



**Prossimità e organizzazione  
delle cure: la medicina generale  
di domani tra demografia e cronicità**

**IL MODELLO DELLA GESTIONE  
DEL DIABETE  
E IL RISCHIO RESIDUO**

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**DMSI & CeSI-MeT Università d'Annunzio – CHIETI  
ITALY**

**76° CONGRESSO  
NAZIONALE**

**7-12 ottobre 2019**  
Tanka Village - Villasimius (CA)

**FI&MG®**  
Federazione Italiana Medici di Famiglia

**M&S**  
SOCIETÀ SCIENTIFICA DEI MEDICI



Ai sensi dell'art. 76 del Regolamento applicativo dell'Accordo Stato-Regioni 02.02.2017, dichiaro che negli ultimi due anni ho avuto i seguenti rapporti anche di finanziamento con i seguenti soggetti portatori di interessi commerciali in campo sanitario:

**Abbot, Astra Zeneca, Boheringer Ingelheim , Eli Lilly, Merck Sharp & Dhome , Menarini Diagnostici, Novo-Nordisk, Sanofi-Aventis, Sigma-Tau, Takeda.**

**(Speaker)**

**Astra Zeneca, Boheringer Ingelheim, Eli Lilly, Janssen Farmaceutici, Merck Sharp & Dhome, Novo-Nordisk, Sanofi-Aventis.**

**(Advisory Board)**

**Astra Zeneca , Novo-Nordisk**

**(Consultant)**

**Astra Zeneca, Eli Lilly, Novo-Nordisk**

**(Research Grant)**

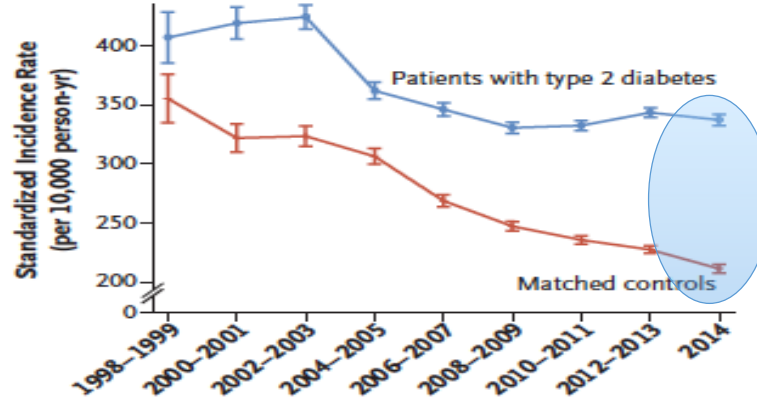
In fede, *AGOSTINO CONSOLI*



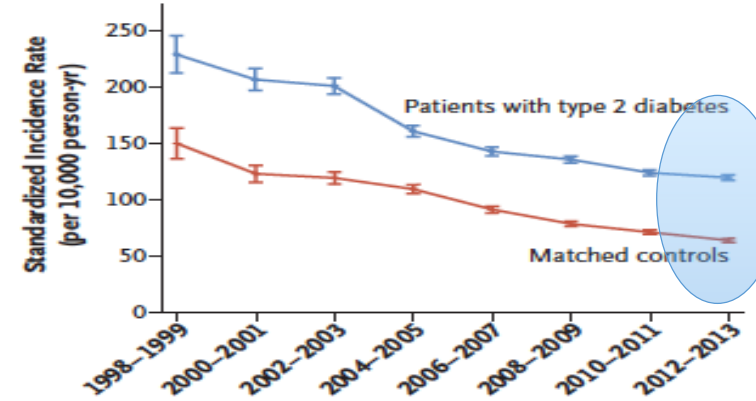
Mortality and Cardiovascular Disease in Type 1 and Type 2 Diabetes

Aidin Rawshani, M.D., Araz Rawshani, M.D., Ph.D., Stefan Franzén, Ph.D., Björn Eliasson, M.D., Ph.D., Ann-Marie Svensson, Ph.D., Mervete Miftaraj, M.Sc., Darren K. McGuire, M.D., M.H.Sc., Naveed Sattar, M.D., Ph.D., Annika Rosengren, M.D., Ph.D., and Soffia Gudbjörnsdottir, M.D., Ph.D.

