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società italiana medicina
d'emergenza-urgenza

HYPOTHESIS

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Introduction

- Hypoglycemia puts patients at risk for unfavorable events and death.
- Severe episodes, defined by the need of external help may be life-threatening
- It is one of the chief and most frequently-observed diabetes-related complaints in emergency departments (ED)
- Because of the high frequency as a cause of altered mental status .... all pts. attending the ED with altered mental status are systematically checked for blood glucose concentration.

Introduction

- Hypoglycemia occurs at a rate around 1.0 per patient-year in T1DM, and reportedly less frequent in insulin-treated T2DM.
- The event rates of severe hypoglycemia are similar in T1DM and insulin-treated T2DM with poor metabolic control and longstanding and complicated disease [*Leese GP, Diabetes Care 2003].*
- The importance of hypoglycemia was highlighted by recent trials of intensive metabolic control in T2DM, where the negative results were partly related to the adverse effects of hypoglycemia.
- The recent availability of new classes of glucose-lowering drugs, further drew the attention of the scientific community.

Introduction

- Very few data exist on the emergency management of hypoglycemia and its related outcomes.
- The use of health resources (ambulance call, on-site treatment, hospital admission is likely to be much higher than estimated by administrative data, and particularly relevant in T2DM, often characterized by long-term disease and complex comorbid profiles.

HYPOTHESIS – HYPOglycemia Treatment in the Hospital Emergency System - Italian Study

Aim: To describe the characteristics of patients attending Emergency Departments (EDs) following a severe episode of hypoglycemia, the factors associated with the management of events and the final outcome.

Data collection

- In 2012, the Study and Research Center of Italian Society of Emergency Medicine (SIMEU) launched a study on all cases attending the EDs for a severe hypoglycemic event between Jan 2011 and Jun 2012.
- According to a predefined case report form, 46 EDs covering an area of approximately 12 million inhabitants, collected data on all cases with an acceptance diagnosis of hypoglycemia. The terms "hypoglycemia" or "hypoglycemic event" were used to search the ED databases

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Clinical data

- Gender, Males (50.5%);
- Mean age, 70 yrs; (median, 76; range, < 1 year to 102 years);
  - Insulin, 65 ± 20; OHA, 79 ± 11; Ins + OHA, 75 ± 12
- Mean duration of disease, < 1 mo to 60 yrs (median, 40 mo).
- Blood glucose at time of event (n = 2314), 45 ± SD 27 mg/dL
  - Below 2 mmol/L, 960 (42%), 2-3 mmol/L, 863 (37%).
- The event required assistance at home by the personnel of the out-of-hospital ED service (*118*) in 1,821 cases (51.8%).
- Treatment: glucose or glucose drinks + i.v. glucose (1,430 cases), i.m. glucagon (22 cases) at home or on ambulance, before arrival to hospital.
- In hospital, oral glucose (564 cases), i.m. glucagon (63 cases) or i.v. glucose (2,483 cases).

Comorbidities

Data	No. of cases (%)	Data	No. of cases (%)
Cardiovascular disease	1,884 (53.6)	Chronic hepatic failure	138 (3.9)
Chronic kidney disease	411 (11.7)	- Hepatocellular carcinoma	9 (0.3)
- On dialysis	34 (1.0)	Alcohol abuse	119 (3.4)
Chronic respiratory disease	313 (8.9)	Pancreatic disease	65 (1.8)
Cancer*	312 (8.9)	- Pancreatic carcinoma	40 (1.1)
Cognitive decline	272 (7.7)	Solid organ transplantation	30 (0.9)
Malnutrition	165 (4.7)	One or more comorbidities	2,320 (76.0)
Psychiatric disease	148 (4.2)		
Hypothyroidism	148 (4.2)		

Traumatic injury was recorded in 287 cases; involvement in a traffic accident in 47

