (24.4)	2 (14.3)	5 (18.5)	0.77
HAD depression scores (3)				
<i>Number of participants</i>	45	14	27	-
No anxiety (score ≤ 7) – n (%)	30 (66.7)	13 (92.9)	23 (85.2)	0.69
Doubt ($8 \leq$ score ≤ 10) – n (%)	10 (22.2)	0 (0.0)	3 (11.1)	0.16
Overt anxiety (score ≥ 11) – n (%)	5 (11.1)	1 (7.1)	1 (3.7)	0.58
BDI depression scores (4)				
<i>Number of participants</i>	34	12	21	
No depression (score ≤ 3) – n (%)	19 (55.9)	7 (58.3)	9 (42.9)	0.84
Mild depression ($4 \leq$ score ≤ 7) – n (%)	7 (20.6)	2 (16.7)	7 (33.3)	0.62
Moderate depression ($8 \leq$ score ≤ 15) – n (%)	5 (14.7)	3 (25.0)	4 (19.0)	0.80
Severe depression (score ≥ 16) – n (%)	3 (8.8)	0 (0.0)	1 (4.8)	0.55

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Supplementary Table S2. DiaRem, Ad-DiaRem and 5y-Ad-DiaRem performances in the two French cohorts, as well as the performances of the 5y-Ad-DiaRem in the two European validations cohorts

In the confusion matrixes, the true condition was non-remission 5-years post-RYGB, and the predicted conditions was set as if a patient's score value was over the score's fixed threshold (>6 for the DiaRem (1), ≥10 for the Ad-DiaRem (2), and >11 for the 5y-Ad-DiaRem).

	BARICAN cohort (n = 175)			French cohort (n = 54)			Italian cohort (n=20)	German cohort (n=50)
	DiaRem	Ad-DiaRem	5y-Ad-DiaRem	DiaRem	Ad-DiaRem	5y-Ad-DiaRem	5y-Ad-DiaRem	5y-Ad-DiaRem
True positives – n (%)	60 (34)	58 (33)	73 (42)	22 (41)	20 (37)	23 (43)	10 (50)	21 (42)
True negatives – n (%)	76 (43)	79 (45)	76 (43)	22 (41)	24 (44)	25 (46)	4 (20)	24 (48)
False positives – n (%)	18 (10)	15 (9)	18 (10)	6 (11)	4 (7)	3 (6)	2 (10)	3 (6)
False negatives – n (%)	21 (12)	23 (13)	8 (5)	4 (7)	6 (11)	3 (6)	4 (20)	2 (4)
Positive predictive value	77%	79%	80%	79%	83%	88%	83%	87%
Negative predictive value	78%	77%	90%	85%	80%	89%	50%	92%
Sensitivity	74%	72%	90%	85%	77%	88%	71%	91%
Specificity	81%	84%	81%	79%	86%	89%	67%	88%
Accuracy	79%	78%	85%	81%	81%	89%	70%	90%
AUC	81%	84%	90%	88%	89%	96%	85%	92%

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Supplementary Table S3. Unstandardized odd-ratios evaluating the risk of undergoing 5-year Relapse and/or remain in non-remission. Both sex and age were included in the regression model.

* The group of patients was used as reference.

† Evolutions during the first year were calculated using the following formula: [(1-year value) – (Baseline value)] / (Baseline value) x 100.