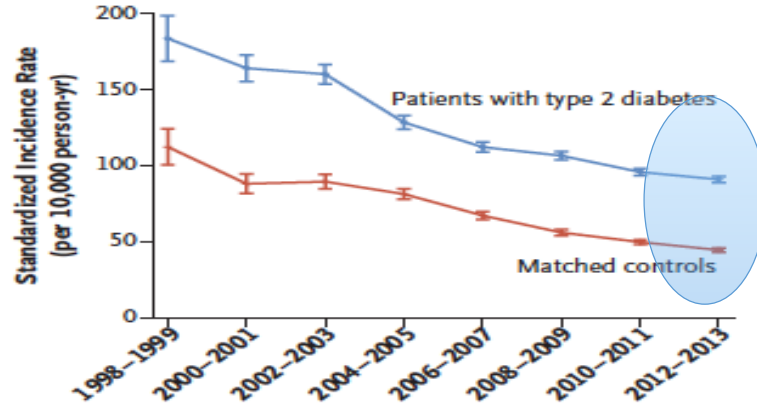
**A Death from Any Cause**



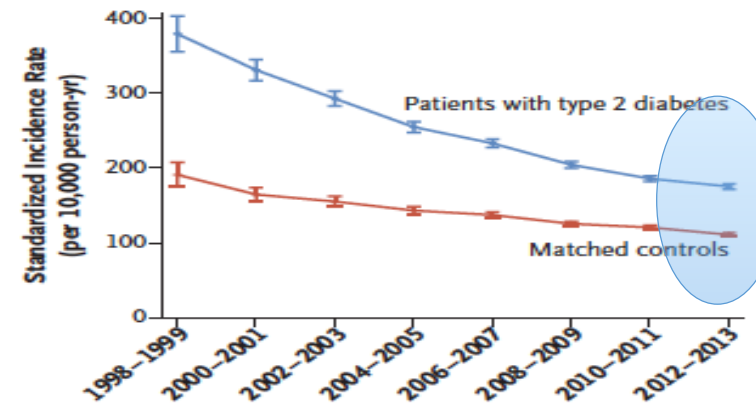
**B Death from Cardiovascular Disease**



**C Death from Coronary Heart Disease**

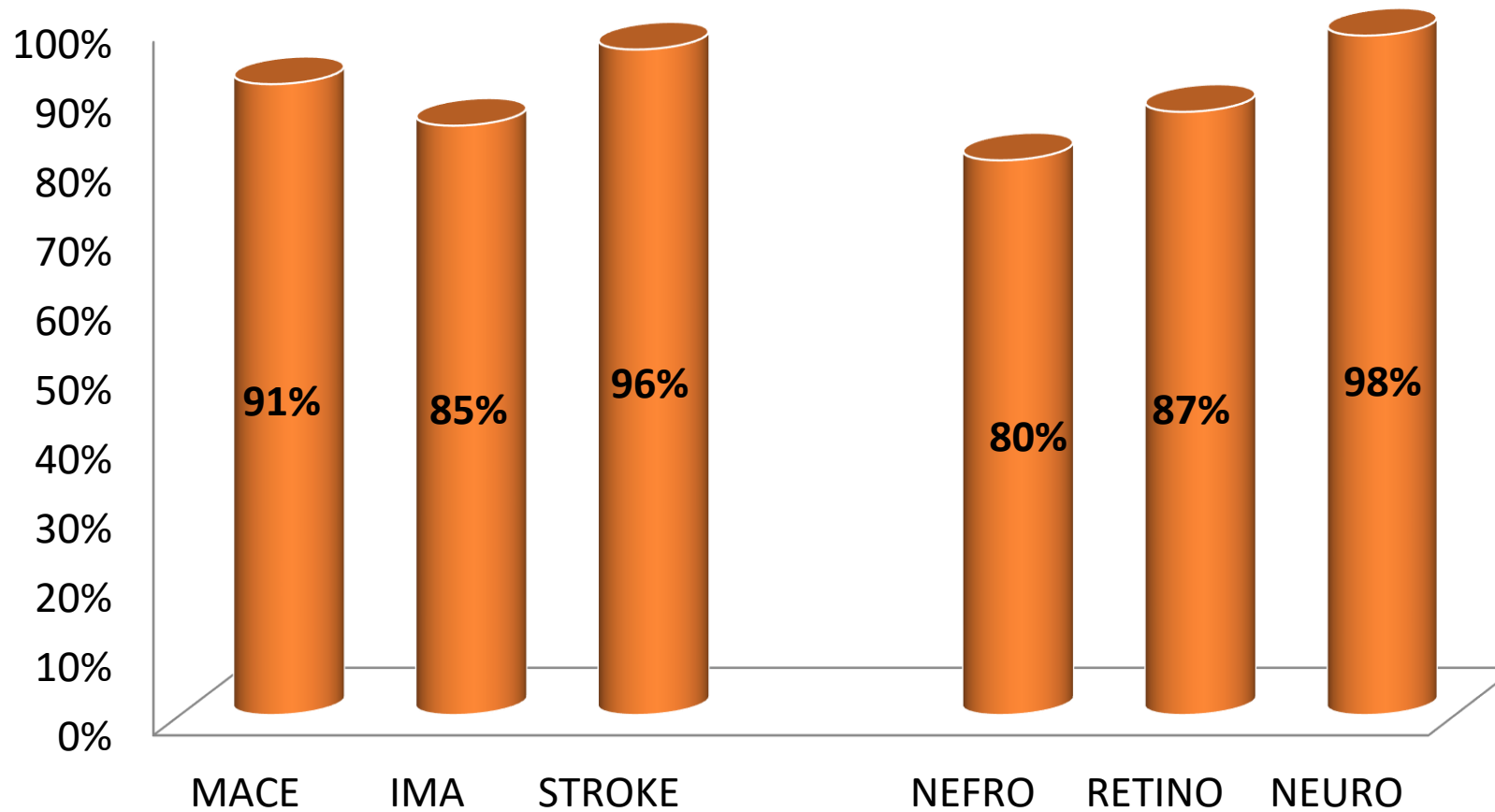


**D Hospitalization for Cardiovascular Disease**





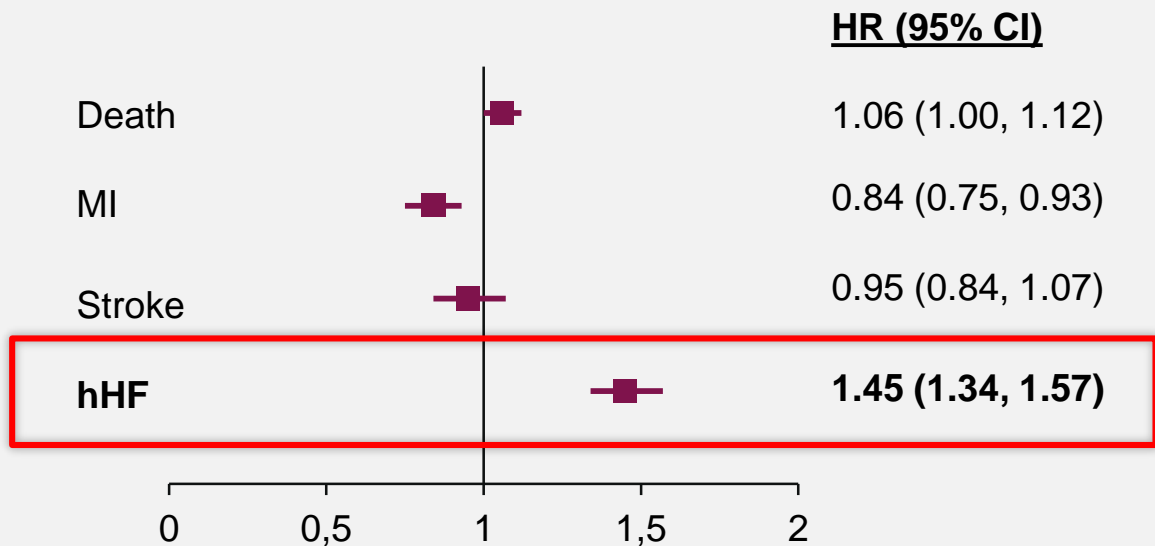
# «Residual» macro- and micro-vascular Risk in DM2 subjects in «standard» treatment



*Giugliano D et al. Endocrine 2018*

# Despite control of known CV risk factors, patients with T2D remain at elevated risk of developing HF

Risk of event in patients with T2D and no risk factors out of target range compared to patients without diabetes

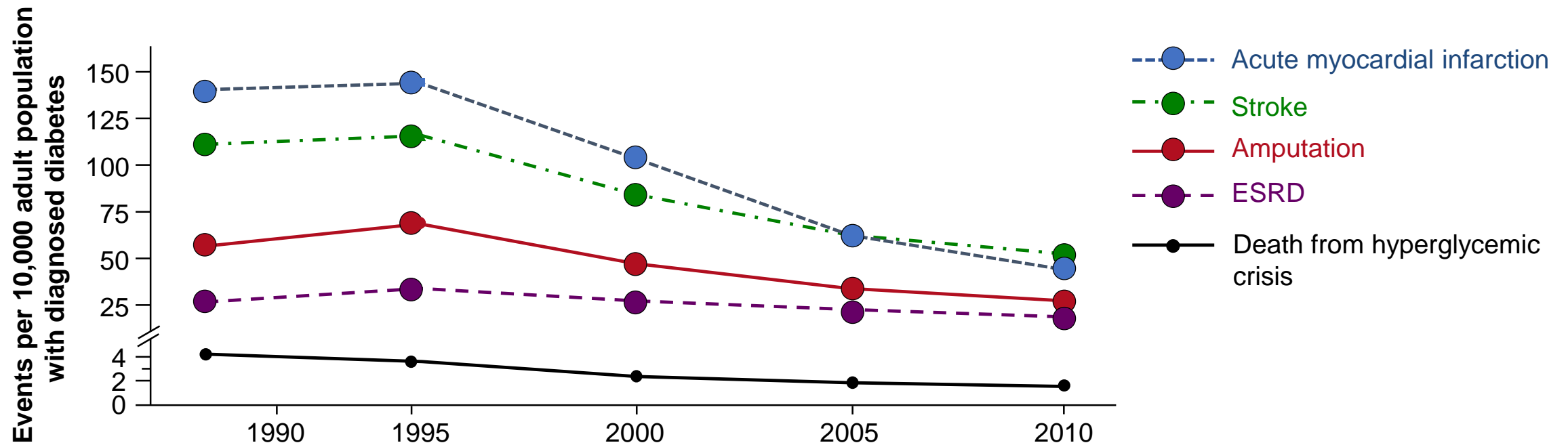


- In this analysis the risk of hHF in patients with T2D (n=271,174) was compared to those without T2D (n=1,355,870)
- The following risk factors were either not present or within guideline range: elevated HbA1c, systolic/diastolic BP, or LDL-C, or albuminuria or tobacco use
- A substantial risk for hHF remained among patients who had all the variables within target range

**On average, the patients with T2D had a 45% increase in the risk of hHF, despite other major risk factors in guideline recommended range or absent**

# Diabetes-related complications in the US 1990–2010

- Ischemic complications such as MI and stroke are declining
- Reductions in rates were smallest for ESRD

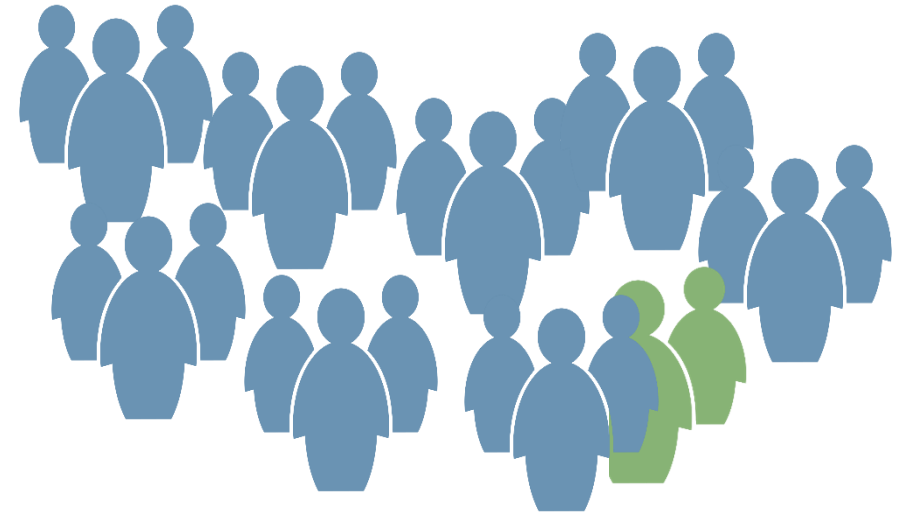


# Prevalence and co-prevalence of comorbidities among patients with type 2 diabetes mellitus

*The vast majority of patients with T2DM have multiple comorbidities*



**97.5% of patients had at least one comorbid condition in addition to T2DM**



**88.5% of them had at least two.**

The comorbidity burden tended to increase in older age groups and was higher in men than women.

# Prevalence of comorbidities in type 2 DM patients according to age and gender

	Overall		Age Groups‡					
	N	Median (IQR) or %	<65 Years		65 to 74 Years		75+ Years	
			N	Median (IQR) or %	N	Median (IQR) or %	N	Median (IQR) or %
Comorbidities								
T2DM only	34,773	2.5	21,952	3.3	6026	1.6	6795	2.0
1 Comorbidity	125,048	9.0	79,735	11.9	22,348	5.9	22,965	6.8
2 Comorbidities	275,415	19.8	157,257	23.4	63,115	16.7	55,043	16.3
3 Comorbidities	459,189	33.1	242,810	36.2	126,932	33.5	89,447	26.4
4+ Comorbidities	494,591	35.6	169,609	25.3	160,594	42.4	164,388	48.5

	Gender§			
	Male		Female	
	N	Median (IQR) or %	N	Median (IQR) or %
Comorbidities				
T2DM only	13,773	2.1	20,978	2.8
1 Comorbidity	46,796	7.2	78,208	10.6
2 Comorbidities	118,829	18.3	156,514	21.1
3 Comorbidities	220,969	34.1	238,178	32.2
4+ Comorbidities	248,057	38.3	246,508	33.3



# Patients with Type 2 diabetes often have multiple comorbidities that contribute to increased CV risk



**71%**  
have high BP<sup>1</sup>



**65%**  
have dyslipidaemia<sup>2</sup>



**85%** are  
overweight<sup>1</sup>



Patients with Type 2 diabetes have up to **2x greater risk of CVD** than those without diabetes<sup>3</sup>

Sustained reductions in **HbA<sub>1c</sub>** and other parameters including **weight, BP and lipids** can benefit the health of patients with Type 2 diabetes<sup>4-8</sup>