*Including cases with hepatocellular and pancreatic carcinoma

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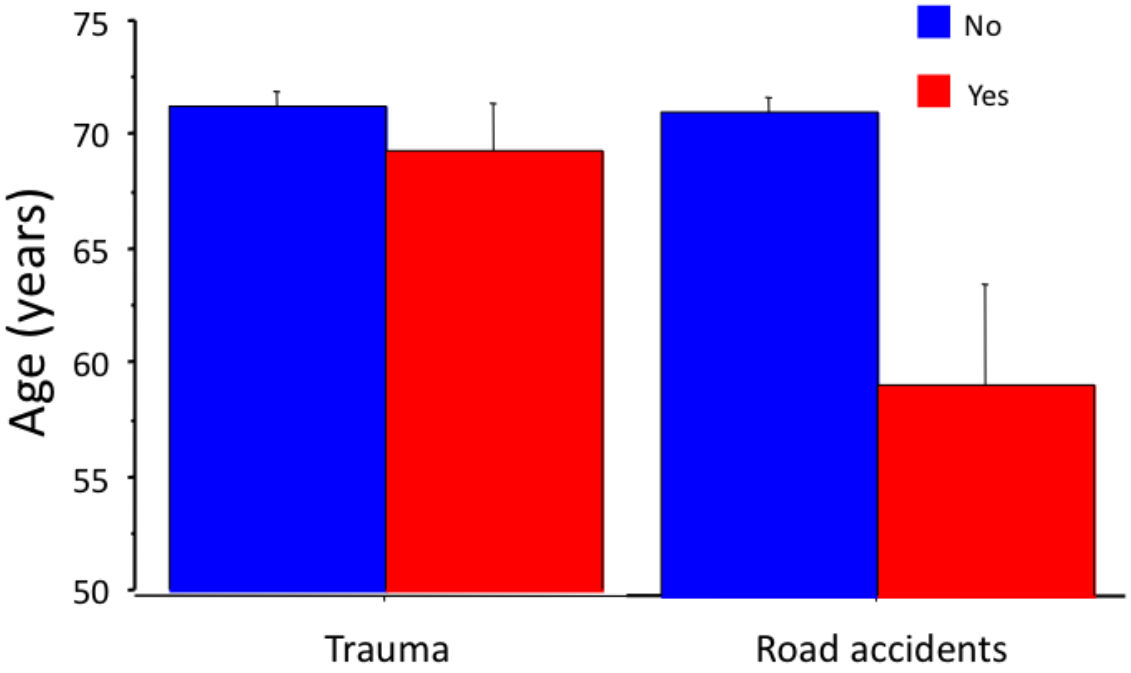
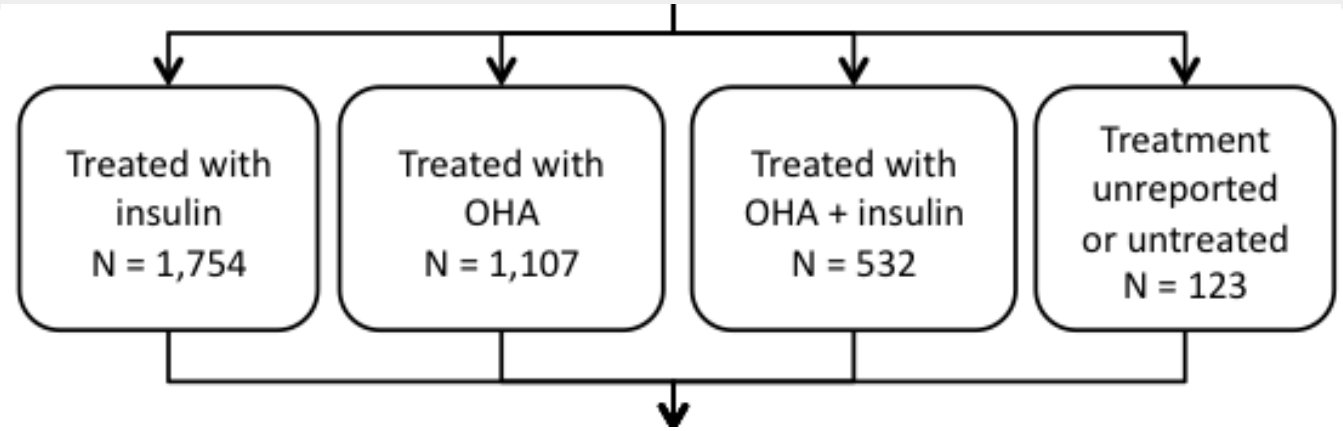
Age by Events

