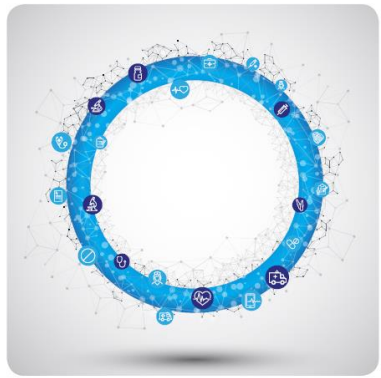


VICENZA

AULA MAGNA ING. GRESELE
POLO UNIVERSITARIO AULSS 8 BERICA
Contrà San Bortolo, 85

10 OTTOBRE 2019

HIGHWAY DIABETES
IL PAZIENTE AL CENTRO?

2019 MOTORE SANITÀ
Gestire il Cambiamento

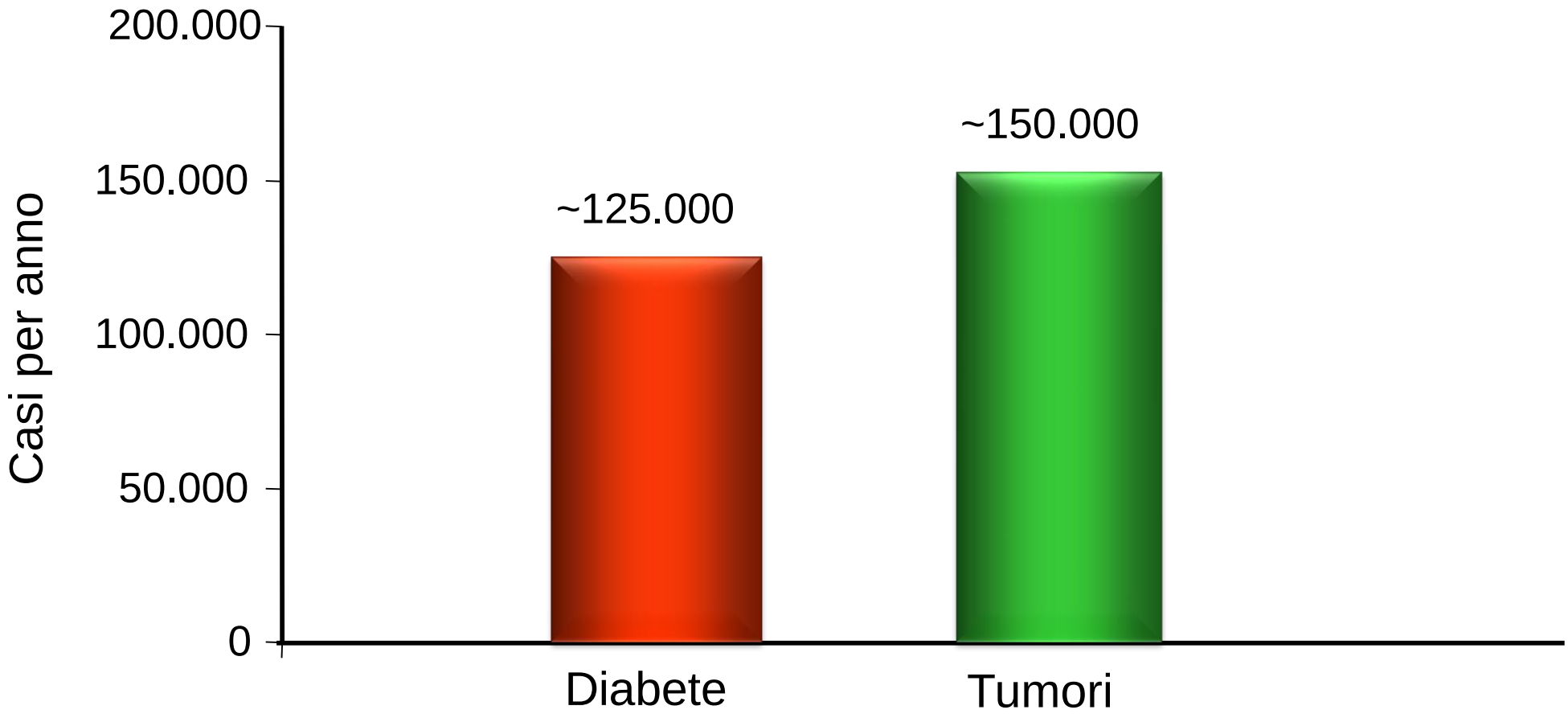
Innovazione tecnologica: cosa sta cambiando nel *real world*

Enzo Bonora

Endocrinologia, Diabete e Malattie del Metabolismo
Università e Azienda Ospedaliera Universitaria Integrata di Verona

Diabete e tumori come causa o concausa di morte in Italia

Elaborazione da Istat 2014 (tumori) e studi epidemiologici osservazionali italiani (diabete)

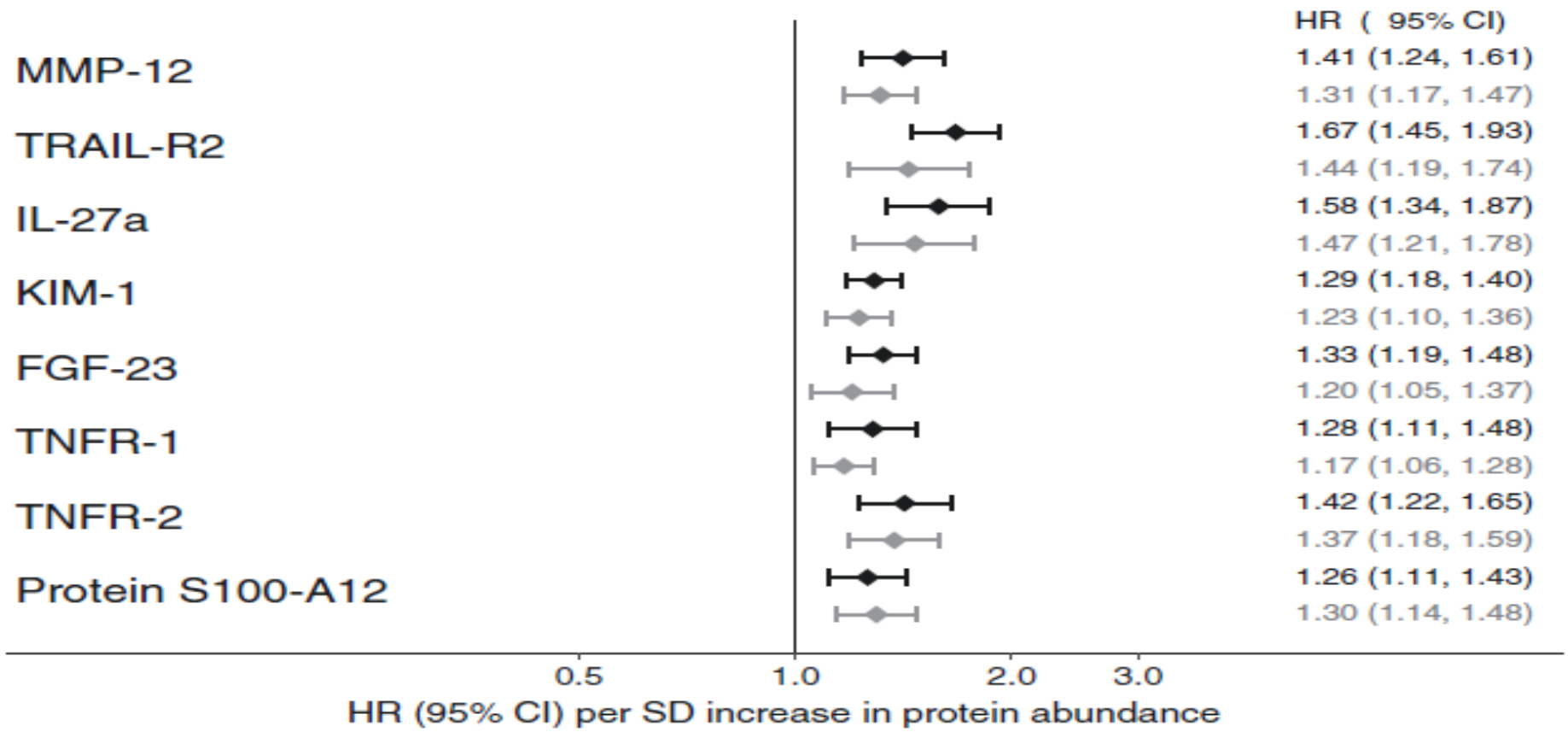


Agenda

- Strumenti diagnostici per una medicina di precisione
- Farmaci e germi
- Dispositivi per monitoraggio e terapia
- Connettività, telemedicina e medicina digitale
- BIG data e intelligenza artificiale come ausilio nella terapia

Multiplex proteomics for prediction of MACE in T2DM

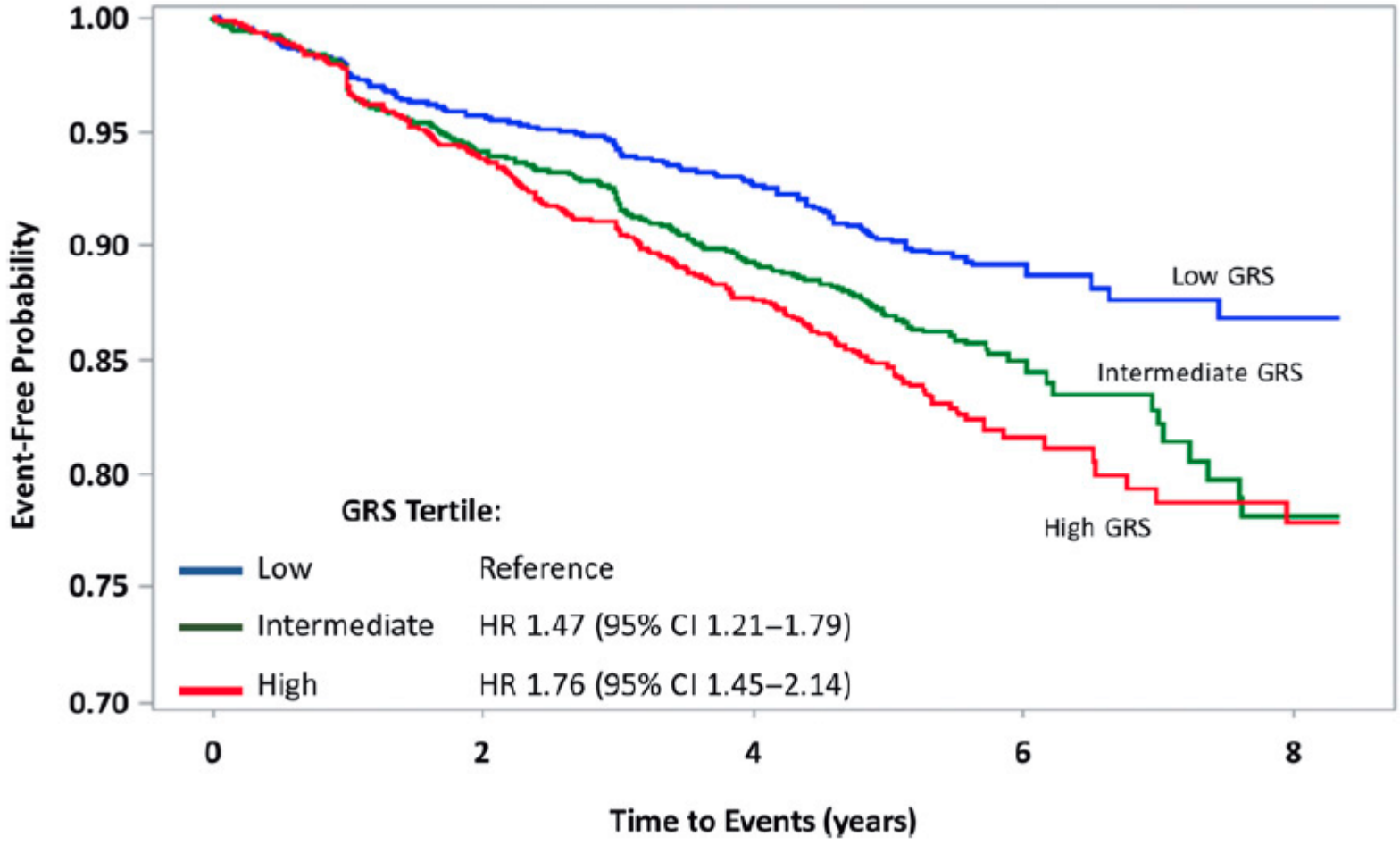
Nowak C et al - Diabetologia 2018; 61:1748–1757



Combined data from 6 prospective epidemiological studies of 30–77-year-old individuals with T2DM in whom **80 circulating proteins** were measured.
Adjusted for sex and age (black symbols) and also for duration of DM, BMI, HbA1c, smoking, AF, LDL-C, statin use, sBP, Albuminuria, eGFR, prior CVD (grey symbols)