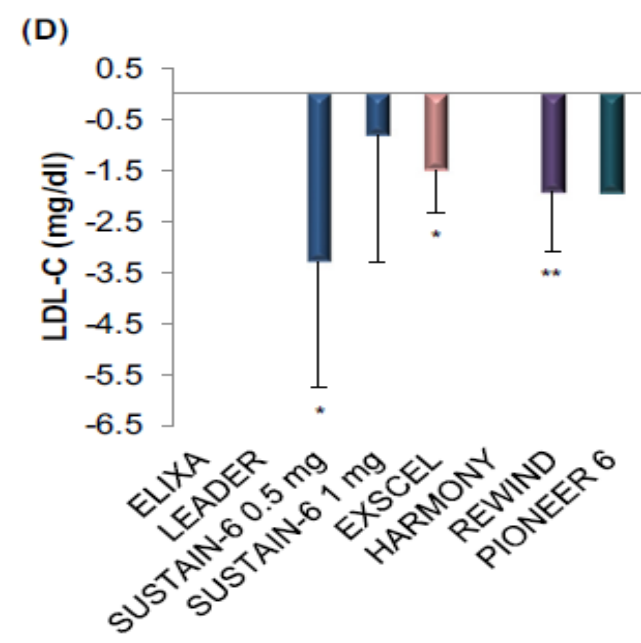
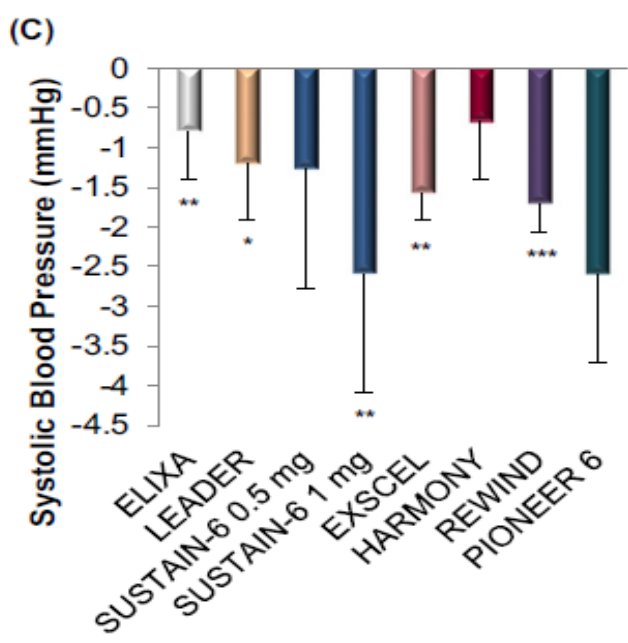
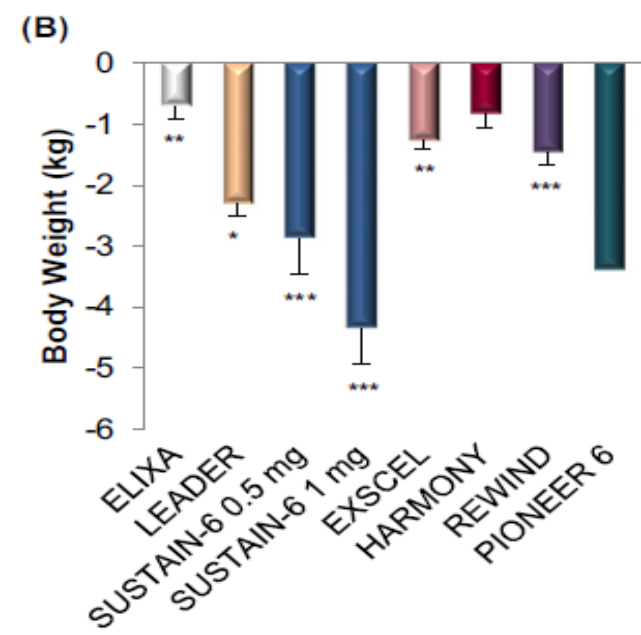
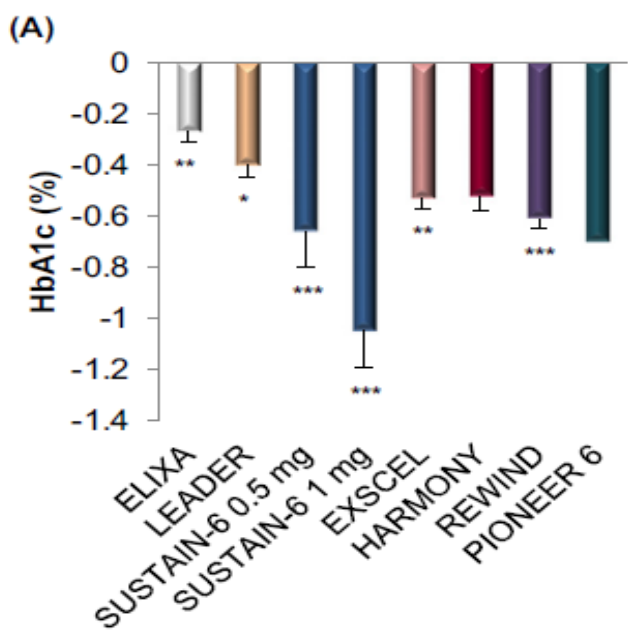
BP, blood pressure; CVD cardiovascular disease.

1. CDC. National Diabetes Statistics Report, 2014. Available at: <http://www.cdc.gov/diabetes/data/statistics/2014StatisticsReport.html>. Last accessed September 2015; 2. CDC. Available at: [http://www.cdc.gov/diabetes/statistics/comp/fig7\\_overweight.htm](http://www.cdc.gov/diabetes/statistics/comp/fig7_overweight.htm). Last accessed September 2015; 3. Gregg EW, et al. *N Engl J Med* 2014;**370**:1514–23; 4. Stratton IM, et al. *BMJ* 2000;**321**:405–12; 5. Pi-Sunyer FX. *Postgrad Med* 2009;**121**:94–107; 6. Williamson DF, et al. *Diabetes Care* 2000;**23**:1499–504; 7. Patel A, ADVANCE Collaborative Group. *Lancet* 2007;**370**:829–40; 8. Pyörälä K, et al. *Diabetes Care* 1997;**20**:614–20.

# Key factors affecting adherence

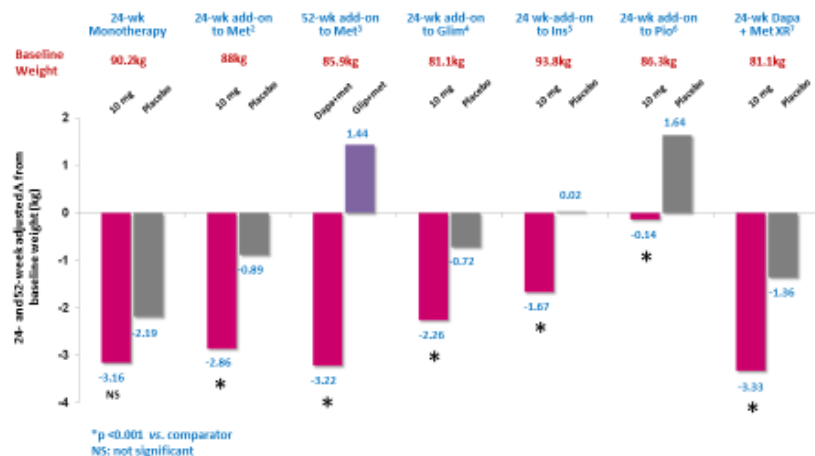
- **Complexity of medication regimen (number of doses, number of concurrent medications)**
- Treatment requires mastery of certain techniques (injection, inhaler)
- Duration of therapy
- Frequent changes in medication regimen
- Lack of immediate therapeutic benefit
- Medications with associated social stigma
- Actual/perceived unpleasant side effects
- Treatment interferes with lifestyle/requires significant behavioural change

**GLP-1 RAs  
improve  
several  
parameters**



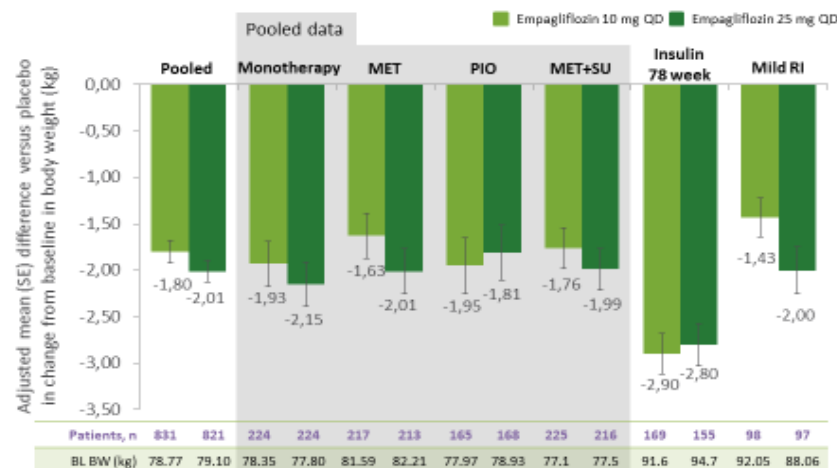
# SGLT2 Inhibitors: Effects on weight

## Body weight changes with dapagliflozin



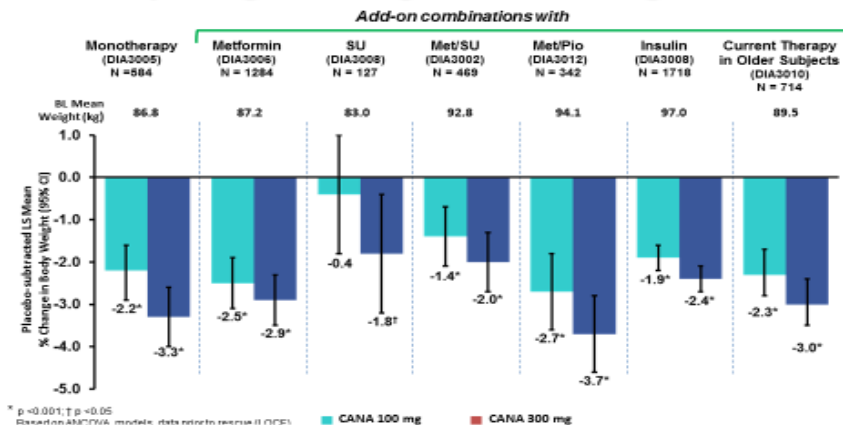
<sup>1</sup>Herrmanni E, et al. Diabetes Care 2010;33:2217-2224; <sup>2</sup>Bailey CJ, et al. Lancet 2010;375:2225-2233; <sup>3</sup>Nauwak MA, et al. Diabetes Care 2011;34:2015-2022; <sup>4</sup>Srojek K, et al. Diabetes Obes Metab 2011;13:928-938; <sup>5</sup>Wilding J, et al. Diabetes 2010;59 (Suppl 1):A21-A22 (Abstract 0078-OR); <sup>6</sup>Rosenzweig I, et al. 71<sup>st</sup> ADA Scientific Sessions, San Diego, 24-28 June, 2011 (Abstract 0986-F); <sup>7</sup>Henry R, et al. 71<sup>st</sup> ADA Scientific Sessions, San Diego, 24-28 June, 2011, Abstract 307-OR.

## Body weight changes with empagliflozin



BL, baseline; BW, body weight; MET, metformin; PIO, pioglitazone; QD, once daily; RI, renal impairment; SE, standard error; SU, sulphonylurea.  
\*Statistically significant versus安慰剂对照.  
<sup>1</sup>Henry R, et al. Diabetes Care 2010;33:2217-2224; <sup>2</sup>Rosenzweig I, et al. Diabetes 2010;59 (Suppl 1):A21-A22 (Abstract 0078-OR); <sup>3</sup>Kovacs C, et al. Diabetes Obes Metab 2010;12 (Suppl 1):A100; <sup>4</sup>Henry R, et al. Diabetes Care 2011;34:2015-2022; <sup>5</sup>Bailey CJ, et al. Lancet 2010;375:2225-2233; <sup>6</sup>Rosenzweig I, et al. 71<sup>st</sup> ADA Scientific Sessions, San Diego, 24-28 June, 2011 (Abstract 0986-F); <sup>7</sup>Henry R, et al. 71<sup>st</sup> ADA Scientific Sessions, San Diego, 24-28 June, 2011, Abstract 307-OR.