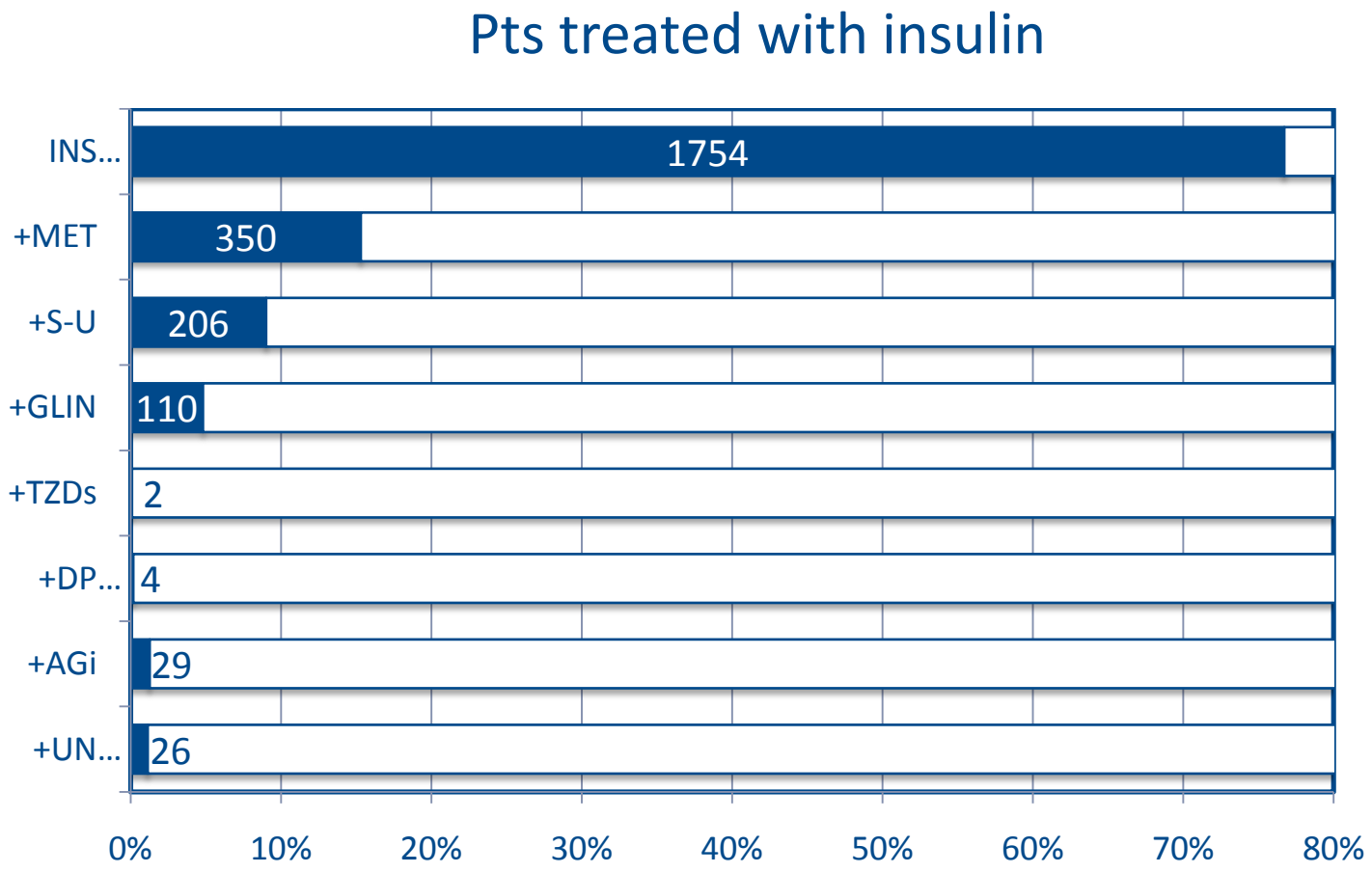


Drug treatment



- Insulin was the sole treatment in 50% of cases,
- 31% were treated by oral agents,
- 15% were on combination treatment (insulin + oral agents).
- In 3.5% of cases treatment was not registered (n = 60, 1.7%) or subjects were reported as untreated (n = 63, 1.8%).
- No hypoglycemic events were reported in association with GLP-1 receptor agonists.