Genetic risk scores and CVD risk in T2DM

Morieri ML et al - Diabetes Care 2018

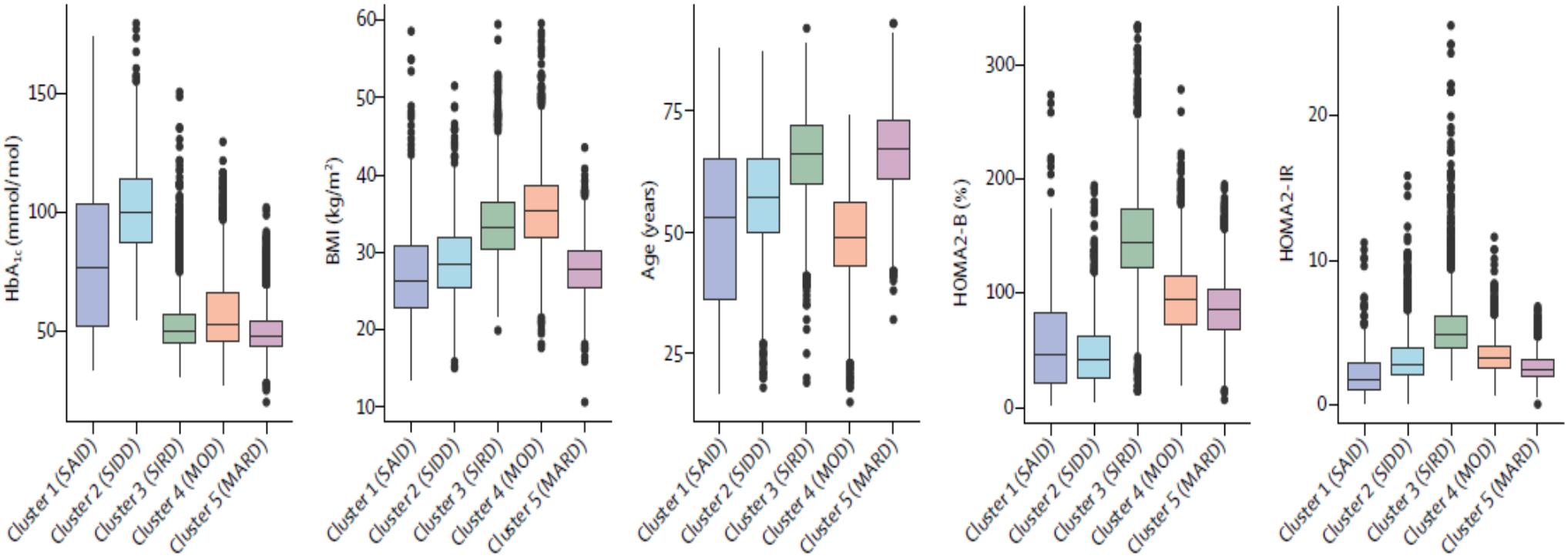


Type 2 diabetes is not a single disease

- Older or younger onset of disease
- Overweight/obesity or normal or quasi-normal weight
- Severe insulin deficiency or severe insulin resistance
- Faster or slower progression toward beta-cell failure
- More or less difficult control of glucose/HbA1c
- Higher fasting or higher post-prandial blood glucose levels
- Stronger or looser genetic background

Clinical features in subgroups (cluster) of patients with T2DM

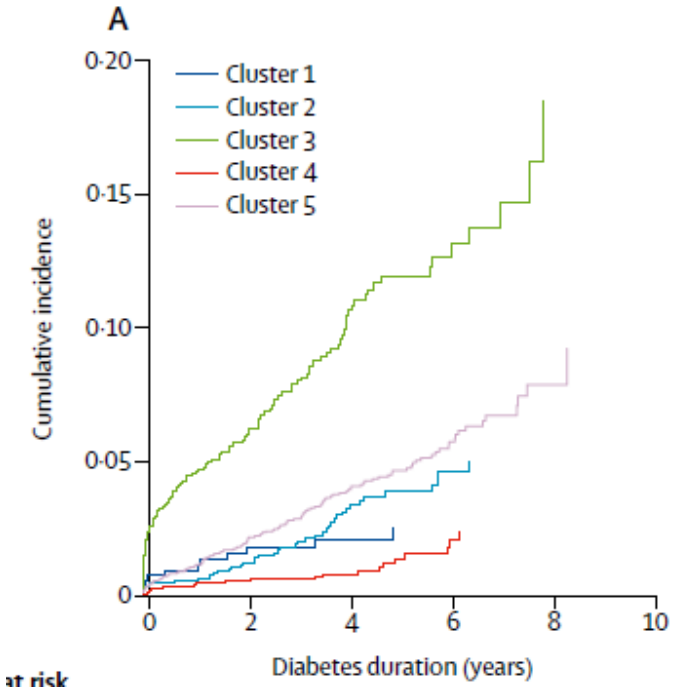
Ahlqvist E et al – Lancet Diabetes Endocrinol 2018; 6:361

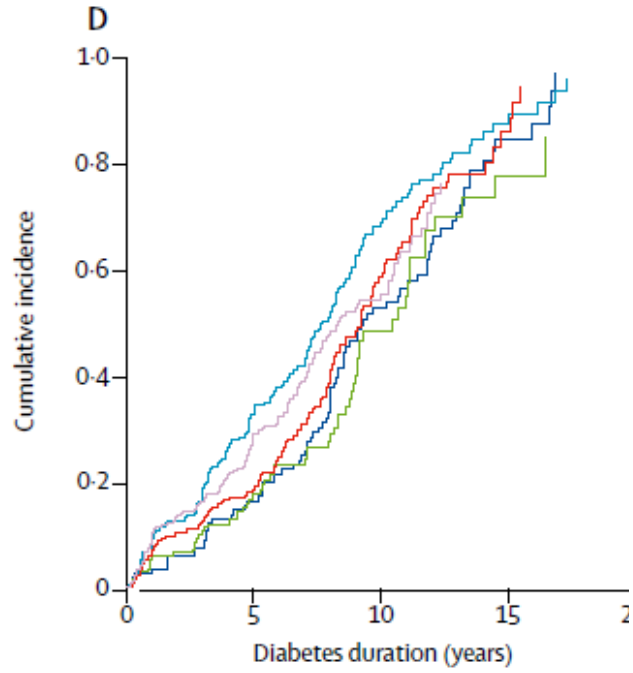


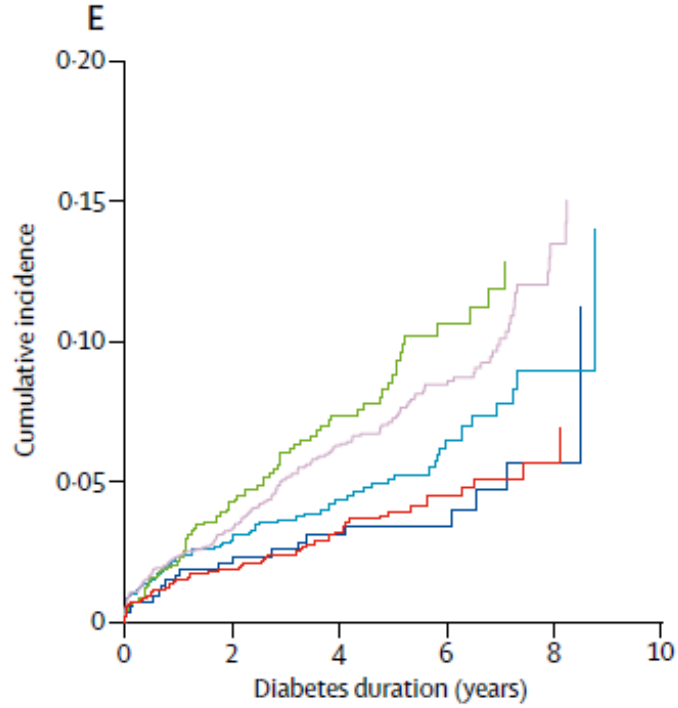
TOTALE = 8980 nuovi casi
SAID = severe autoimmune diabetes (6.4%) = early-onset, relatively low BMI, poor control, insulin deficiency, GADA +
SIDD = severe insulin-deficient diabetes (17.5%) = early-onset, relatively low BMI, poor control, insulin deficiency, GADA -
SIRD = severe insulin-resistant diabetes (15.3) = high BMI, insulin resistance
MOD = mild obesity-related diabetes (21.6%) = high BMI, no insulin resistance
MARD = mild age-related diabetes (39.1%) = older age, lower BMI, no insulin resistance

Incidence of complications in subgroups (cluster) of patients with T2DM

Ahlqvist E et al – Lancet Diabetes Endocrinol 2018; 6:361







Nephropathy

Retinopathy

CVD

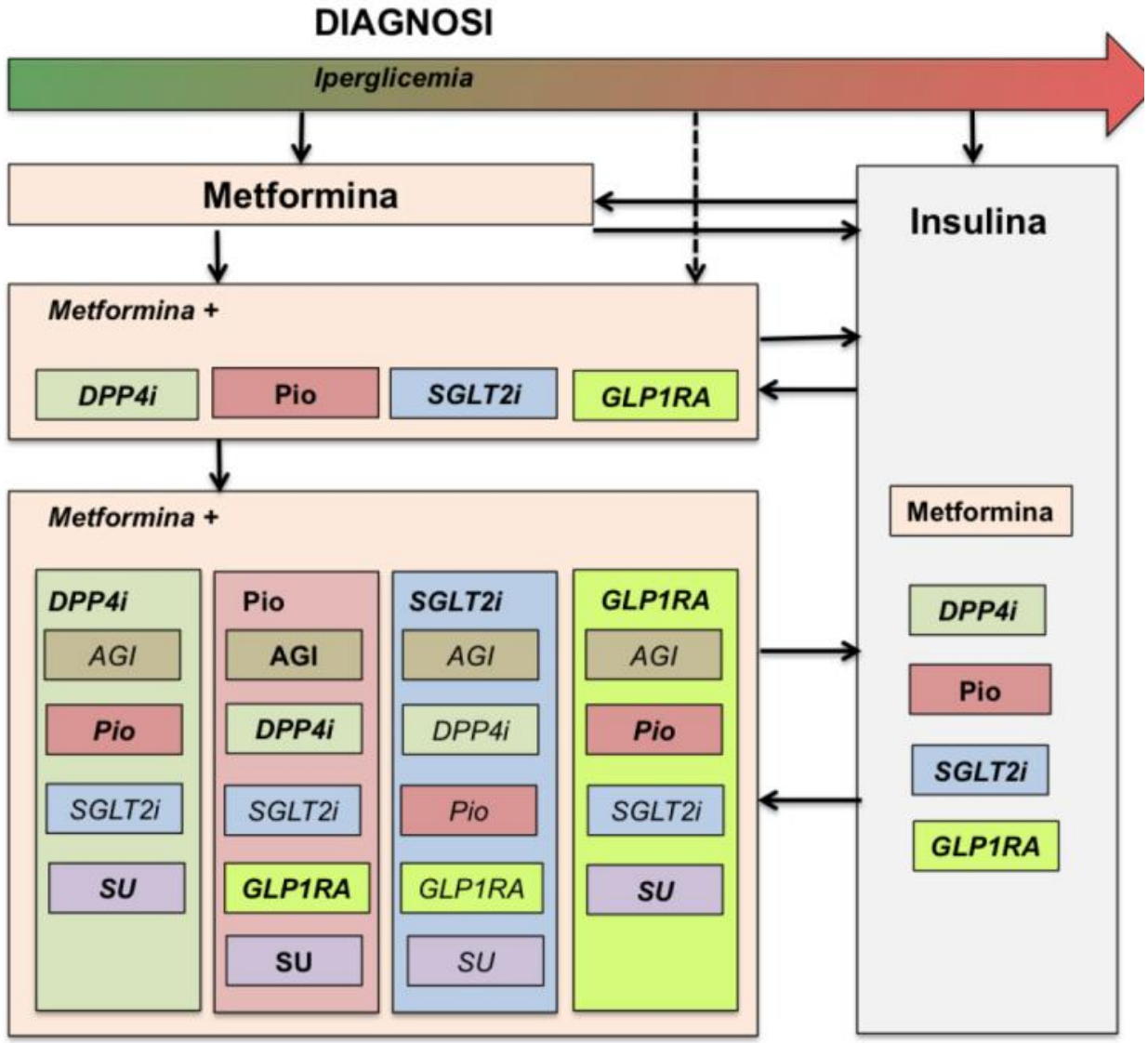
Innovazione e terapia del diabete

Negli ultimi 10 anni si sono resi disponibili:

- Inibitori DPP-4 da soli o in combinazione fissa con altri farmaci
- Agonisti recettoriali GLP-1 da soli in combinazione fissa con insulina
- Inibitori SGLT-2 da soli o in combinazione fissa con altri farmaci
- Analoghi insulina rapidissimi
- Analoghi insulina ultralenti