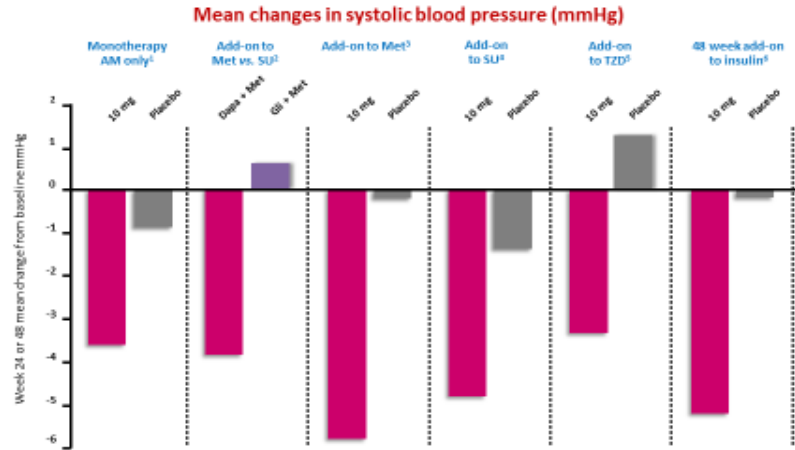
## Body weight changes with canagliflozin



BL, baseline; LS, least squares; MET, metformin; PIO, pioglitazone; QD, once daily; RI, renal impairment; SE, standard error; SU, sulphonylurea.  
\*Statistically significant versus安慰剂对照.  
<sup>1</sup>Henry R, et al. Diabetes Care 2010;33:2217-2224; <sup>2</sup>Rosenzweig I, et al. Diabetes 2010;59 (Suppl 1):A21-A22 (Abstract 0078-OR); <sup>3</sup>Kovacs C, et al. Diabetes Obes Metab 2010;12 (Suppl 1):A100; <sup>4</sup>Henry R, et al. Diabetes Care 2011;34:2015-2022; <sup>5</sup>Bailey CJ, et al. Lancet 2010;375:2225-2233; <sup>6</sup>Rosenzweig I, et al. 71<sup>st</sup> ADA Scientific Sessions, San Diego, 24-28 June, 2011 (Abstract 0986-F); <sup>7</sup>Henry R, et al. 71<sup>st</sup> ADA Scientific Sessions, San Diego, 24-28 June, 2011, Abstract 307-OR.

# SGLT2 Inhibitors: Effects on Blood Pressure

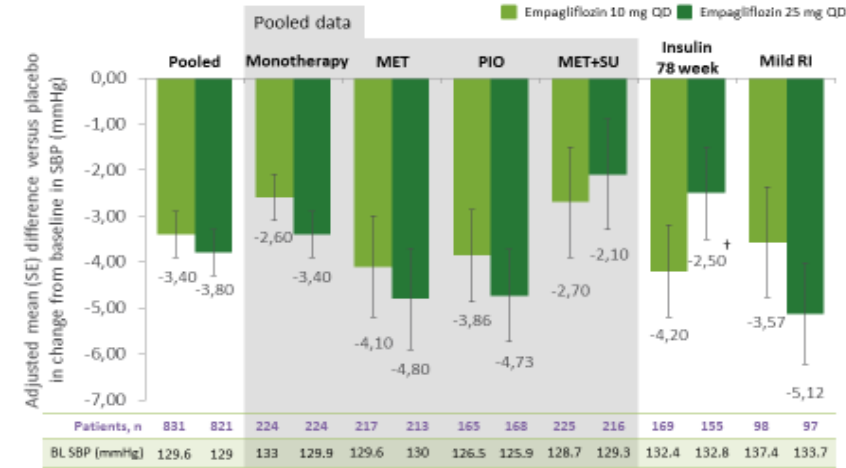
## Blood pressure reductions consistently observed with dapagliflozin in phase III studies



<sup>1</sup>Ferrannini E, et al. *Diabetes Care* 2010;33:2217-2224. <sup>2</sup>Yaluck MA, et al. *Diabetes Care* 2011;34:2015-22. <sup>3</sup>Bailey C, et al. *Cancer* 2010;375:2225-33. <sup>4</sup>Stojek K, et al. *Diabetes Obes Metab* 2011;13:338-38. <sup>5</sup>Rosenstock J, et al. 71st ADA Scientific Sessions, San Diego, 24-28 June, 2011 [Abstract 0986-F]. <sup>6</sup>Walding, et al. *Diabetes* 2010;59(Suppl 1):A21-A22 [Abstract 0678-0R].

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## Blood pressure reductions observed with empagliflozin in phase III studies

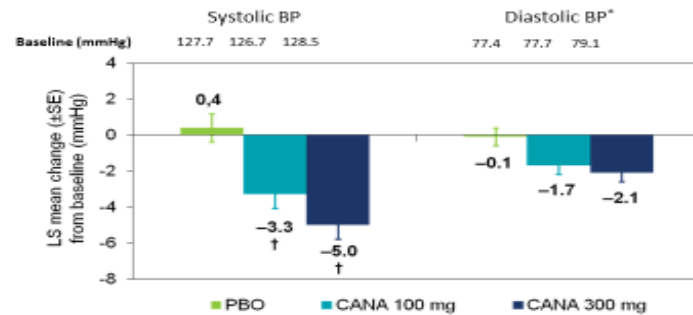


BL, baseline; MET, metformin; PIO, pioglitazone; QD, once daily; RI, renal impairment; SBP, systolic blood pressure; SE, standard error; SU, sulphonylurea. \*All statistical significance unless otherwise marked. †Not statistically significant.

Hoch T, et al. *Diabetes Obes Metab* 2013 Aug 1. doi:10.1111/dom.12188. Haring H-J, et al. *Diabetes Care* 2014. doi:10.2337/14-2073. Kovacs C, et al. *Diabetes Obes Metab* 2013 Aug 1. doi:10.1111/dom.12188. Haring H-J, et al. *Diabetes Care* 2014. doi:10.2337/14-2073. Rayner A, et al. *Lancet Diabetes Endocrinol* 2014 May 29(5):369-84. doi:10.1016/S2213-8587(13)70259-0. Rosenstock J, et al. Poster: 351, 49th Annual Meeting of the European Association for the Study of Diabetes, 23-27 September 2013.

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## Reduction in Blood Pressure with canagliflozin treatment at Week 26



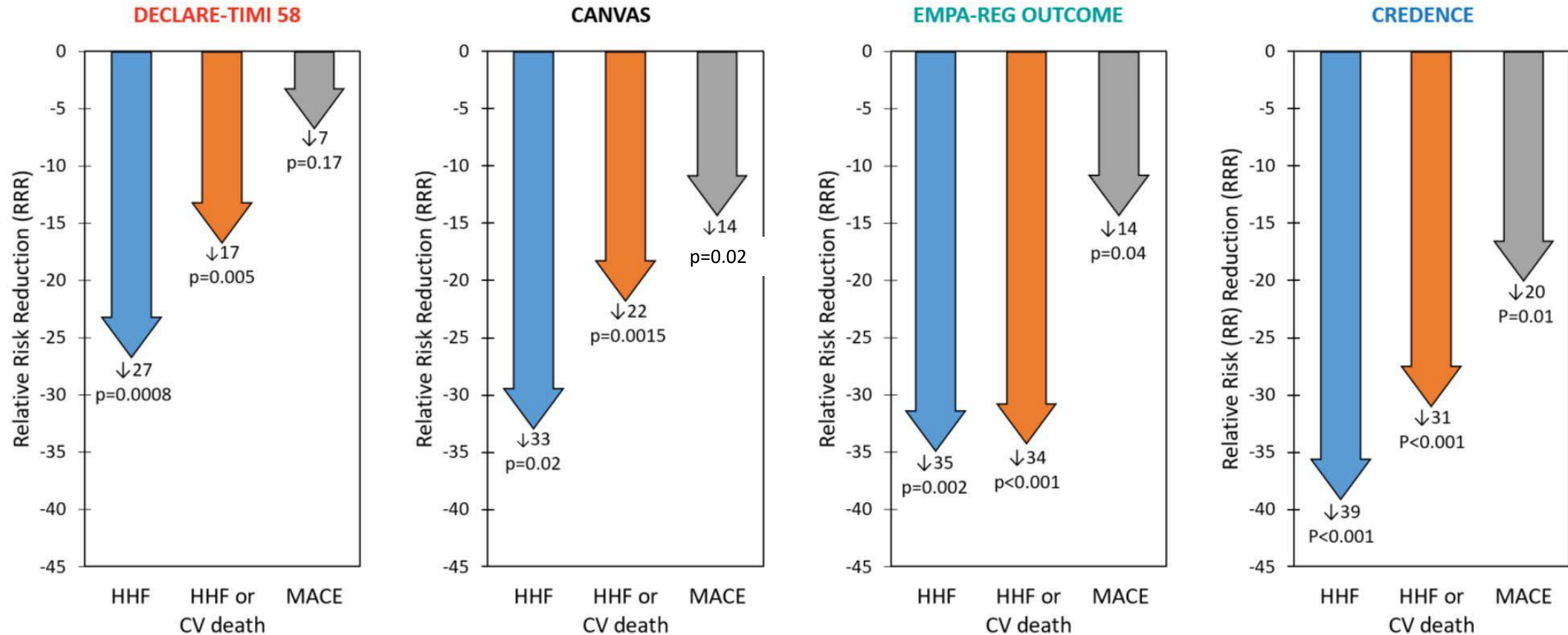
\*P < 0.001 vs placebo; †Statistical comparison for Canagliflozin 100 and 300 mg vs placebo not performed (not pre-specified).

BP, blood pressure; LS, least-squares; SE, standard error; PBO, placebo; CANA, canagliflozin; MITT, modified intent-to-treat; LOCF, last observation carried forward.