Drug treatment



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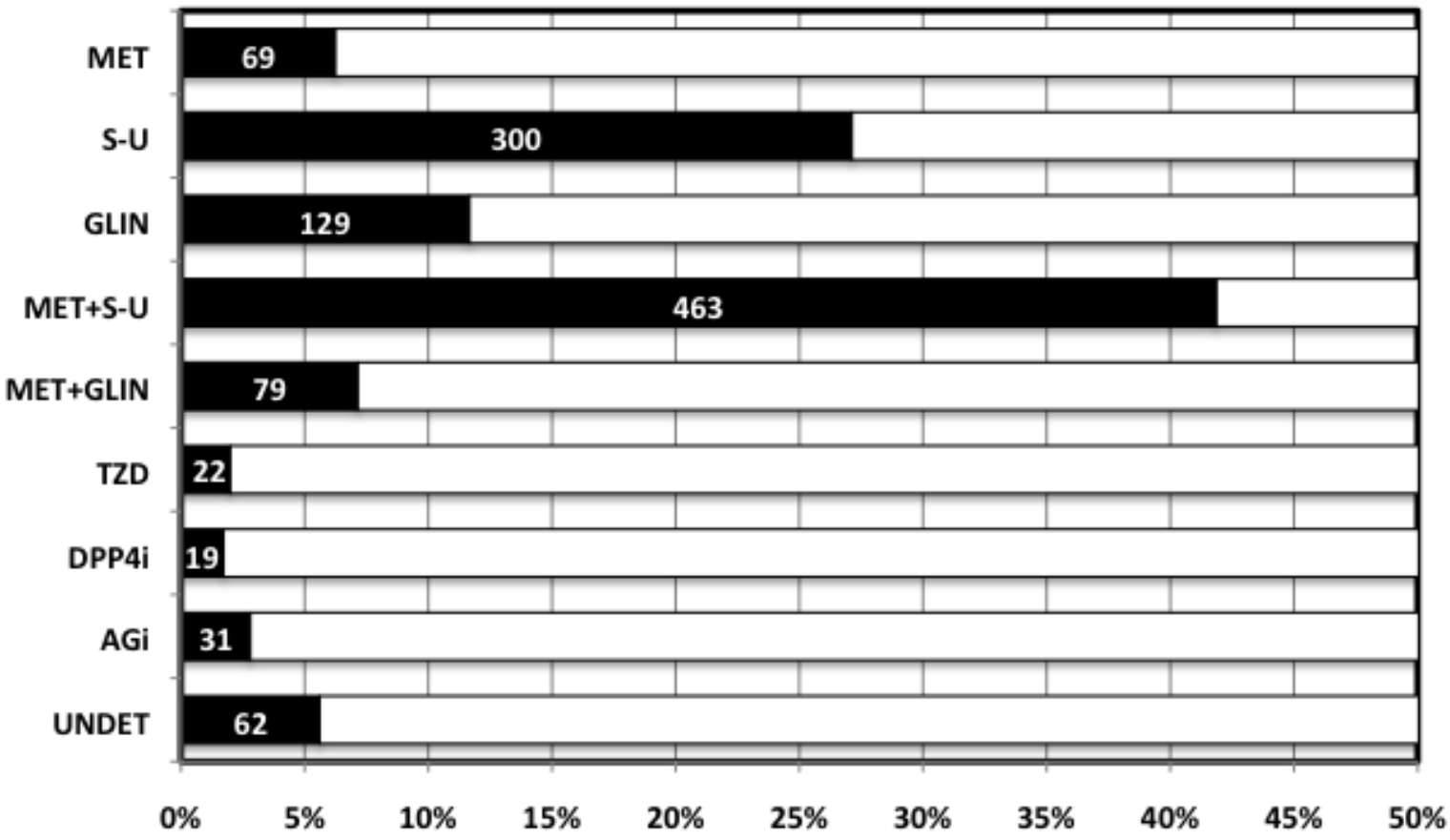
Drug treatment: Oral Agents