OR odd-ratio, CI confidence interval

	Risk of 5y-Relapse compared to 5y-DR*			Risk or 5y-NDR compared to 5y-Relapse*			Risk of 5y-NDR compared to 5y-DR*		
	OR	95% CI	p	OR	95% CI	p	OR	95% CI	p
Baseline variables									
Fasting glucose (mmol/L)	1.07	[0.88;1.28]	0.55	1.12	[0.94;1.36]	0.30	1.29	[1.12;1.51]	0.002
HbA1C (%)	1.17	[0.8;1.69]	0.48	2.39	[1.5;4.23]	0.004	3.27	[2.18;5.29]	<0.001
Number of anti-diabetic treatments	1.81	[1.18;2.84]	0.04	3.54	[1.86;7.76]	0.002	3.70	[2.44;6.06]	<0.001
Age (years)	1.00	[0.96;1.04]	0.94	1.08	[1.03;1.15]	0.02	1.06	[1.02;1.10]	0.004
Type 2 diabetes duration (years)	1.10	[0.98;1.23]	0.18	1.27	[1.13;1.48]	0.002	1.32	[1.21;1.47]	<0.001
Kinetic variables (during the 1st year) †									
Weight lost (% baseline)	1.13	[1.06;1.22]	0.01	0.94	[0.87;1]	0.13	1.08	[1.02;1.14]	0.01
Fat mass lost (% baseline)	1.09	[1.02;1.17]	0.04	0.95	[0.88;1.01]	0.14	1.03	[0.99;1.07]	0.23
Fat-free mass lost (% baseline)	0.91	[0.84;0.97]	0.04	1.05	[0.98;1.14]	0.22	0.95	[0.91;0.99]	0.06
Trunk-fat mass lost (% baseline)	1.04	[1.01;1.09]	0.06	0.99	[0.95;1.03]	0.66	1.03	[1;1.06]	0.06
1-year variables									
1-year fasting glycaemia (mmol/L)	1.33	[0.8;2.19]	0.33	1.84	[1.13;3.4]	0.07	2.03	[1.46;2.97]	<0.001
1-year HbA1C (%)	1.02	[0.44;2.26]	0.95	9.00	[3.04;36.2]	0.002	5.32	[2.87;10.88]	<0.001
1-year number of anti-diabetic treatments	-	-	-	-	-	-	25.82	[9.5;99.9]	<0.001

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Supplementary Table S4. Comparison of the test cohort (BARICAN) and the French confirmation cohort from Louis-Mourier Hospital. Between cohorts comparisons were performed using Mann-Whitney tests for continuous variables and Chi-square test for categorical variables (noted *).

	Test cohort	French confirmation cohort	p-value
Baseline characteristics			
Number of patients	175	54	
Male - n (%)	39 (22.3%)	7 (13.0%)	0.193*
Age (years)	48.26 ± 10.33	48.22 ± 9.38	0.976
T2D duration (years)	6.75 ± 6.53	6.69 ± 6.92	0.954
Body weight (kg)	128.92 ± 22.07	120.31 ± 21.97	0.013
BMI (kg/m ²)	47.37 ± 7.43	45.10 ± 6.18	0.043
HbA1c (%)	7.54 ± 1.56	7.65 ± 1.15	0.620
Fasting glycemia (mmol/L)	7.88 ± 2.65	8.63 ± 3.03	0.081
Number of Anti-T2D drug(s) - n (%)			0.796*
0	33 (18.9%)	7 (13.0%)	
1	46 (26.3%)	18 (33.3%)	
2	53 (30.3%)	17 (31.5%)	
3	32 (18.3%)	9 (16.7%)	
>3	11 (6.3%)	3 (5.6%)	
Post-operative comparisons			
Body weight loss during the first year (% baseline)	-26.93 ± 7.61	-28.96 ± 7.09	0.082
Body weight loss during the 5 years of follow-up (% baseline)	-24.40 ± 10.42	-28.08 ± 8.00	0.018
5-years T2D remission status			0.202*
5y-DR	94 (53.7%)	28 (51.9%)	
5y-Relapse	27 (15.4%)	4 (7.4%)	
5y-NDR	54 (30.9%)	22 (40.7%)	
1-year T2D remission status			0.929*
1y-DR	66 (37.7%)	21 (38.9%)	
1y-PDR	40 (22.9%)	11 (20.4%)	
1y-NDR	69 (39.4%)	22 (40.7%)	

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Supplementary Table S5. Comparison of the test cohort (BARICAN) and the Italian confirmation cohort from Geltrude Mingrone’s department (5). Between cohorts comparisons were performed using Mann-Whitney tests for continuous variables and Chi-square test for categorical variables (noted *).