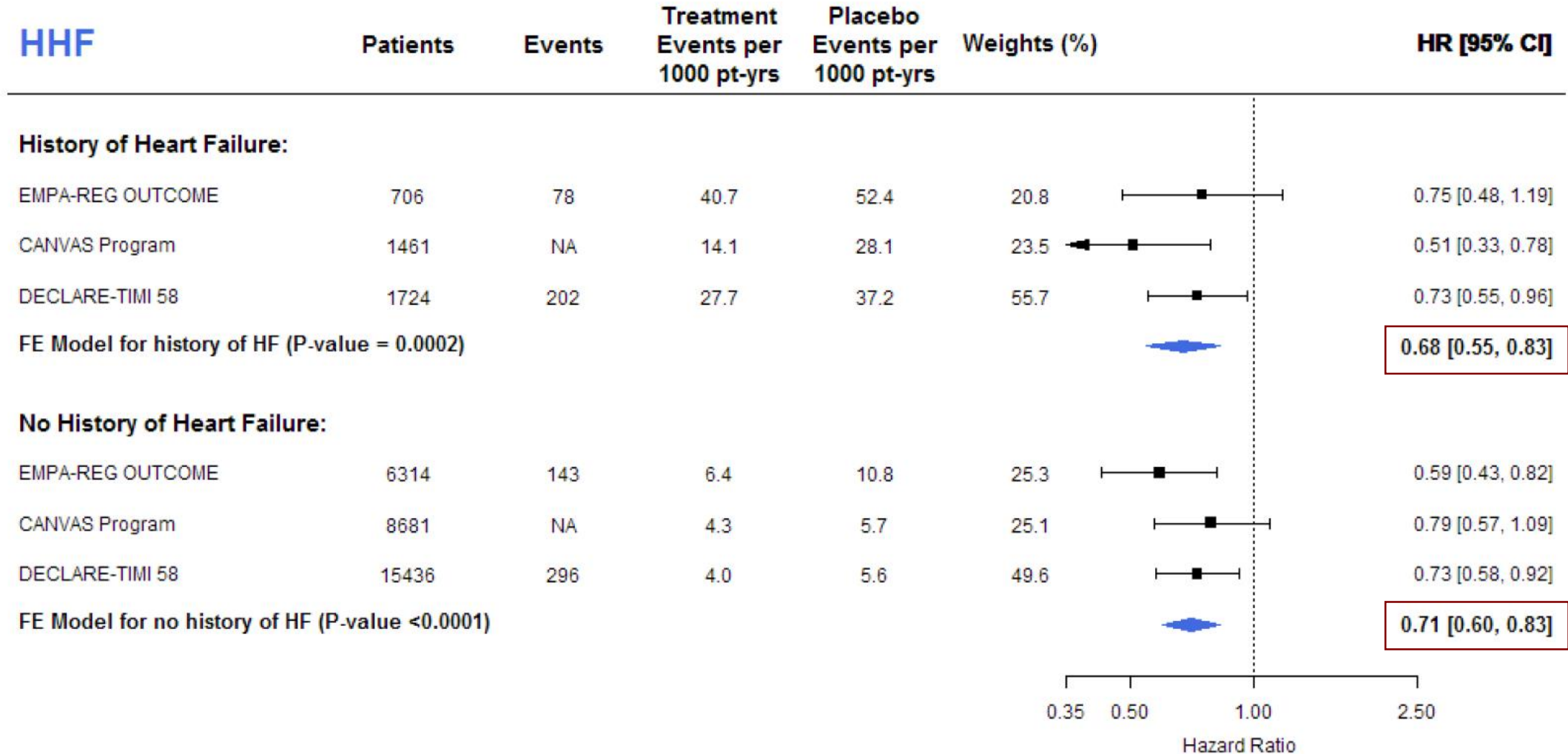
†Minimal changes in pulse rate were observed with canagliflozin 100 and 300 mg compared with placebo (-1.6, -0.5 and 1.4 beats per min, respectively).



# Heart failure hospitalization (HHF), HHF and CV death, and MACE relative risk reductions (RRRs) in SGLT2 inhibitors CVOTs