Altre classi di farmaci non sono lontane

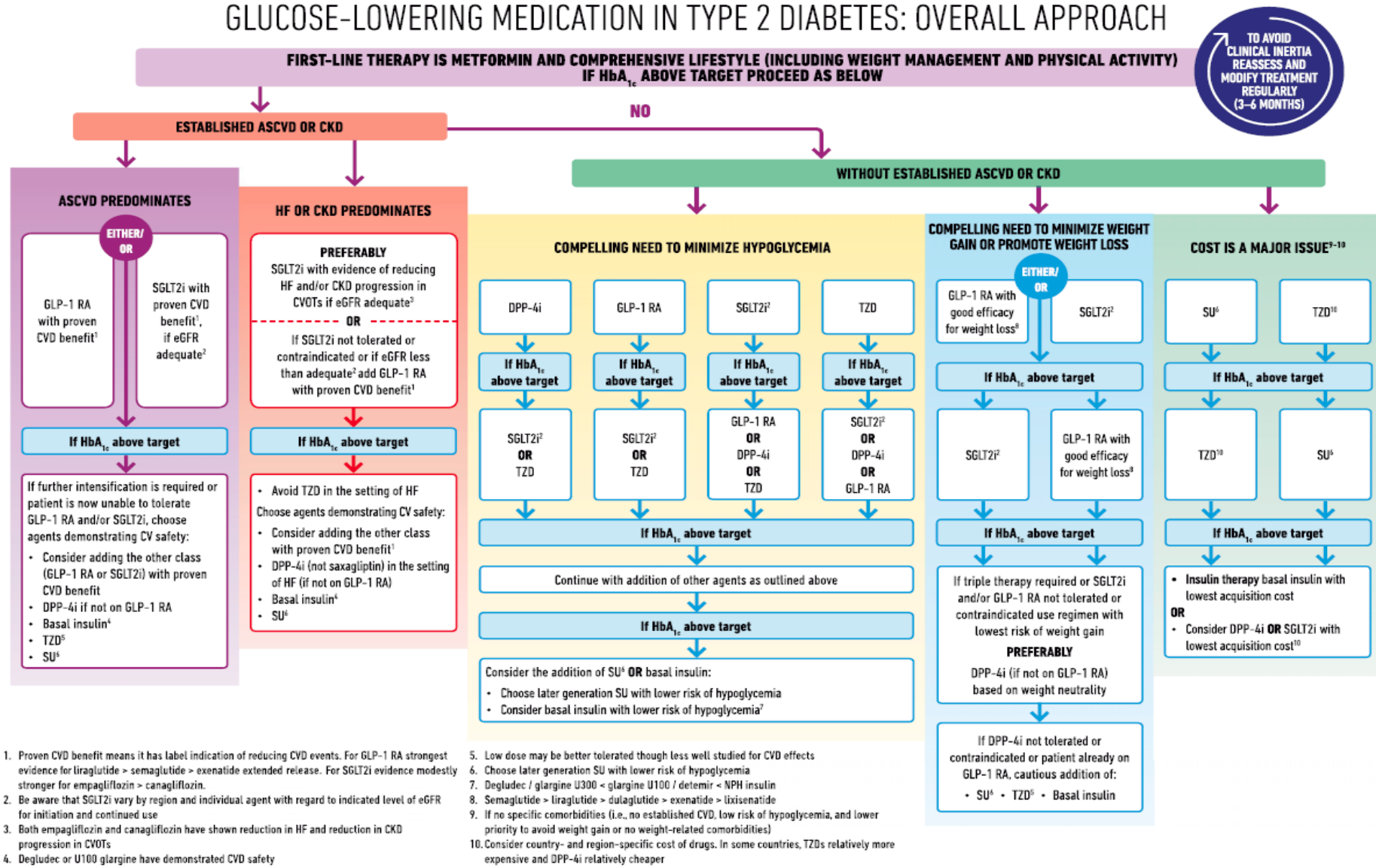
Standard Italiani per la Cura del Diabete Mellito - 2018



SU/Glinidi oggi sono farmaci di terza/quarta linea

Algoritmo terapeutico nel diabete tipo 2

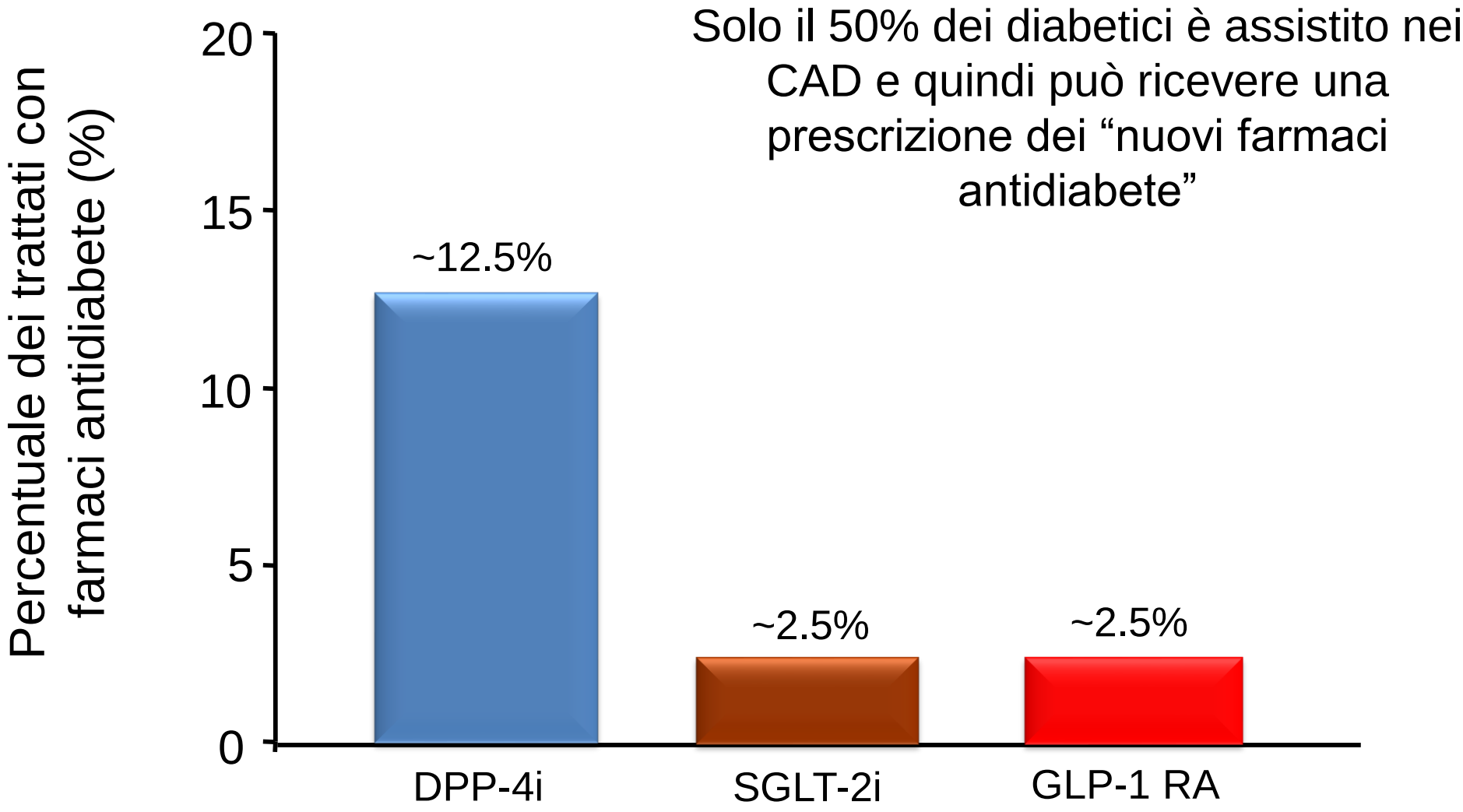
Consensus ADA-EASD 2018



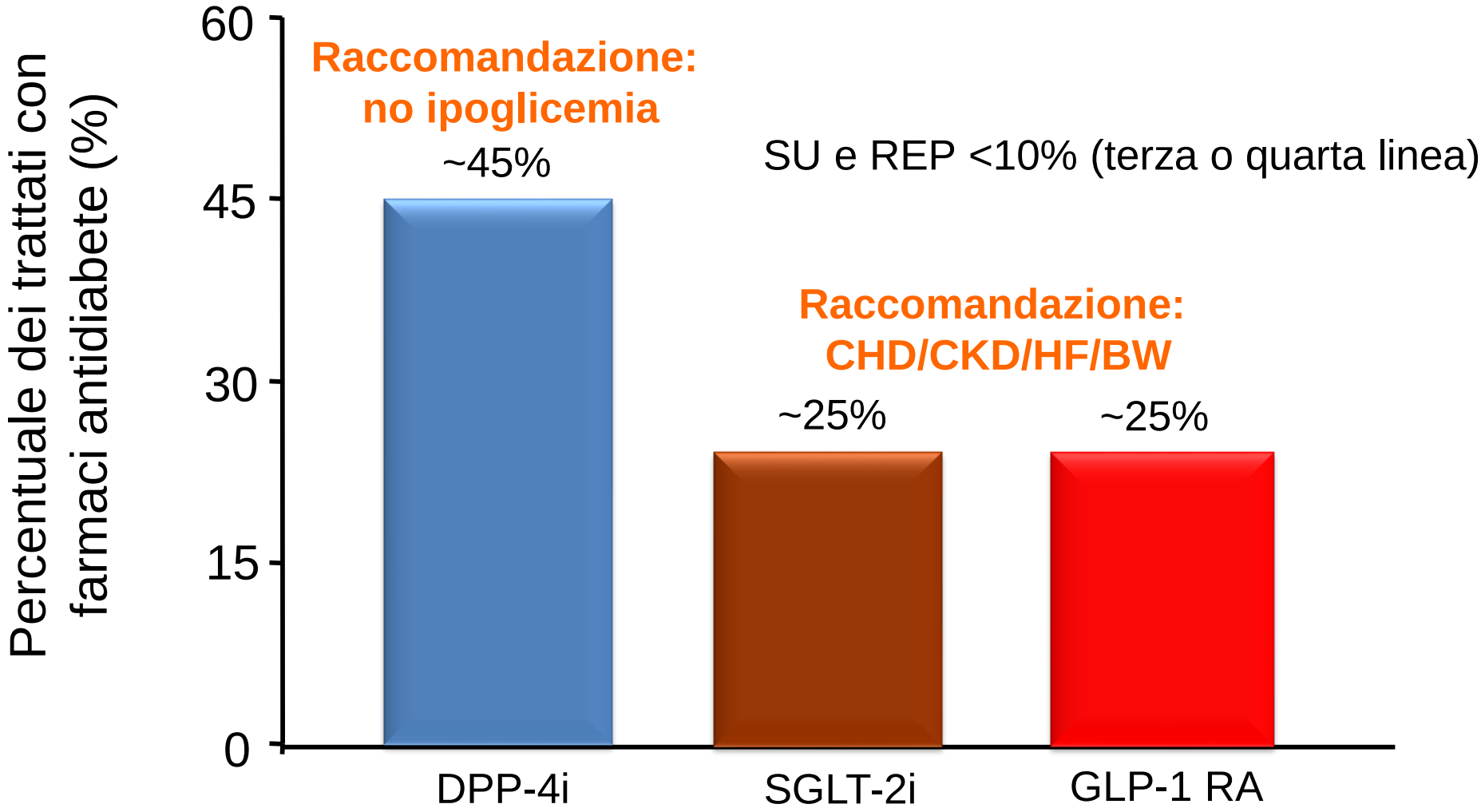
1. Proven CVD benefit means it has label indication of reducing CVD events. For GLP-1 RA strongest evidence for liraglutide > semaglutide > exenatide extended release. For SGLT2i evidence modestly stronger for empagliflozin > canagliflozin.
2. Be aware that SGLT2i vary by region and individual agent with regard to indicated level of eGFR for initiation and continued use
3. Both empagliflozin and canagliflozin have shown reduction in HF and reduction in CKD progression in CVOTs
4. Degludec or U100 glargine have demonstrated CVD safety
5. Low dose may be better tolerated though less well studied for CVD effects
6. Choose later generation SU with lower risk of hypoglycemia
7. Degludec / glargine U300 < glargine U100 / detemir < NPH insulin
8. Semaglutide > liraglutide > dulaglutide > exenatide > lixisenatide
9. If no specific comorbidities (i.e., no established CVD, low risk of hypoglycemia, and lower priority to avoid weight gain or no weight-related comorbidities)
10. Consider country- and region-specific cost of drugs. In some countries, TZDs relatively more expensive and DPP-4i relatively cheaper

Trattati con “nuovi” farmaci antidiabete in Italia

Osservatorio ARNO Diabete SID-CINECA - 2017 (anno 2016)