Of note, among the 23 cases where DPP4i were recorded, insulin was present in 4, MET in 18, S-U in 11, repaglinide in 4, TZDs in 2, variably combined

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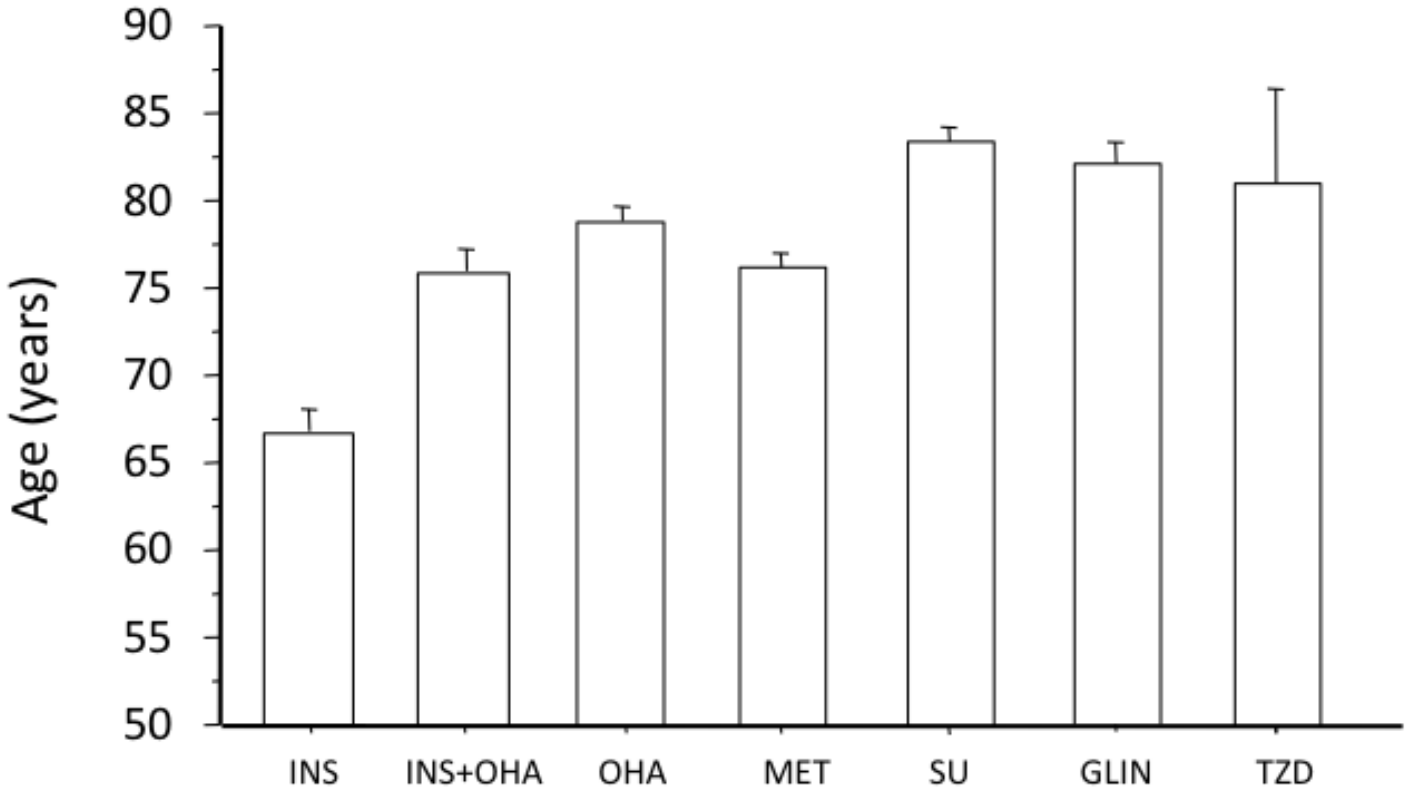
Type of Therapy and Decades