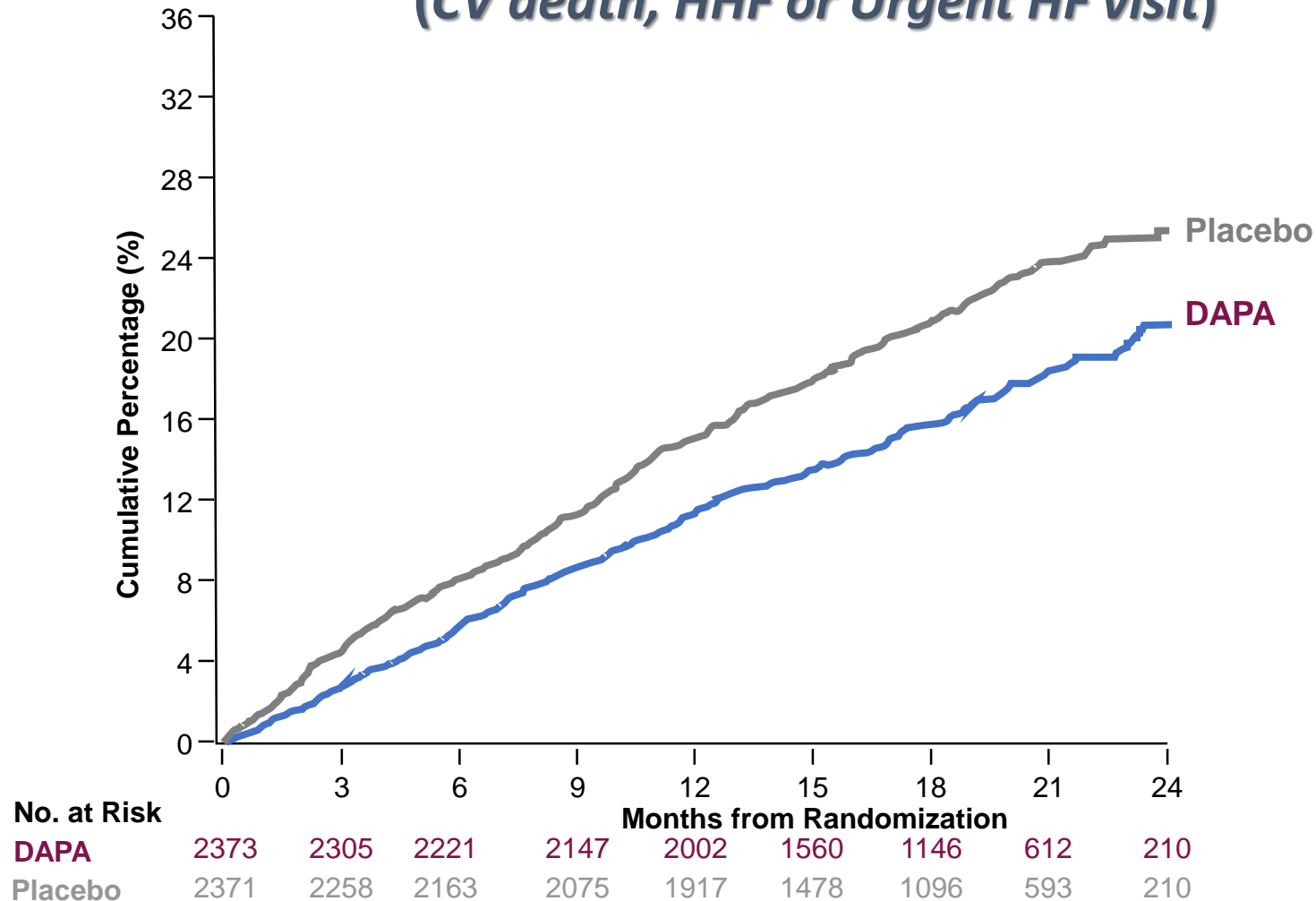


# SGLT2 inhibitors CVOT: meta-analysis of hospitalization for heart failure stratified by history of heart failure



# DAPA-HF STUDY

## Cumulative Occurrence of PRIMARY COMPOSITE ENDPOINT (CV death, HHF or Urgent HF visit)



**26% RRR**

HR 0.74 (0.65, 0.85)  
p=0.00001

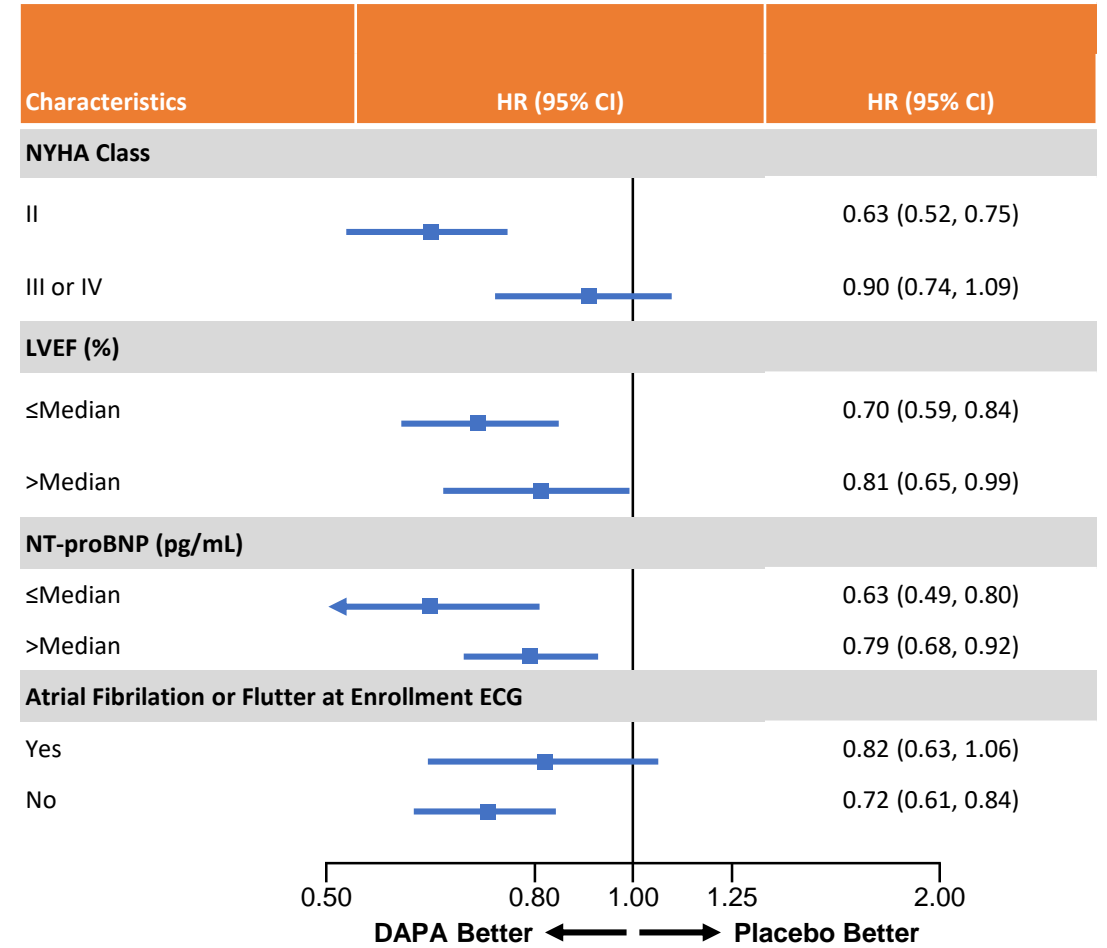
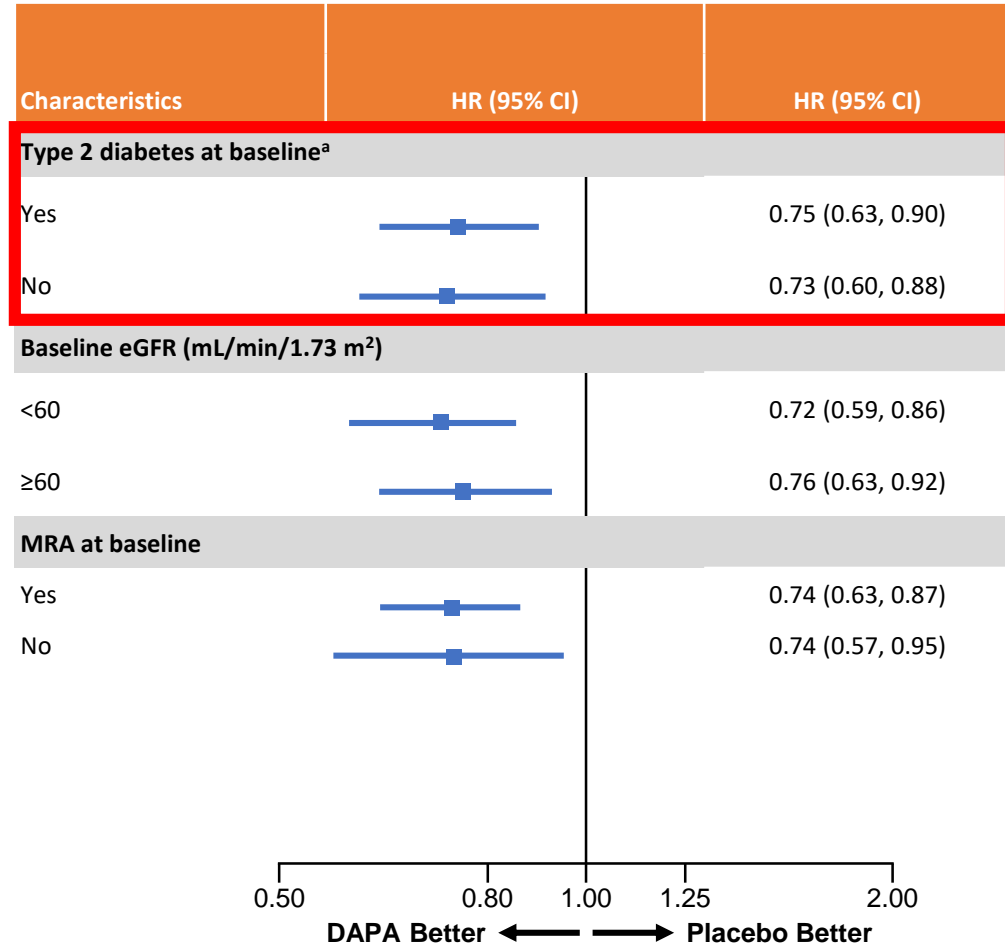
NNT = 21

### 4744 patients

- ≥18 years of age
- With or without T2D
- **Diagnosis of symptomatic HFrEF (NYHA class II-IV) for ≥ 2 months**
- **LVEF ≤40% within last 12 months**
- Elevated NT-proBNP
- eGFR ≥30 ml/min/1.73 m<sup>2</sup>
- Stable SoC HFrEF treatment

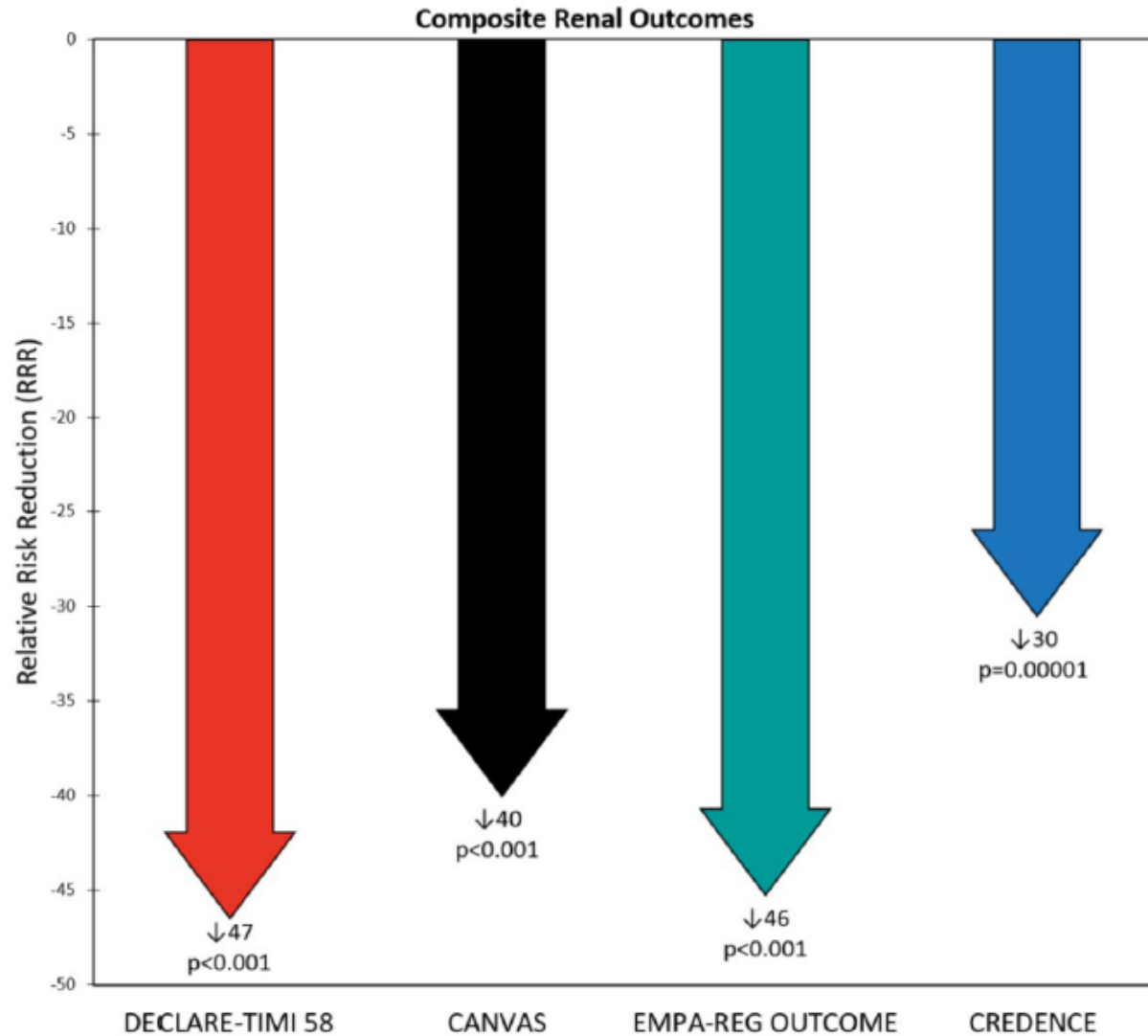
# DAPA-HF STUDY

## PRIMARY COMPOSITE ENDPOINT in pre-specified sub-groups



<sup>a</sup>Defined as history of T2DM or HbA1c ≥6.5% at both enrollment and randomization visits.

# Composite renal outcome relative risk reductions (RRRs) in SGLT2i Outcome Trials

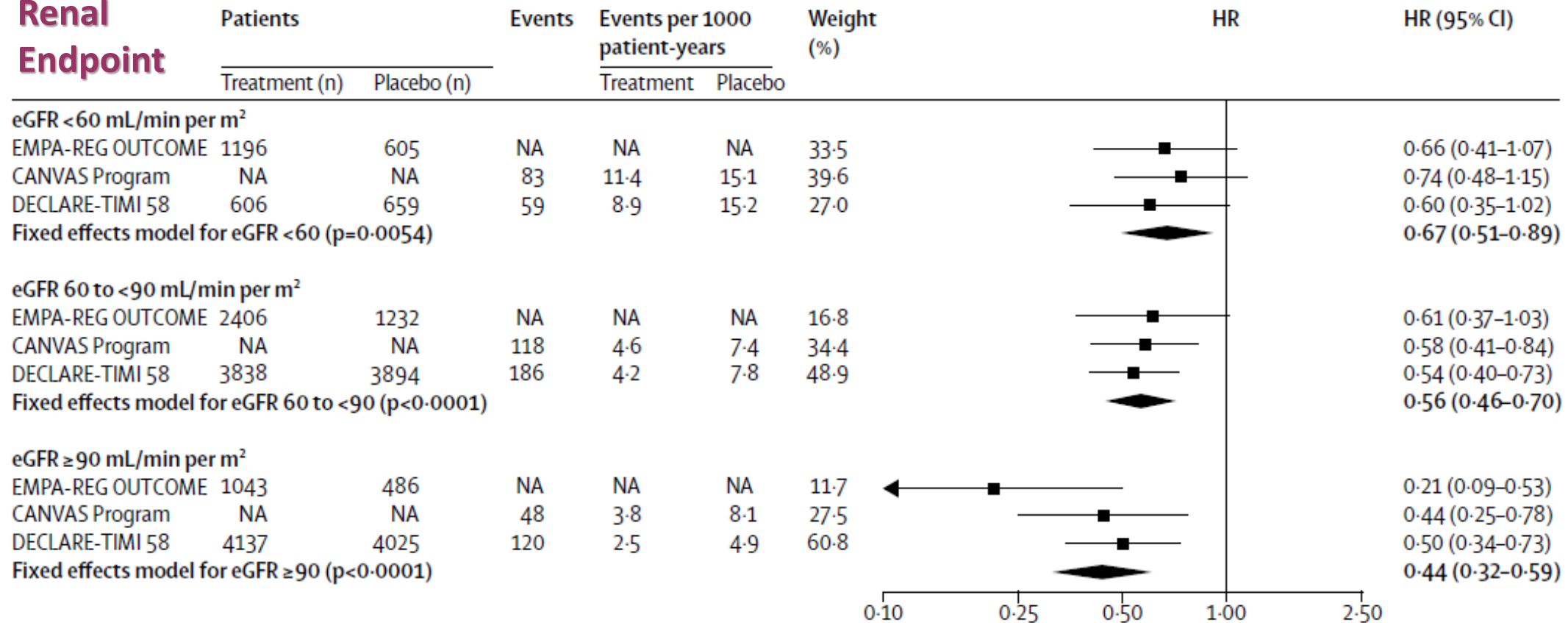




# SGLT2 inhibitors for primary and secondary prevention of cardiovascular and renal outcomes in type 2 diabetes: a systematic review and meta-analysis of cardiovascular outcome trials