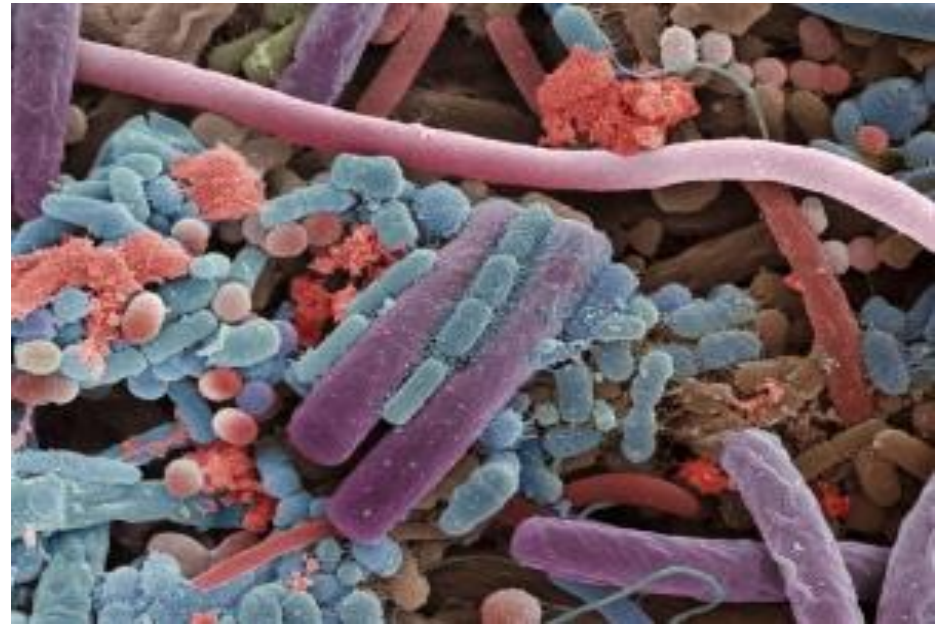


Scenario dei trattati con “nuovi” farmaci antidiabete in Italia rispetto al totale in terapia farmacologica se fossero puntualmente applicate le nuove linee guida



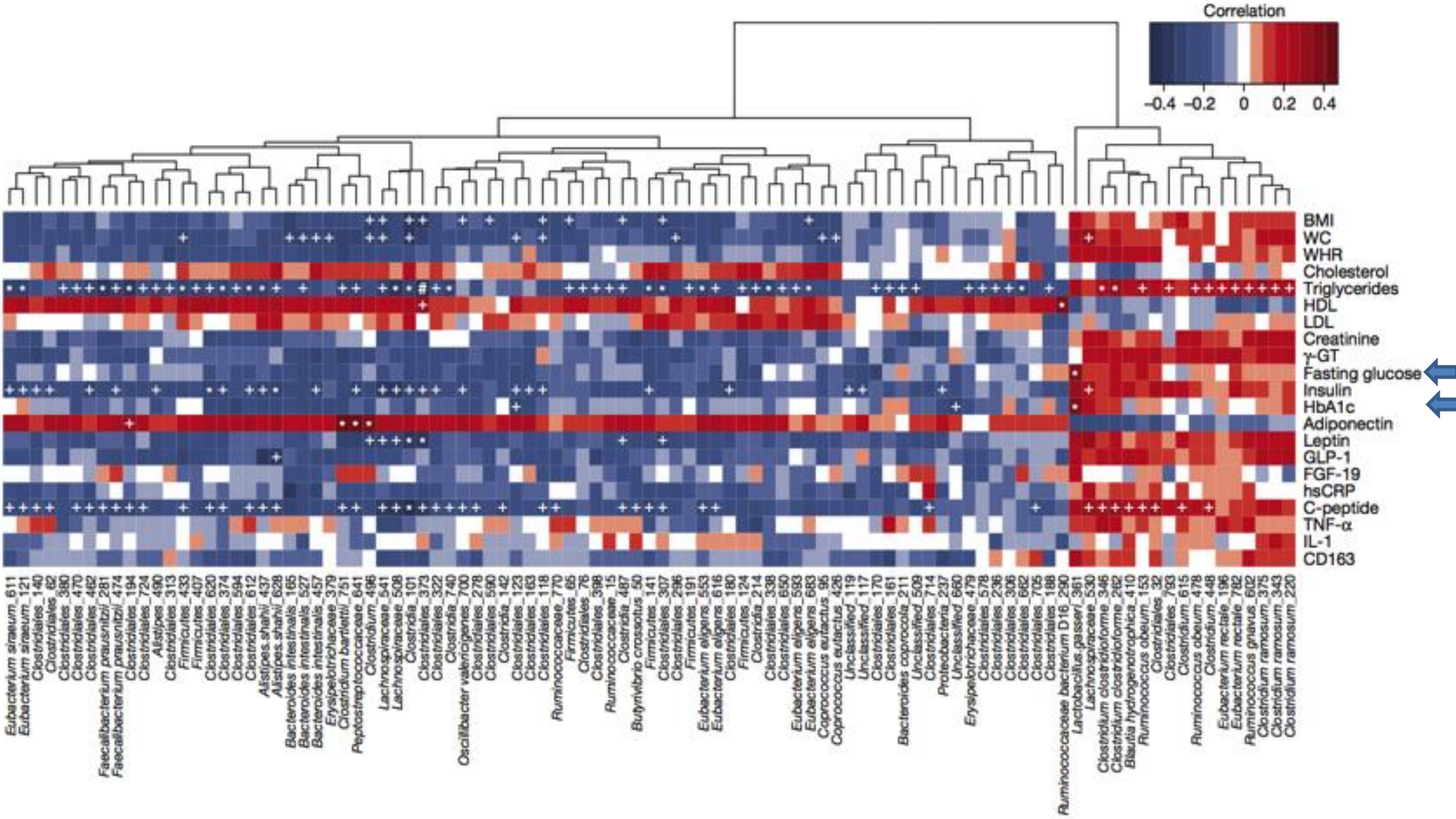
Gut microbiota and diabetes

Dysbiosis is common



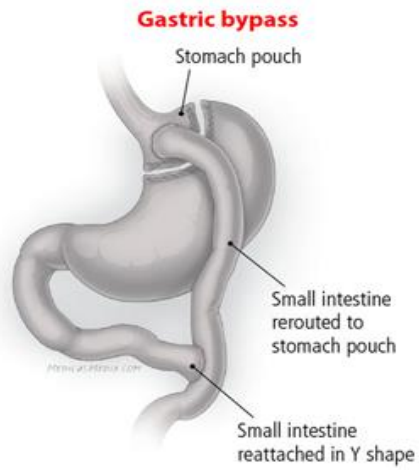
Associations of metagenome with metabolic biomarkers in European women with normal, impaired and diabetic glucose control

Nature 2013; 498:99-103

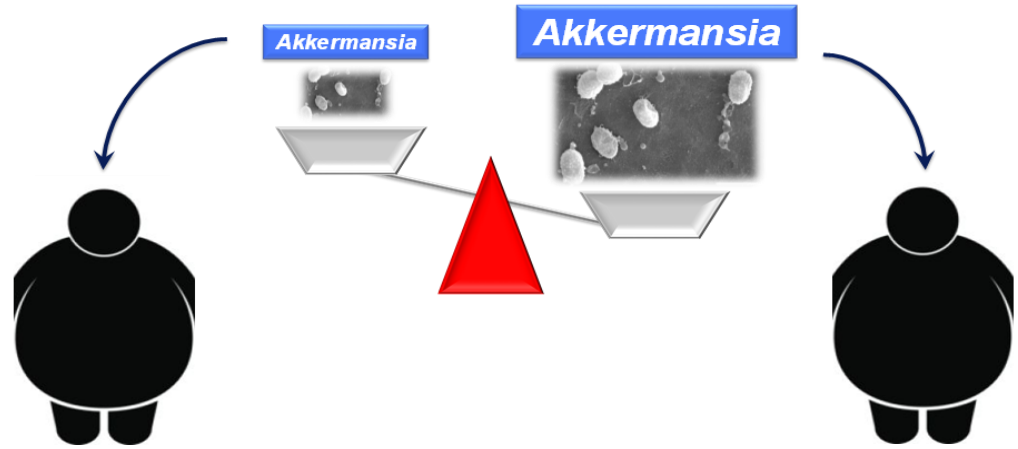


Akkermansia muciniphila and its beneficial effects

Dao et al *Gut* 2016; Dao et al *Clin Exp Nutr* 2016



A. muciniphila



Higher cholesterol
Higher Inflammation
Higher insulin resistance
Higher waist circumference
Larger adipocyte size

Lower cholesterol
Lower Inflammation
Less insulin resistance
Lower waist circumference
Smaller adipocyte size

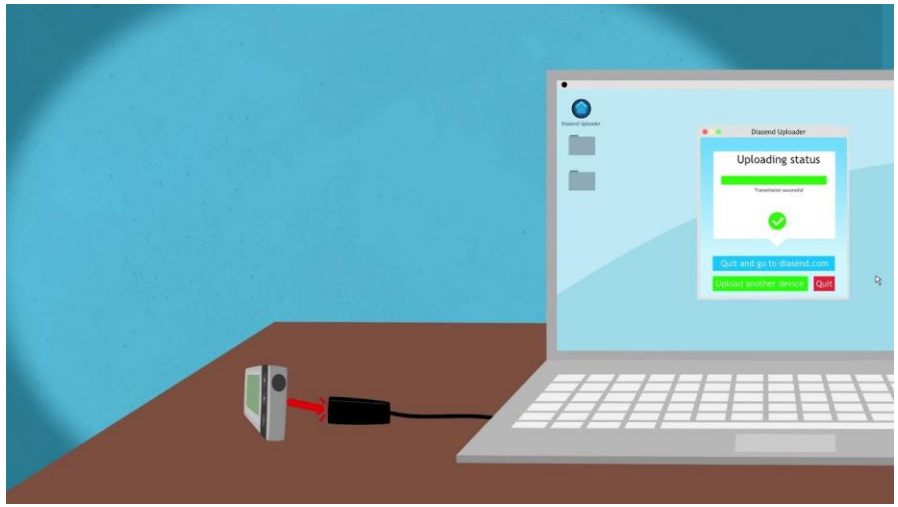
Strumenti per il monitoraggio glicemico domiciliare: “a ciascuno il suo”

Dispositivi prescritti per la cura del diabete in Italia

Osservatorio ARNO Diabete SID-CINECA - 2017 (anno 2016)

Tipo	N. soggetti trattati	% trattati su popolazione con diabete (n=640.846)
Strisce	322.295	50,3
Siringhe/aghi	274.197	42,8
Lancette pungidito	138.807	21,7
Totale	325.279	50,8

Scarico dati su smartphone, pc o piattaforma da sfruttare maggiormente



diasend®

#1 in diabetes data management

[redacted] t Explorer

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Google

Preferiti [redacted]

Pagina Sicurezza Strumenti

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V 3.01 | Crea rapporto | Cancella rapporto | Leggi dispositivo

Impostazioni

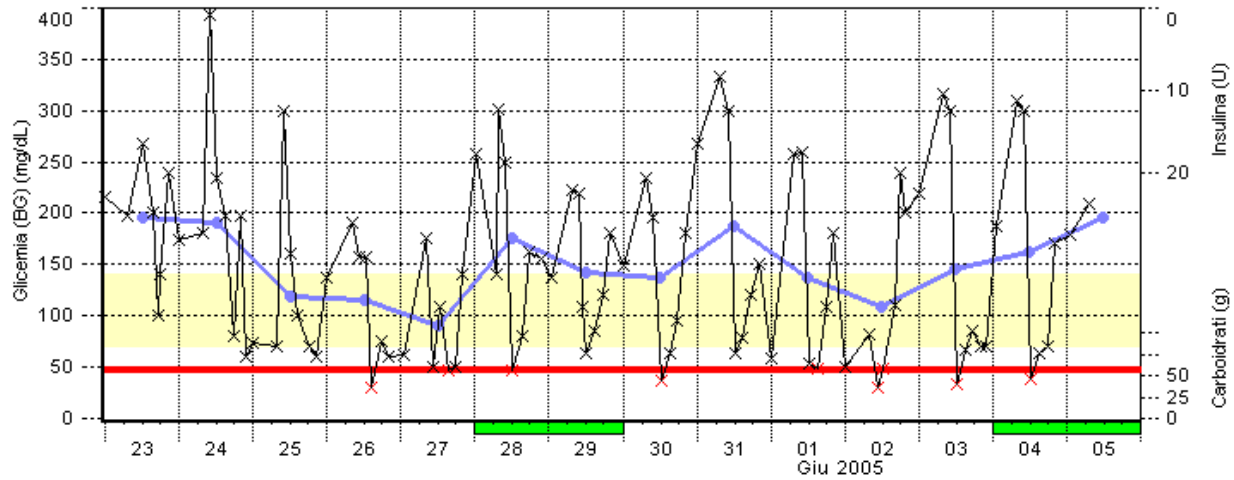
Glucometro

- Grafico dell'andamento
- Andamento giornaliero
- Andamento settimanale
- Controllo metabolico
- Distribuzione
- Diario
- Panoramica
- Elenco

Grafico dell'andamento

2 settimane fino al 05.06.2005

Numero di serie
01161150



Stampa pagina

× Glicemia (BG) × Ipo Glicemia media (MBG) Fine settimana

[redacted]

[redacted]