	Test cohort	Italian confirmation cohort	p
Baseline characteristics			
Number of patients	175	20	
Male - n (%)	39 (22.3%)	12 (60.0%)	0.001*
Age (years)	48.26 ± 10.33	43.90 ± 7.57	0.068
T2D duration (years)	6.75 ± 6.53	6.05 ± 1.15	0.636
Body weight (kg)	128.92 ± 22.07	129.84 ± 22.58	0.861
BMI (kg/m ²)	47.37 ± 7.43	44.85 ± 5.16	0.143
HbA1c (%)	7.54 ± 1.56	8.55 ± 1.40	0.006
Fasting glycemia (mmol/L)	7.88 ± 2.65	9.55 ± 3.35	0.010
Number of Anti-T2D drug(s) - n (%)			<0.001*
0	33 (18.9%)	0 (0.0%)	
1	46 (26.3%)	3 (15.0%)	
2	53 (30.3%)	0 (0.0%)	
3	32 (18.3%)	11 (55.0%)	
>3	11 (6.3%)	6 (30.0%)	
Post-operative comparisons			
Body weight loss during the first year (% baseline)	-26.93 ± 7.61	-31.81 ± 7.72	0.007
Body weight loss during the 5 years of follow-up (% baseline)	-24.40 ± 10.42	-28.59 ± 7.26	0.090
5-years T2D remission status			0.005*
5y-DR	94 (53.7%)	5 (25.0%)	
5y-Relapse	27 (15.4%)	9 (45.0%)	
5y-NDR	54 (30.9%)	6 (30.0%)	
1-year T2D remission status			0.349*
1y-DR	66 (37.7%)	8 (40.0%)	
1y-PDR	40 (22.9%)	5 (25.0%)	
1y-NDR	69 (39.4%)	7 (35.0%)	

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Supplementary Table S6. Comparison of the test cohort (BARICAN) and the German confirmation cohort from Leipzig hospital. Between cohorts comparisons were performed using Mann-Whitney tests for continuous variables and Chi-square test for categorical variables (noted *).

	Test cohort	German confirmation cohort	p-value
Baseline characteristics			
Number of patients	175	50	
Male - n (%)	39 (22.3)	15 (30.0)	0.348*
Age (years)	48.26 (10.33)	51.59 (9.55)	0.043
T2D duration (years)	6.75 (6.53)	7.72 (8.12)	0.388
Body weight (kg)	128.92 (22.07)	143.53 (23.37)	<0.001
BMI (kg/m ²)	47.37 (7.43)	50.42 (7.26)	0.011
HbA1c (%)	7.54 (1.56)	7.09 (1.83)	0.087
Fasting glycemia (mmol/L)	7.88 (2.65)	8.37 (3.69)	0.300
Number of Anti-T2D drug(s) - n (%)			0.060*
0	33 (18.9)	6 (12.0)	
1	46 (26.3)	20 (40.0)	
2	53 (30.3)	19 (38.0)	
3	32 (18.3)	5 (10.0)	
>3	11 (6.3)	0 (0.0)	
Post-operative comparisons			
Body weight loss during the first year (% baseline)	-26.93 (7.61)	-29.07 (8.72)	0.091
Body weight loss during the 5 years of follow-up (% baseline)	-24.40 (10.42)	-28.74 (11.58)	0.012
5-years T2D remission status			0.805*
5y-DR	94 (53.7%)	27 (54.0)	
5y-Relapse	27 (15.4%)	6 (12.0)	
5y-NDR	54 (30.9%)	17 (34.0)	
1-year T2D remission status			0.036*
1y-DR	66 (37.7%)	28 (56.0)	
1y-PDR	40 (22.9%)	5 (10.0)	
1y-NDR	69 (39.4%)	17 (34.0)	

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Supplementary Table S7. Evolution of clinical parameters before, 1-year and 5-years after RYGB for patients who maintained their T2D.