## Renal Endpoint



Use on innovative treatment strategies in T2DM  
can reduce:

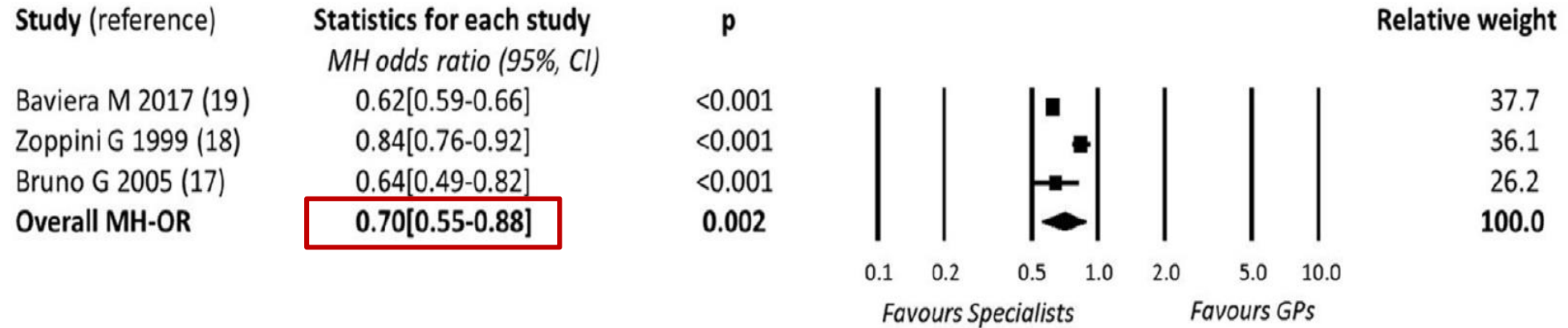
- **Medication Burden**
- **Advers drugs events**
- **Hypoglycemia**
- **Treatment Adherence**
- **RESIDUAL RISK**

# Diabete Mellito: il fattore C

- **COMUNE:** *una persona su 15 in Italia ha diabete noto*
- **CRESCENTE:** *2 milioni di Italiani 30 aa fa, 4 milioni oggi*
- **CRONICO:** *decadi di vita con la malattia*
- **COINVOLGENTE:** *ogni apparato, organo, cellula soffre per l'iperglicemia*
- **CALEIDOSCOPICO:** *il quadro clinico cambia nel tempo*
- **CONDIZIONANTE:** *impone fino a 500 mila «azioni» nel corso della vita*
- **Non CURABILE:** *non si guarisce dal diabete*
- **CATTIVO:** *può comportare grave disabilità e premorienza*
- **COSTOSISSIMO:** *molti miliardi di euro*

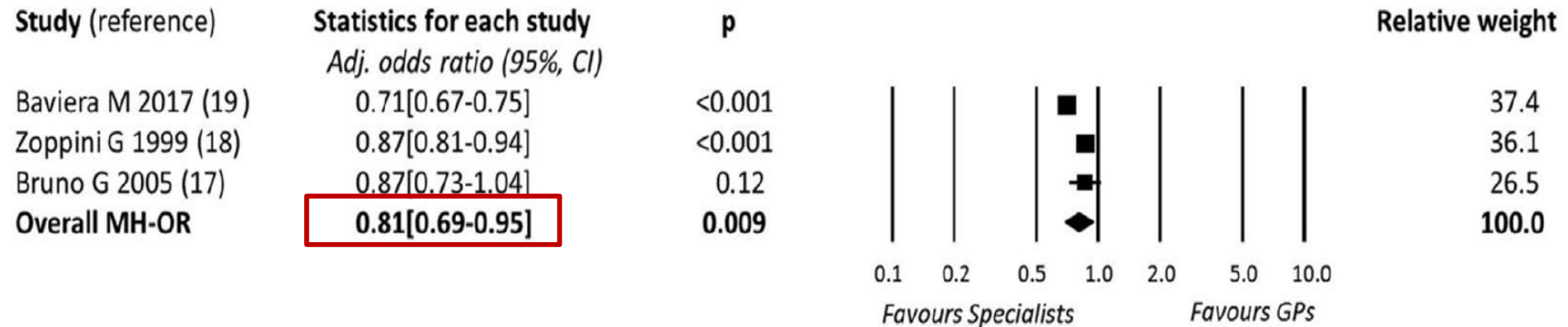
# Attending Diabetes Clinics is associated with a lower all-cause mortality. A meta-analysis of observational studies performed in Italy

## Unadjusted analysis



## Adjusted analysis\*

Panel B



\*Variables used for adjustment in individual studies always included gender and age; the other confounders were insulin therapy and place of residence in the study of Zoppini et al., and duration of diabetes in the study of Bruno et al.

Per ottenere i migliori risultati possibili nella cura delle persone con diabete, attraverso la forte integrazione tra i diversi punti di erogazione dell'assistenza, è necessaria una più precisa definizione organizzativa istituzionalizzata delle attività e dei ruoli delle Strutture Diabetologiche e della Medicina Generale.

Il programma di cura della persona con diabete non può prescindere da una Gestione Integrata della patologia che veda al centro il paziente stesso e preveda la sinergia tra il Medico di Medicina Generale (MMG) e il Team Diabetologico.

Per una corretta gestione integrata nell'assistenza del paziente diabetico sono necessari:

1. un percorso diagnostico terapeutico e assistenziale (PDTA) condiviso;
2. un modulo di informazione e consenso sottoscritto dal paziente che aderisce alla gestione integrata, così come previsto dal PDTA;
3. l'utilizzo della cartella clinica informatizzata;
4. l'attivazione di strumenti di comunicazione diretta, on-line, attraverso l'integrazione delle cartelle cliniche dei MMG e dei Team Diabetologici;
5. la formazione continua dei professionisti;
6. la raccolta dati e la valutazione periodica della Gestione Integrata, attraverso l'utilizzo di indicatori di struttura, di processo e di esito e l'avvio di percorsi di self-audit, audit di gruppo e di Associazioni Funzionali Territoriali e Unità Complessa di Cure Primarie.

n. 45/2016 del 05 LUG. 2016  
Allegato al Decreto del Commissario  
ad ACTA

  
**ASR ABRUZZO**  
AGENZIA SANITARIA REGIONALE

*Att. A)*  
Allegato al Decreto del Commissario  
ad ACTA

n. 45/2016 del 05 LUG. 2016



# PDTA DEL DIABETE



**Il programma di cura della persona con diabete non può prescindere da una Gestione Integrata della patologia che veda al centro il paziente stesso e preveda la sinergia tra il Medico di Medicina Generale (MMG) e il Team Diabetologico**

**In tutte le fasi del percorso è necessaria comunque una stretta interazione tra il Team Diabetologico, il MMG e gli altri specialisti, da realizzarsi attraverso l'uso di supporti informatici.**