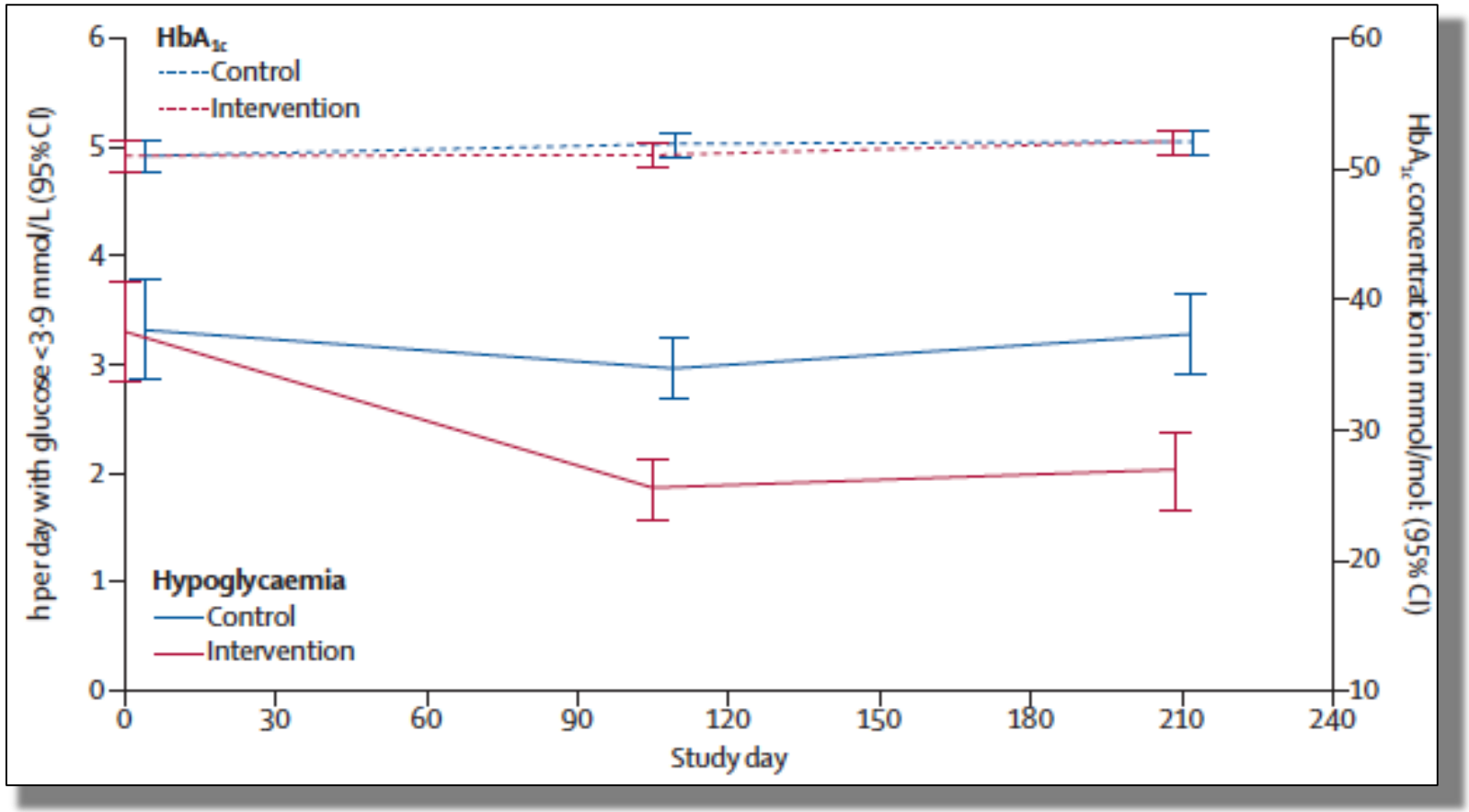
Fine | Computer | Modalità protetta: disattivata | 100%

Sensori glicemici intermittenti (FGM o iCGM)

Oltre 5 mila nel Veneto
Numeri in aumento

Impatto del FGM sul tempo trascorso con glicemia <70 mg/dl nel T1DM

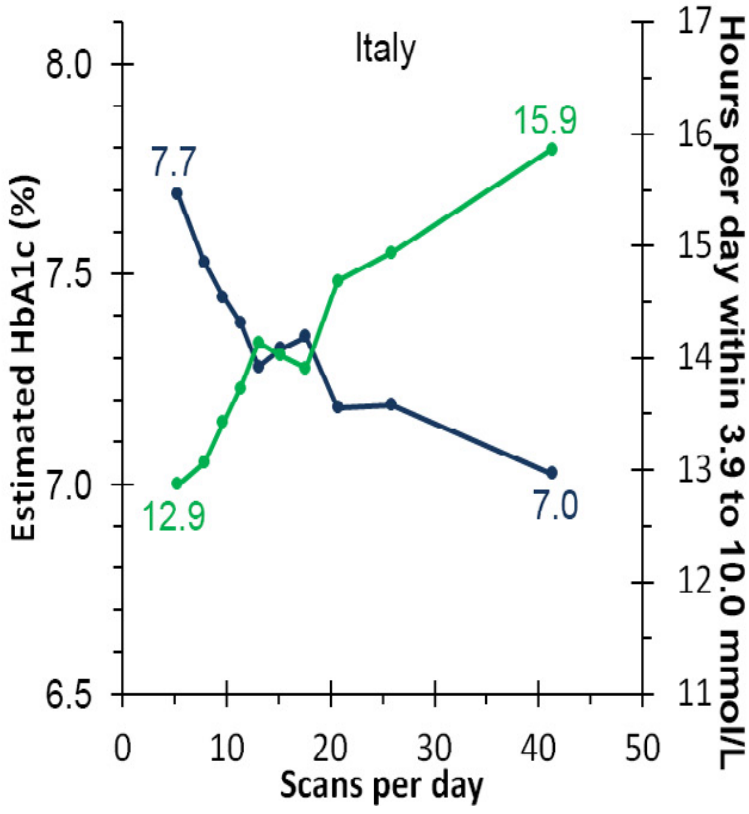
Bolinder J et al - Lancet 2016; 388: 2254-63

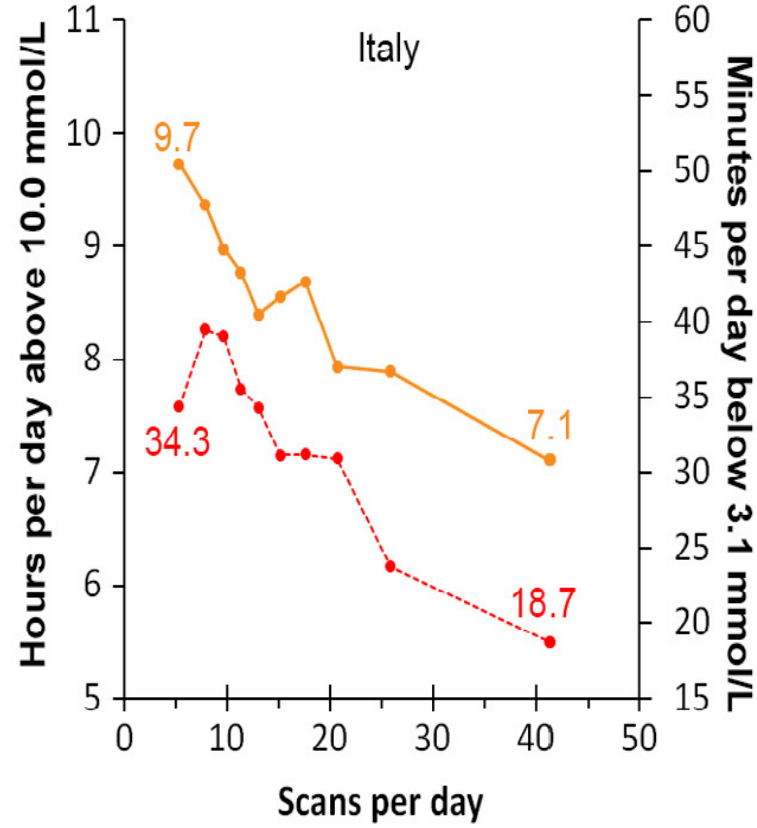


241 soggetti con T1DM, follow-up 240 giorni

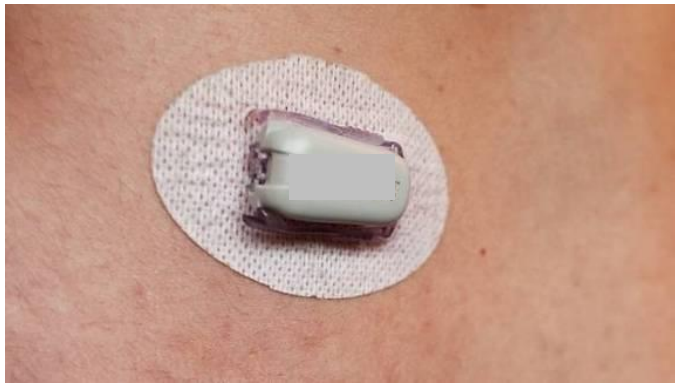
Il numero delle scansioni del sensore (FGM) per giorno riduce la HbA1c, le ore trascorse con glicemia >180 mg/dl, i minuti trascorsi con glicemia inferiore a 55 mg/dl e aumenta il Time-in-Range

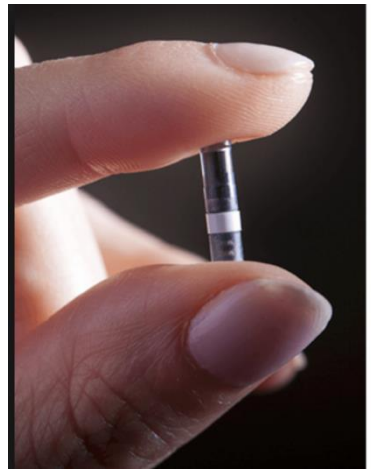
Dunn T et al - Diab Res Clin Pract 2018; 137:37





Sensori glicemici *Real Time* (CGM)

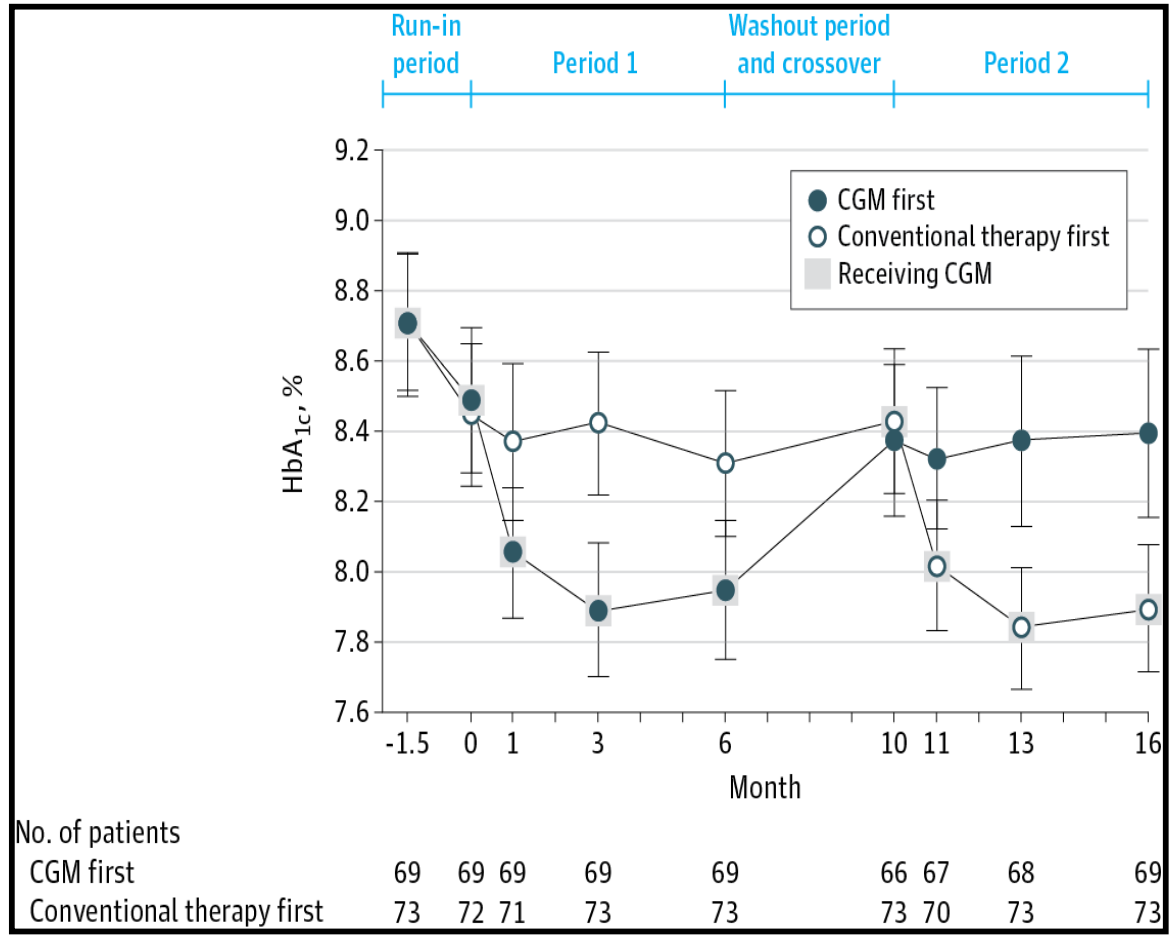




Oltre un centinaio nel Veneto
Numeri in aumento

Controllo glicemico migliore con rtCGM rispetto a monitoraggio con glucometro nel T1DM