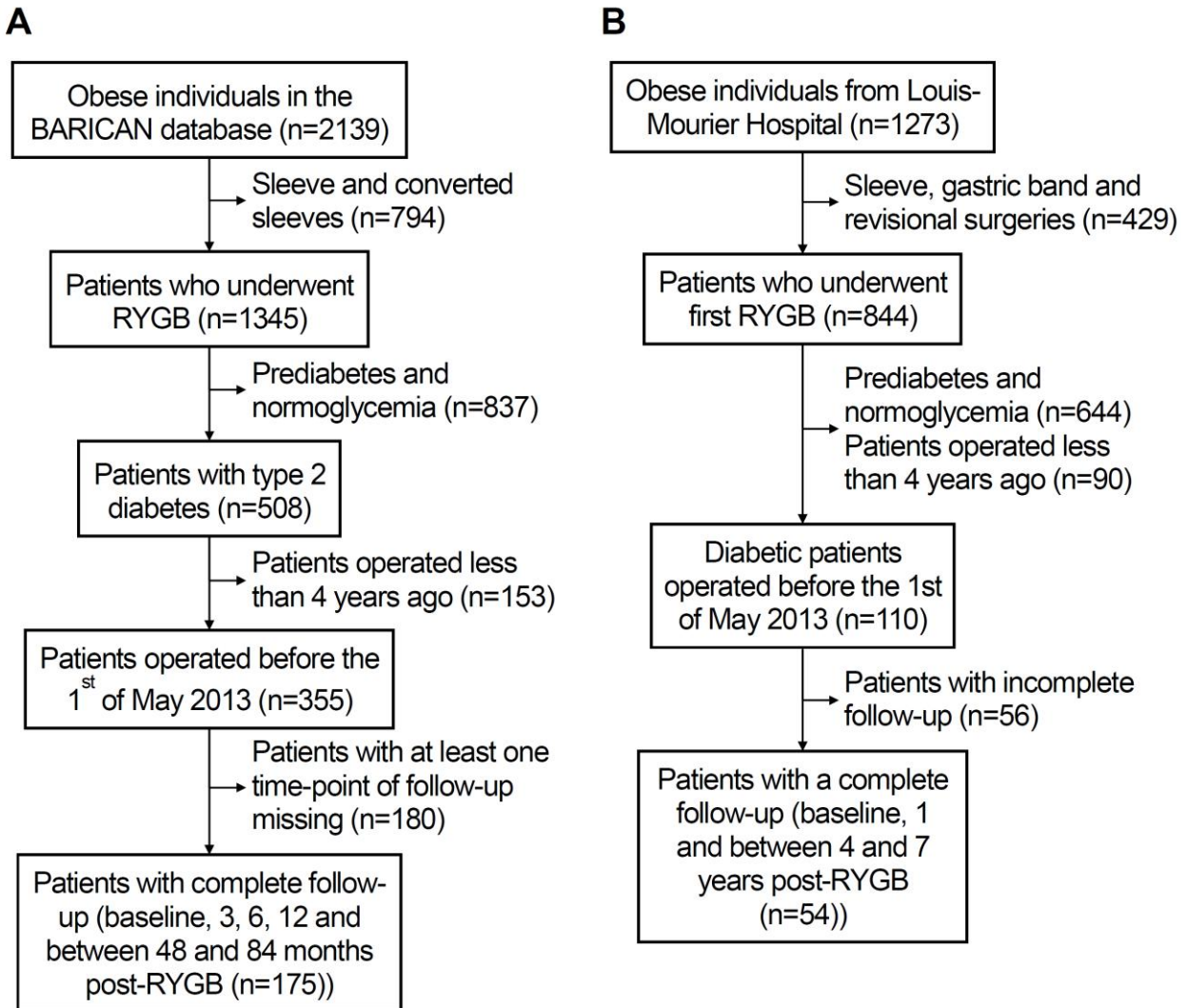
Data are presented as mean ± standard deviation unless stated otherwise. Between time-point comparisons were performed using Mann-Whitney tests for continuous variables and Chi-square test for categorical variables (noted *).

BMI body mass index, HBP high blood pressure, ALP alkaline phosphatase, AST aspartate aminotransferase, ALT alanine aminotransferase, GGT gamma glutamyltransferase