# INTEGRAZIONE GESTIONE ASSISTENZA UNA SOLUZIONE POSSIBILE

Cartelle Cliniche MMG / Quick Connect / My Star Connect Diabetologo

## Cartelle Cliniche MMG

Referto del 26/11/2012 al 01/05/2011  
Paziente ACETELLI MARILENA

Esami del 26/11/2012

Problemi del 12/11/2012

Esami del 12/11/2012

Esami del 10/11/2012

Prescrizioni del 25/10/2012

Esami del 25/10/2012

Visualizzazione del Referto specialistico



## Cartella Clinica Diabetologo

DIABETOLOGIA

[admin] Esami - APPROVA ANGELO età 70

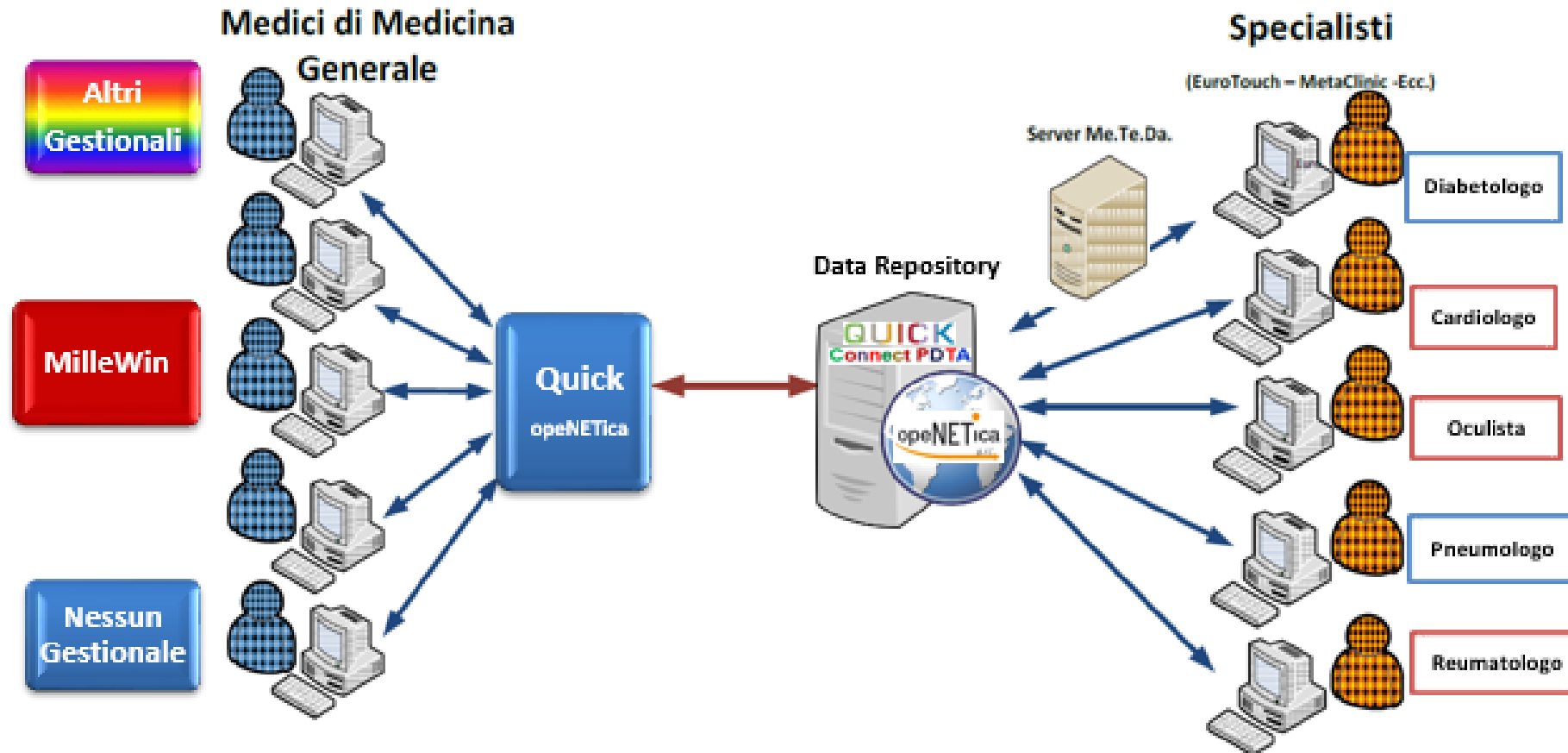
Descrizione	08/02/2013	09/01/2013	20/12/2012	20/06/2012
Peso kg	68.0			68.0
IM	24.1	24.1		
Peso Max Kg	70.6			
Peso Min Kg	53.6			
Altezza cm	168	168		
Emoglobina Glicata HbA1c %	7.3		7.4	
Pressione Sistolica mmHg	130	130		
Pressione Diastolica mmHg	81	82		
Glucosio HCL mg/dl	239	240		
Creatinina mg/dl	49	50		
Trigliceridi post 12h dig. mg/dl	138	140		
Cholesterol a digiuno mg/dl	125	130		
Creatinina mg/dl	0.88	0.90		
Proteina mg/dl				
Microalbuminuria mg/24h	10	12		

Gestione integrata (Invio referti)

Gestione integrata (Invio referti)

Gestione integrata (Invio referti)

# UNA SOLUZIONE POSSIBILE



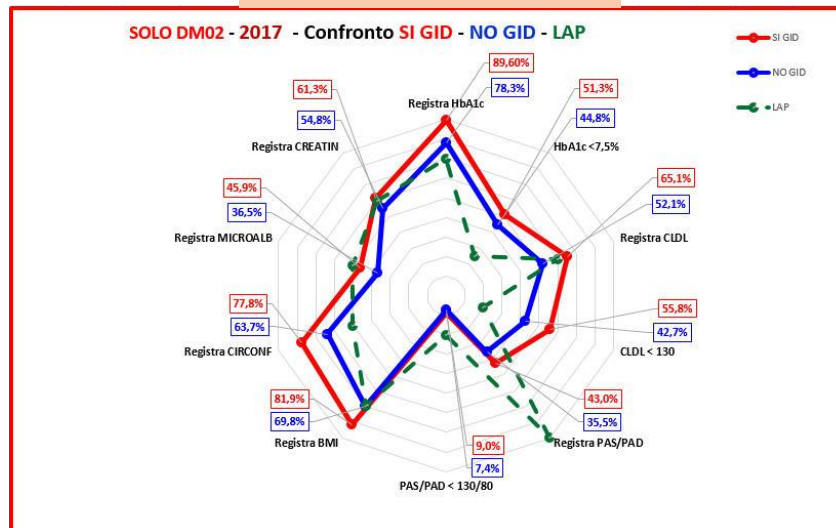
# LA GESTIONE INTEGRATA DEL DIABETE NELLA AUSL DI PESCARA

## RISULTATI PRELIMINARI

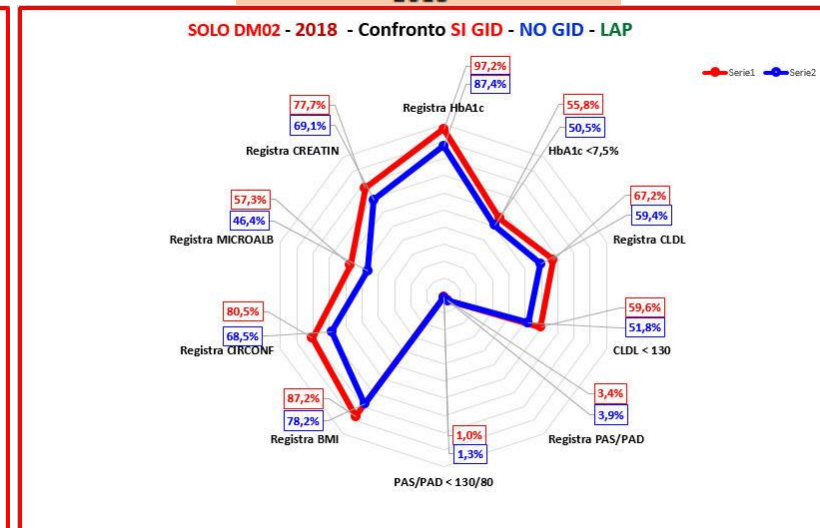
TOTALE	2017			diff %
	SI GID	NO GID	LAP	
DIABETICI SI GID NO GID	1943	4895		
% DIAB SI GID NO GID	32,22%	67,78%	3%	
DIABETOLOGIA PESCARA	SI GID	NO GID	LAP	
Registra HbA1c	89,60%	78,3%	70%	12,61
HbA1c <7,5%	51,3%	44,8%	25%	12,67
Registra CLDL	65,1%	52,1%	60%	19,97
CLDL < 130	55,8%	42,7%	20%	23,48
Registra PAS/PAD	43,0%	35,5%	90%	17,44
PAS/PAD < 130/80	9,0%	7,4%	20%	17,78
Registra BMI	81,9%	69,8%	70%	14,77
Registra CIRCONF	77,8%	63,7%	50%	18,12
Registra MICROALB	45,9%	36,5%	50%	20,48
Registra CREATIN	61,3%	54,8%	60%	10,60

TOTALE	2018			diff %
	SI GID	NO GID	LAP	
DIABETICI SI GID NO GID	2165	2690		
% DIAB SI GID NO GID	35,2%	64,8%	3%	
DIABETOLOGIA PESCARA	SI GID	NO GID	LAP	
Registra HbA1c	97,2%	87,4%	70%	10,08
HbA1c <7,5%	55,8%	50,5%	25%	9,50
Registra CLDL	67,2%	59,4%	60%	20,07
CLDL < 130	59,6%	51,8%	20%	20,86
Registra PAS/PAD	3,4%	3,9%	90%	18,35
PAS/PAD < 130/80	1,0%	1,3%	20%	13,04
Registra BMI	87,2%	78,2%	70%	18,59
Registra CIRCONF	80,5%	68,5%	50%	20,99
Registra MICROALB	57,3%	46,4%	50%	25,37
Registra CREATIN	77,7%	69,1%	60%	18,09

2017



2018





<http://www.siditalia.it/pdf/Diabetologi%20per%20curare%20e%20diabetologi%20per%20risparmiare.pdf>

	AREA D'INTERVENTO	RISPARMIO ASL PESCARA euro/anno	RISPARMIO ASL TERAMO euro/anno	RISPARMIO ASL L'AQUILA euro/anno	RISPARMIO ASL CHIETI euro/anno	RISPARMIO REGIONALE euro/anno	RISPARMIO NAZIONALE euro/anno
1	"Strisce appropriate" Ottimizzazione dell'autocontrollo glicemico domiciliare;	€ 241.298,84	€ 232.726,66	€ 230.524,52	€ 295.449,98	€ 1.000.000,00	€ 30.000.000,00
2	"L'esame serve davvero?" Appropriatezza nella prescrizione di esami di laboratorio e strumentali (propria e indotta);	€ 482.597,67	€ 465.453,33	€ 461.049,03	€ 590.899,97	€ 2.000.000,00	€ 60.000.000,00
3	"No ipoglicemia" Prevenzione delle ipoglicemie con una scelta oculata dei farmaci anti-diabetici;	€ 313.688,49	€ 302.544,66	€ 299.681,87	€ 384.084,98	€ 1.300.000,00	€ 41.000.000,00
4	"Guarda la convenienza" Uso efficace delle varie opportunità offerte dal ricco armamentario terapeutico;	€ 289.558,60	€ 279.272,00	€ 276.629,42	€ 354.539,98	€ 1.200.000,00	€ 35.000.000,00
5	"Un click solo" Corretta istruzione dell'esecuzione della terapia insulinica per evitare spreco di insulina con la dose test che precede l'iniezione;	€ 144.779,30	€ 139.636,00	€ 138.314,71	€ 177.269,99	€ 600.000,00	€ 19.000.000,00
6	"Cerca la bozza" Prevenzione delle lipodistrofie nei pazienti insulino-trattati;	€ 168.909,19	€ 162.908,67	€ 161.367,16	€ 206.814,99	€ 700.000,00	€ 21.000.000,00
7	"Guarda prima i piedi" Prevenzione del 'piede diabetico';	€ 386.078,14	€ 372.362,66	€ 368.839,23	€ 472.719,97	€ 1.600.000,00	€ 50.000.000,00
	<b>TOTALE PRIMI SETTE INTERVENTI</b>	€ 2.026.910,23	€ 1.954.903,98	€ 1.936.405,93	€ 2.481.779,86	€ 8.400.000,00	€ 256.000.000,00
8							





**CONTINUARE AD IGNORARE I VANTAGGI CLINICI ED  
ECONOMICI DELLA GESTIONE INTEGRATA PRIVA LE  
PERSONE CON DIABETE DELL'OPPORTUNITA' DI UNA  
CURA MIGLIORE ED IMPEDISCE UNA CORRETTA  
RAZIONALIZZAZIONE DELLE RISORSE**



*Grazie per l'attenzione*