DIAMOND Study - Beck RW et al - JAMA 2017; 317: 371-378

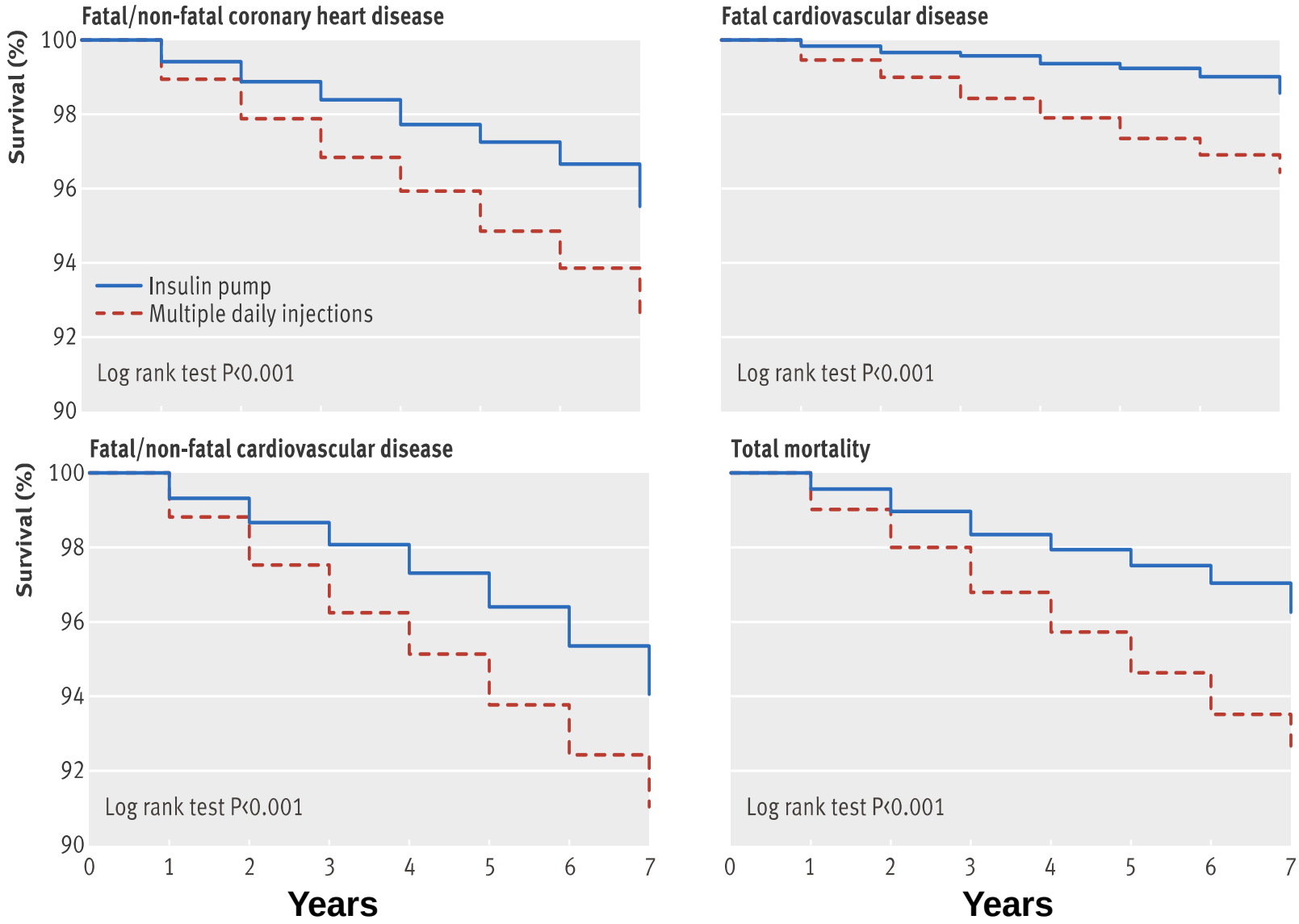


Microinfusori insulinici e patch pumps

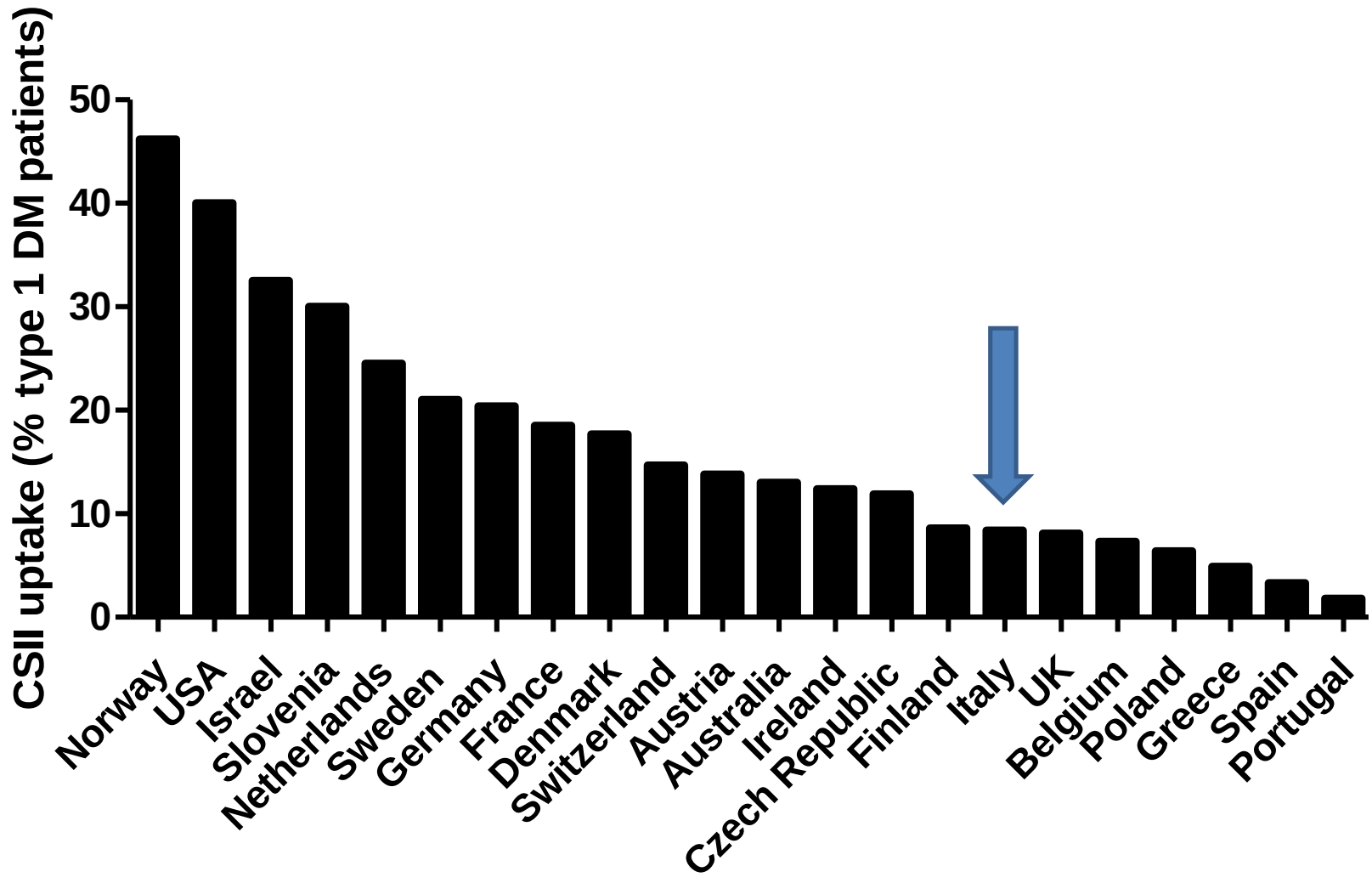
Oltre 600 nel Veneto
Numeri in aumento

Patients on insulin pump therapy have lower cardiovascular morbidity and lower total mortality

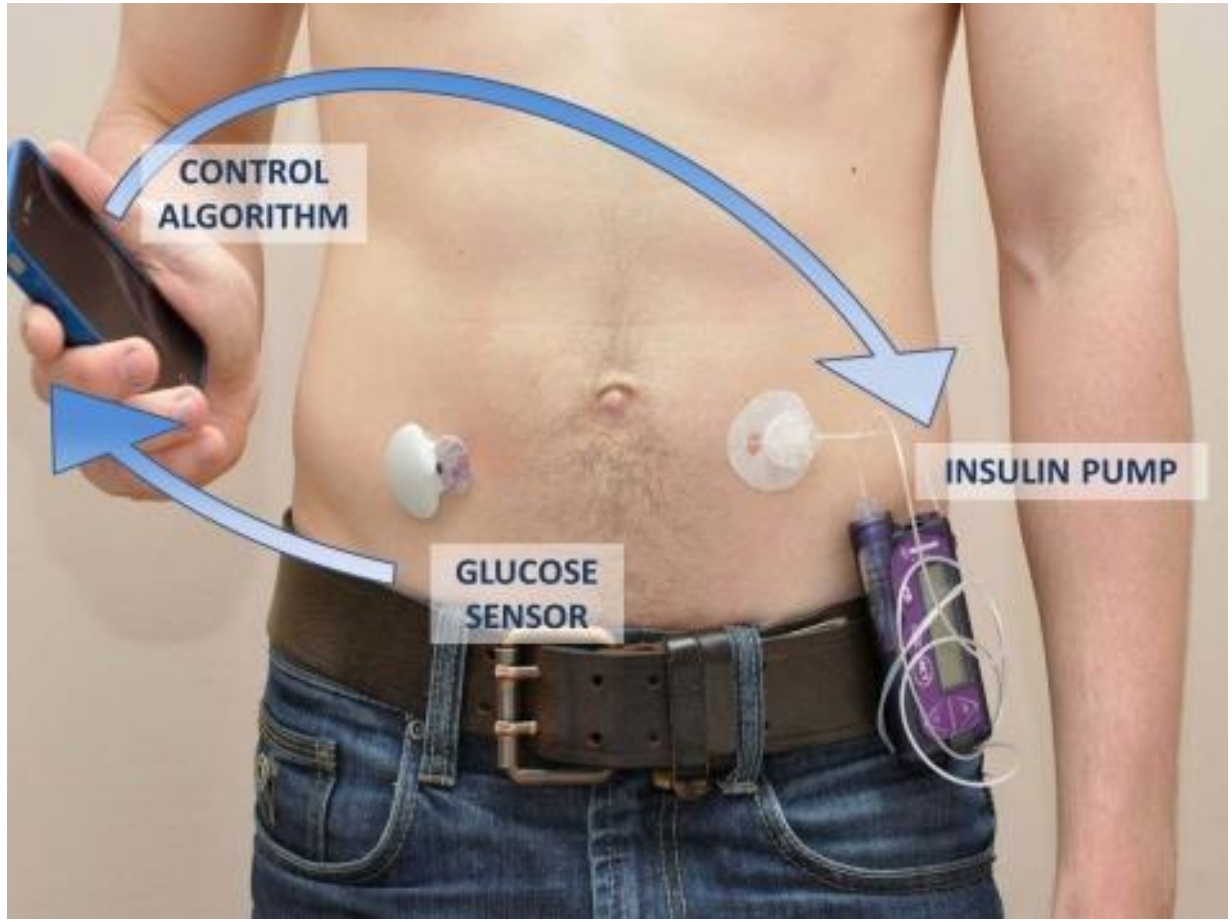
The Swedish National Diabetes Register – BMJ 2015



Pazienti con T1DM trattati con microinfusore insulinico nel mondo occidentale



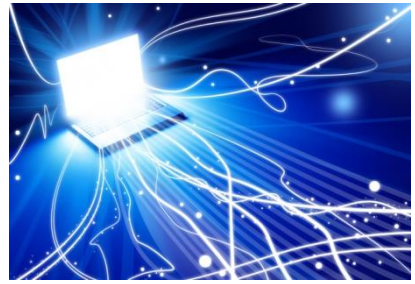
Il pancreas artificiale è ormai una realtà: ci sono già pazienti che lo usano in Italia