n=54	Before RYGB	1-year post-RYGB	5-years post-RYGB	1-year vs baseline	5-years vs baseline	5-years vs 1-year
Body weight (kg)	123.5 ± 21.0	92.7 ± 17.3	94.7 ± 18.1	<0.001	<0.001	0.09
BMI (kg/m ²)	45.7 ± 7.3	34.3 ± 6.1	35.0 ± 6.4	<0.001	<0.001	0.09
Body composition						
Fat mass (%)	46.9 ± 5.0	38.8 ± 6.3	41.4 ± 6.0	<0.001	0.005	<0.001
Fat-free mass (%)	50.8 ± 4.9	58.2 ± 6.1	55.8 ± 5.8	<0.001	0.006	<0.001
Trunk-fat mass (%)	32.1 ± 6.9	18.8 ± 5.8	19.1 ± 5.1	<0.001	<0.001	0.13
Android/Gynoid fat mass ratio	2.4 ± 0.6	2.1 ± 0.5	2.0 ± 0.5	0.008	0.02	1.00
Diabetes condition						
Number of anti-diabetic drugs	2.6 ± 1	1.5 ± 1	1.5 ± 1.1	<0.001	<0.001	1.00
Patients requiring Insulin - n (%)*	35 (65%)	19 (35%)	15 (28%)	0.002	0.001	0.40
Fasting glycemia (mmol/L)	8.8 ± 3.2	6.1 ± 1.4	7.9 ± 2.8	<0.001	0.23	<0.001
HbA1C (%)	8.6 ± 1.9	6.6 ± 0.8	7.6 ± 1.2	<0.001	0.002	<0.001
Patients with HbA1C <7% - n (%)*	6 (11%)	34 (67%)	18 (34%)	<0.001	0.005	<0.001
Comorbidities						
Patients taking anti-HBP drugs – n (%)*	47 (87%)	37 (69%)	32 (59%)	0.02	0.001	0.32
Patients taking anti-Dyslipidemia drugs – n (%)*	40 (74%)	15 (28%)	16 (30%)	<0.001	<0.001	1.00
HDL-cholesterol (mmol/L)	1.2 ± 0.3	1.4 ± 0.3	1.6 ± 0.6	<0.001	0.05	0.57
LDL-cholesterol (mmol/L)	2.4 ± 0.7	2.5 ± 0.9	2.5 ± 1.0	0.41	0.84	1.00
ALP (IU/L)	72.4 ± 18.1	82.5 ± 31.5	74.8 ± 17.1	0.17	0.59	0.61
AST (IU/L)	30.1 ± 15.0	27.2 ± 7.8	24.8 ± 4.8	0.50	0.24	0.11
ALT (IU/L)	35.9 ± 22.9	29.8 ± 14.2	27.1 ± 8.8	0.23	0.34	0.85
GGT (IU/L)	54.1 ± 40.5	33.5 ± 46.7	20.5 ± 8.7	0.001	0.001	1.00

Supplementary Figure S1. Study flow charts

(A) Flow-chart of the test cohort, which includes 175 obese individuals with type 2 diabetes who underwent RYGB. (B) Flow-chart of the French validation cohort from Louis-Mourier hospital, including 54 obese individuals with type 2 diabetes who underwent RYGB as an external validation of the 5y-Ad-DiaRem.

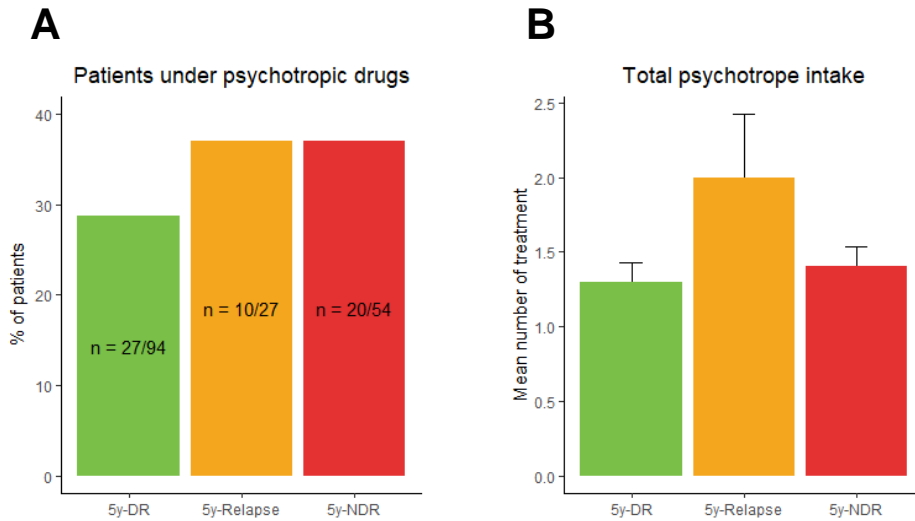


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Supplementary Figure S2. Baseline psychotropic drugs usage in our test cohort (n=175)

- A. Baseline prevalence of psychotropic drug usage
- B. Mean ± standard error of the total number of anti-psychotropic drugs taken by the treated patients

In both panels, Green represents patients in 5-years diabetes remission, Orange, those who relapsed after a transient remission and Red, those who remained with T2D all along the post-RYGB follow-up.