Circa 15 nel Veneto
Numeri in aumento

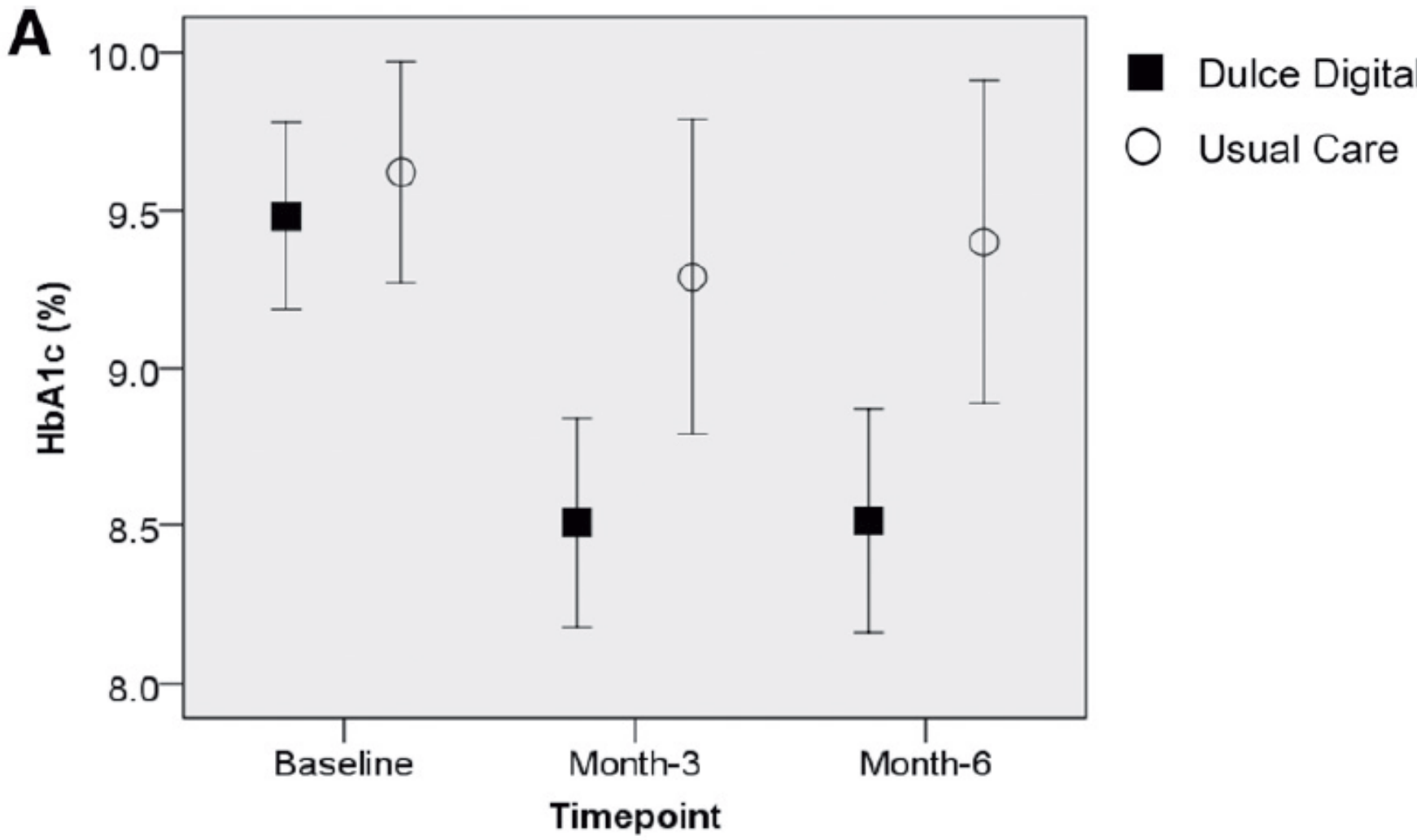
Tecnologia e connettività

- Scarico delle misurazioni glicemiche da glucometro o sensore o i dati del microinfusore sul proprio smartphone o PC o nel server del Centro Diabetologico (valutazione più agevole ed esaustiva)
- Archiviazione dei valori glicemici sulla “nube” (condivisione dei diari glicemici in remoto da parte della persona con diabete e del Centro Diabetologico)
- Valutazione attenta dei diari glicemici arricchiti di altre informazioni (alimentazione, attività fisica, stress, terapia, ecc.) per individuare la strategia di cura migliore



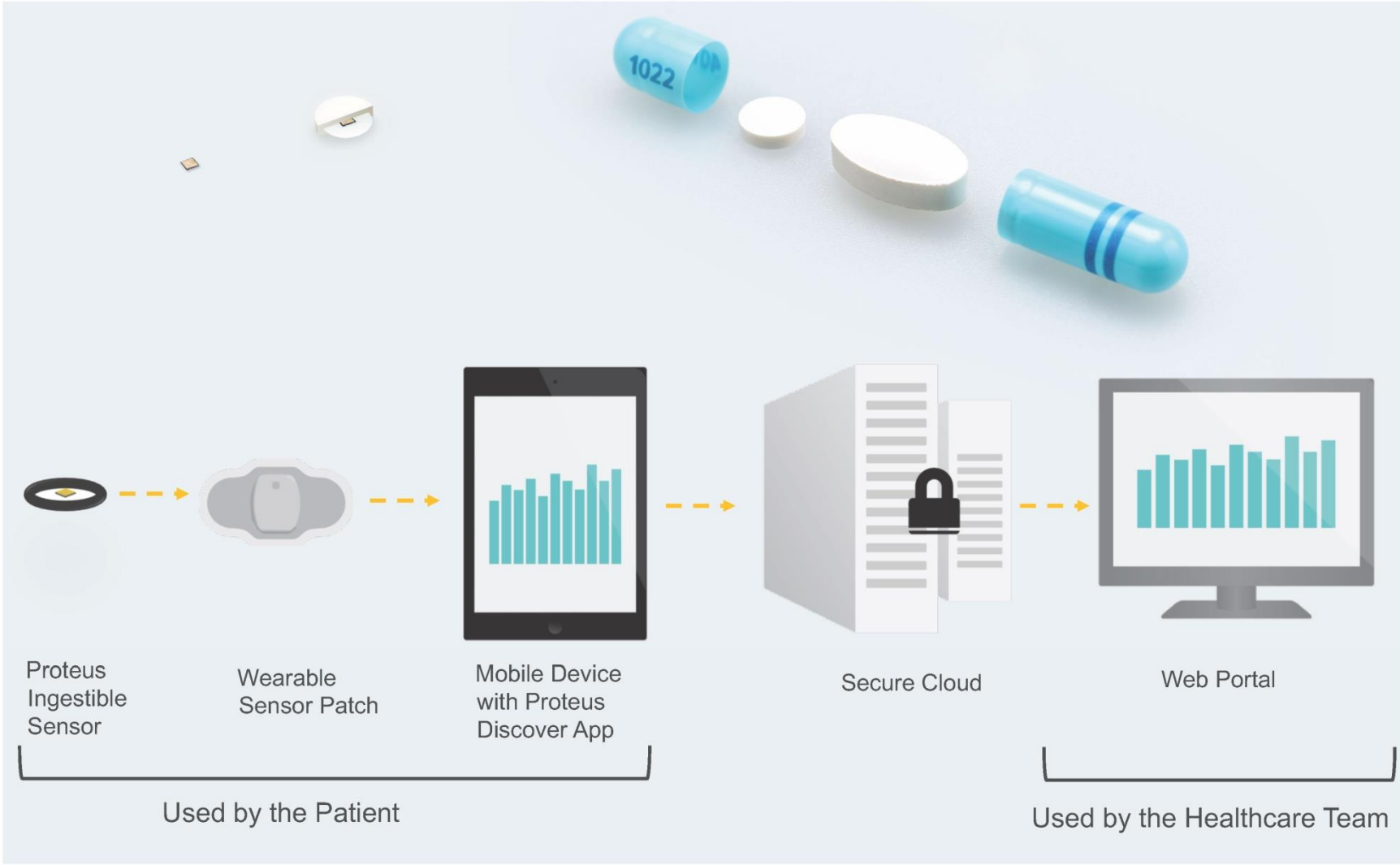
Digital medicine (SMS) to improve SMBG and glucose control in T2DM

Fortmann AL et al - Diabetes Care 2017; 40:1349



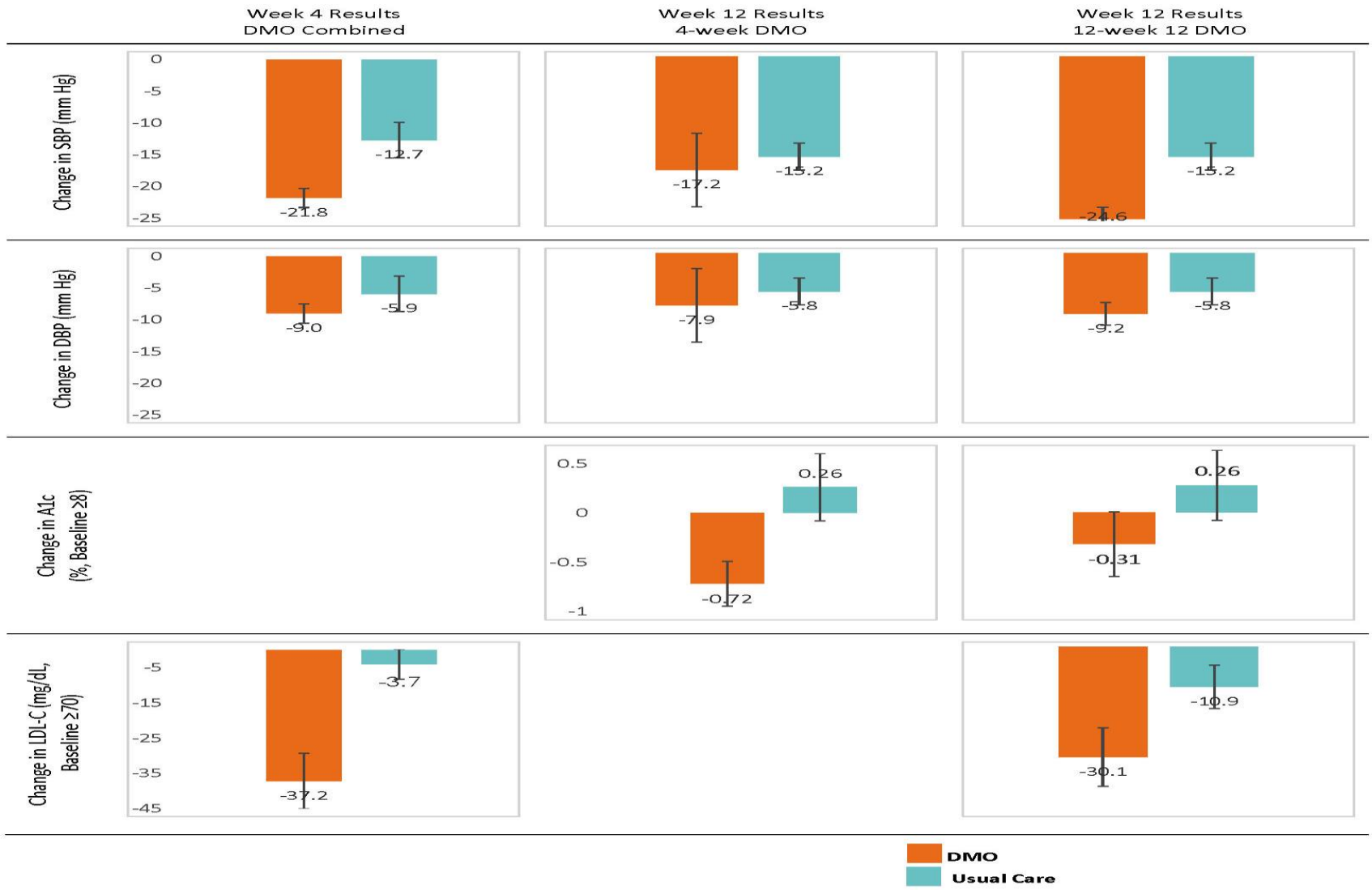
Digital medicine to improve adherence in taking drugs and exercising

Fries J et al - J Med Internet Res 2017; 19:e246



Digital medicine improves adherence and control of blood pressure, HbA1c and LDL-Cholesterol in T2DM

Fries J et al - J Med Internet Res 2017; 19:e246



Digital medicine improves HbA1c in T2DM

A meta-analysis

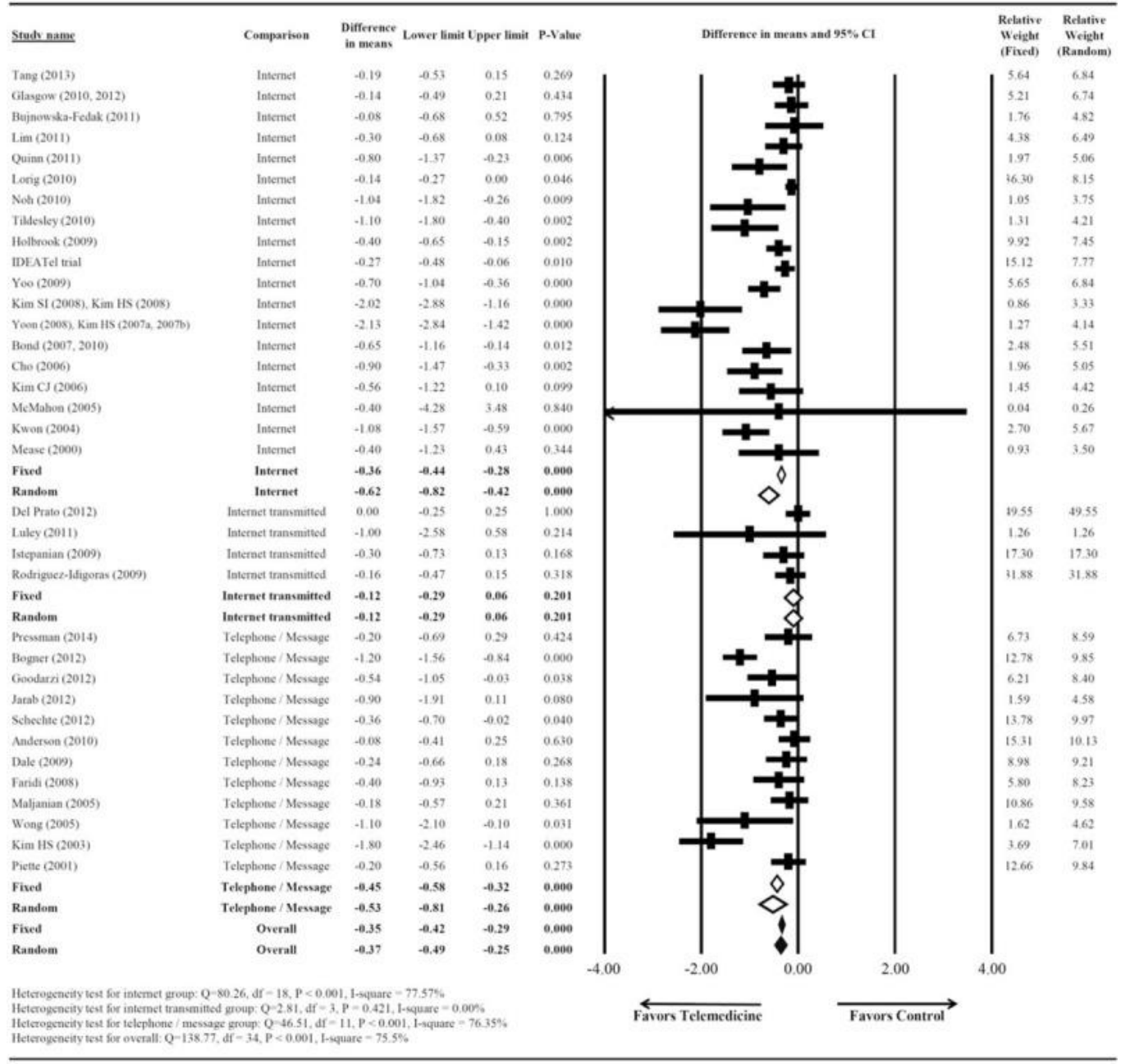
Zhai YK et al - Medicine Res 2014; 93:e312

HbA1c reduction

Internet education = -0.62%

Internet dialogues = -0.12%

Calls/sms = -0.53%



Study name	Comparison	Difference in means	Lower limit	Upper limit	P-Value	Relative Weight (Fixed)	Relative Weight (Random)
Tang (2013)	Internet	-0.19	-0.53	0.15	0.269	5.64	6.84
Glasgow (2010, 2012)	Internet	-0.14	-0.49	0.21	0.434	5.21	6.74
Bujnowska-Fedak (2011)	Internet	-0.08	-0.68	0.52	0.795	1.76	4.82
Lim (2011)	Internet	-0.30	-0.68	0.08	0.124	4.38	6.49
Quinn (2011)	Internet	-0.80	-1.37	-0.23	0.006	1.97	5.06
Lorig (2010)	Internet	-0.14	-0.27	0.00	0.046	16.30	8.15
Noh (2010)	Internet	-1.04	-1.82	-0.26	0.009	1.05	3.75
Tildesley (2010)	Internet	-1.10	-1.80	-0.40	0.002	1.31	4.21
Holbrook (2009)	Internet	-0.40	-0.65	-0.15	0.002	9.92	7.45
IDEATel trial	Internet	-0.27	-0.48	-0.06	0.010	15.12	7.77
Yoo (2009)	Internet	-0.70	-1.04	-0.36	0.000	5.65	6.84
Kim SI (2008), Kim HS (2008)	Internet	-2.02	-2.88	-1.16	0.000	0.86	3.33
Yoon (2008), Kim HS (2007a, 2007b)	Internet	-2.13	-2.84	-1.42	0.000	1.27	4.14
Bond (2007, 2010)	Internet	-0.65	-1.16	-0.14	0.012	2.48	5.51
Cho (2006)	Internet	-0.90	-1.47	-0.33	0.002	1.96	5.05
Kim CJ (2006)	Internet	-0.56	-1.22	0.10	0.099	1.45	4.42
McMahon (2005)	Internet	-0.40	-4.28	3.48	0.840	0.04	0.26
Kwon (2004)	Internet	-1.08	-1.57	-0.59	0.000	2.70	5.67
Mease (2000)	Internet	-0.40	-1.23	0.43	0.344	0.93	3.50
Fixed	**Internet**	**-0.36**	**-0.44**	**-0.28**	**0.000**		
Random	**Internet**	**-0.62**	**-0.82**	**-0.42**	**0.000**		
Del Prato (2012)	Internet transmitted	0.00	-0.25	0.25	1.000	49.55	49.55
Luley (2011)	Internet transmitted	-1.00	-2.58	0.58	0.214	1.26	1.26
Istepanian (2009)	Internet transmitted	-0.30	-0.73	0.13	0.168	17.30	17.30
Rodriguez-Idigoras (2009)	Internet transmitted	-0.16	-0.47	0.15	0.318	31.88	31.88
Fixed	**Internet transmitted**	**-0.12**	**-0.29**	**0.06**	**0.201**		
Random	**Internet transmitted**	**-0.12**	**-0.29**	**0.06**	**0.201**		
Pressman (2014)	Telephone / Message	-0.20	-0.69	0.29	0.424	6.73	8.59
Bogner (2012)	Telephone / Message	-1.20	-1.56	-0.84	0.000	12.78	9.85
Goodarzi (2012)	Telephone / Message	-0.54	-1.05	-0.03	0.038	6.21	8.40
Jarab (2012)	Telephone / Message	-0.90	-1.91	0.11	0.080	1.59	4.58
Schechte (2012)	Telephone / Message	-0.36	-0.70	-0.02	0.040	13.78	9.97
Anderson (2010)	Telephone / Message	-0.08	-0.41	0.25	0.630	15.31	10.13
Dale (2009)	Telephone / Message	-0.24	-0.66	0.18	0.268	8.98	9.21
Faridi (2008)	Telephone / Message	-0.40	-0.93	0.13	0.138	5.80	8.23
Maljanian (2005)	Telephone / Message	-0.18	-0.57	0.21	0.361	10.86	9.58
Wong (2005)	Telephone / Message	-1.10	-2.10	-0.10	0.031	1.62	4.62
Kim HS (2003)	Telephone / Message	-1.80	-2.46	-1.14	0.000	3.69	7.01
Piette (2001)	Telephone / Message	-0.20	-0.56	0.16	0.273	12.66	9.84
Fixed	**Telephone / Message**	**-0.45**	**-0.58**	**-0.32**	**0.000**		
Random	**Telephone / Message**	**-0.53**	**-0.81**	**-0.26**	**0.000**		
Fixed	**Overall**	**-0.35**	**-0.42**	**-0.29**	**0.000**		
Random	**Overall**	**-0.37**	**-0.49**	**-0.25**	**0.000**		

Heterogeneity test for internet group: Q=80.26, df = 18, P < 0.001, I-square = 77.57%
Heterogeneity test for internet transmitted group: Q=2.81, df = 3, P = 0.421, I-square = 0.00%
Heterogeneity test for telephone / message group: Q=46.51, df = 11, P < 0.001, I-square = 76.35%
Heterogeneity test for overall: Q=138.77, df = 34, P < 0.001, I-square = 75.5%

Digital & Telemedicine programs to improve metabolic control in T2DM

- Website for basic and general education
- SMS for personal remote coaching
- Phone calls for helping and consulting

- Diabetes educators, nurses, dietitians, physicians (specialists)

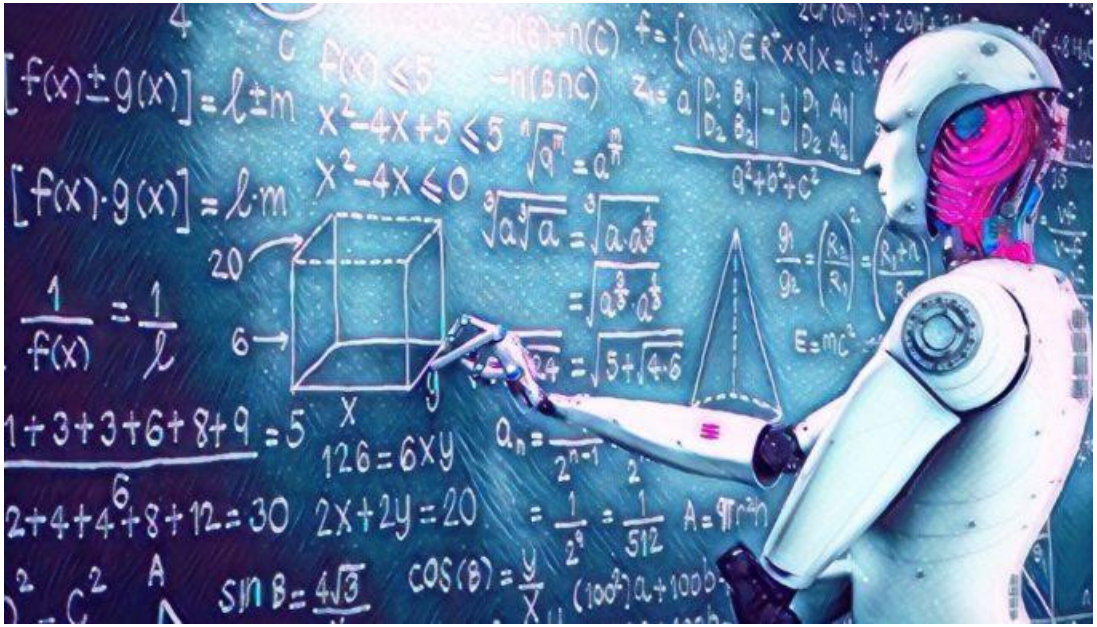
- Supported by National Health Systems in UK and Sweden

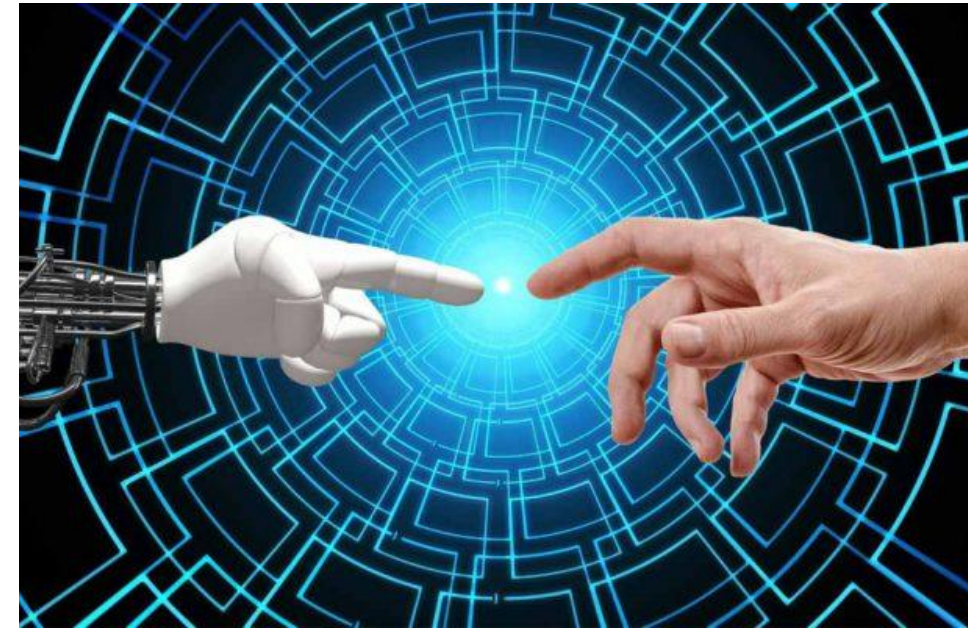
- Cost ~€ 300 per patient per year

Big data to assist in insulin dosing and improve metabolic control in insulin treated patients

- Personal database with hundreds/thousands of glucose assessments before and after meals, insulin injected doses, ingested foods, physical activity sessions, stress level
- An algorithm searches among previous (historical) data the conditions most resembling the current one and identifies the insulin dose which better yielded an optimal glucose control
- The system suggests the insulin dose
- The database continuously expands and the system continuously learns. The greater is the database the more accurate is the suggestion

Intelligenza artificiale





Prospettive future

- Medicina digitale per una gestione più consapevole, responsabile e partecipata
- Medico in remoto (connettività, disponibilità, regole, remunerazione)
- Intelligenza artificiale (molto meglio dell'ignoranza naturale)
- Medicina di precisione (biomarkers e genetica per predire malattia e danno d'organo; farmacogenetica e nutrigenetica per guidare la terapia; farmacogenomica e nutrigenomica per prevenire o cambiare la storia naturale della malattia)
- Alta tecnologia (pancreas artificiale non solo per la basale ma anche per la prandiale)
- Medicina rigenerativa (rimpiazzo delle beta-cellule o degli organi danneggiati)

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