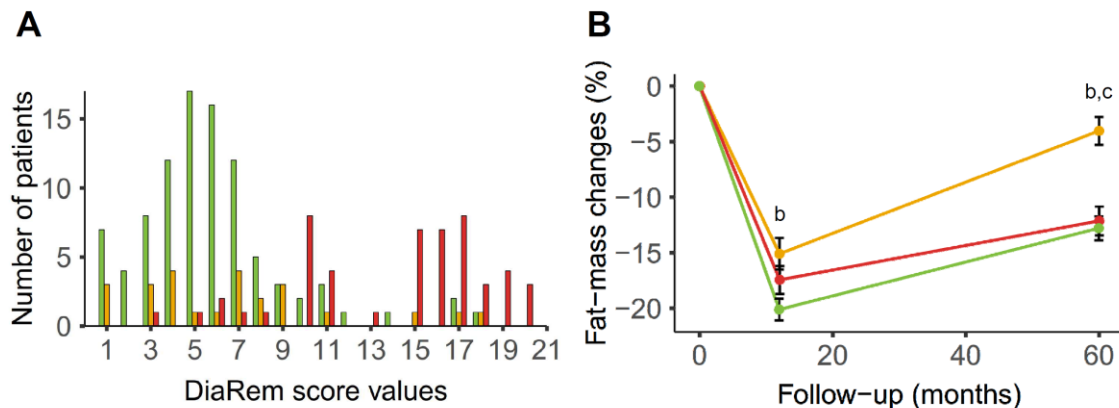


Supplementary Figure S3. DiaRem patient’s distribution in the test cohort (n=175) and evolution of fat mass during the follow-up

(A) Distribution of patients (n=175) in the test cohort according to their DiaRem score values.

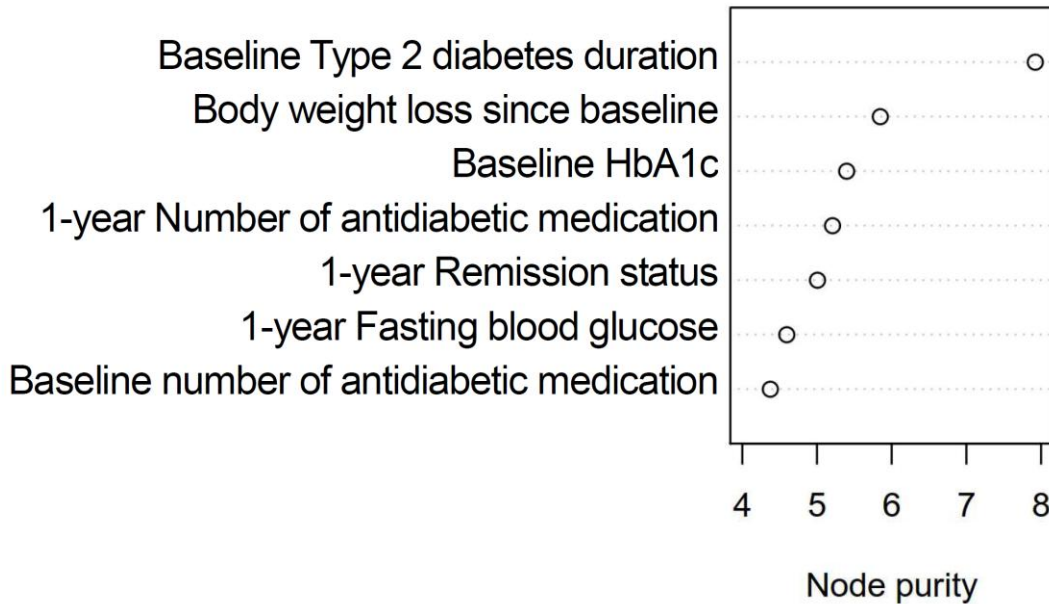
(B) Patients’ IMS score values colored according to their 5-year remission status (BARICAN cohort, n=175). (B) Evolution of patient’s fat mass during the follow-up (determined via DXA)

In both panels, Green represents patients in 5-years diabetes remission, Orange, those who relapsed after a transient remission and Red, those who remained with T2D all along the post-RYGB follow-up. In panel B, b means statistical difference (p<0.05) between 5y-DR and 5y-Relapse, and c between 5y-NDR and 5y-Relapse



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Supplementary Figure S4. Random forest analysis evaluating the impact of each item of the 5y-Ad-DiaRem in terms of long-term diabetes remission



Supplementary Figure S5. 5y-Ad-DiaRem patient’s distribution in our three confirmation cohorts.

- A. Patient’s distribution in the French confirmation cohort (n=54)
- B. Patient’s distribution in the Italian confirmation cohort from (n=20)
- C. Patient’s distribution in the German confirmation cohort from (n=50)

In all panels, Green represents patients in 5-years diabetes remission, Orange, those who relapsed after a transient remission and Red, those who remained with T2D all along the post-RYGB follow-up.