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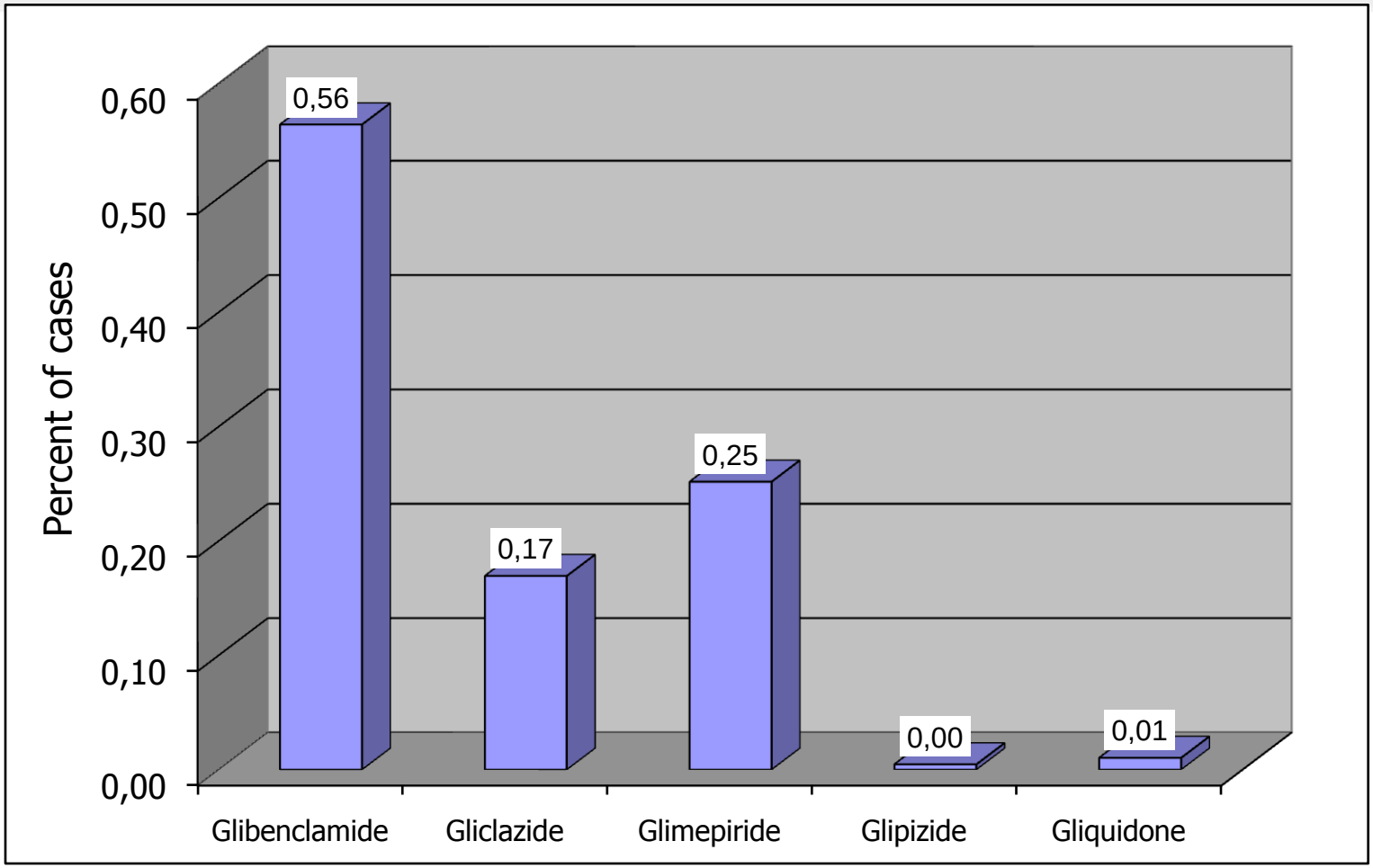
Tipi di farmaci



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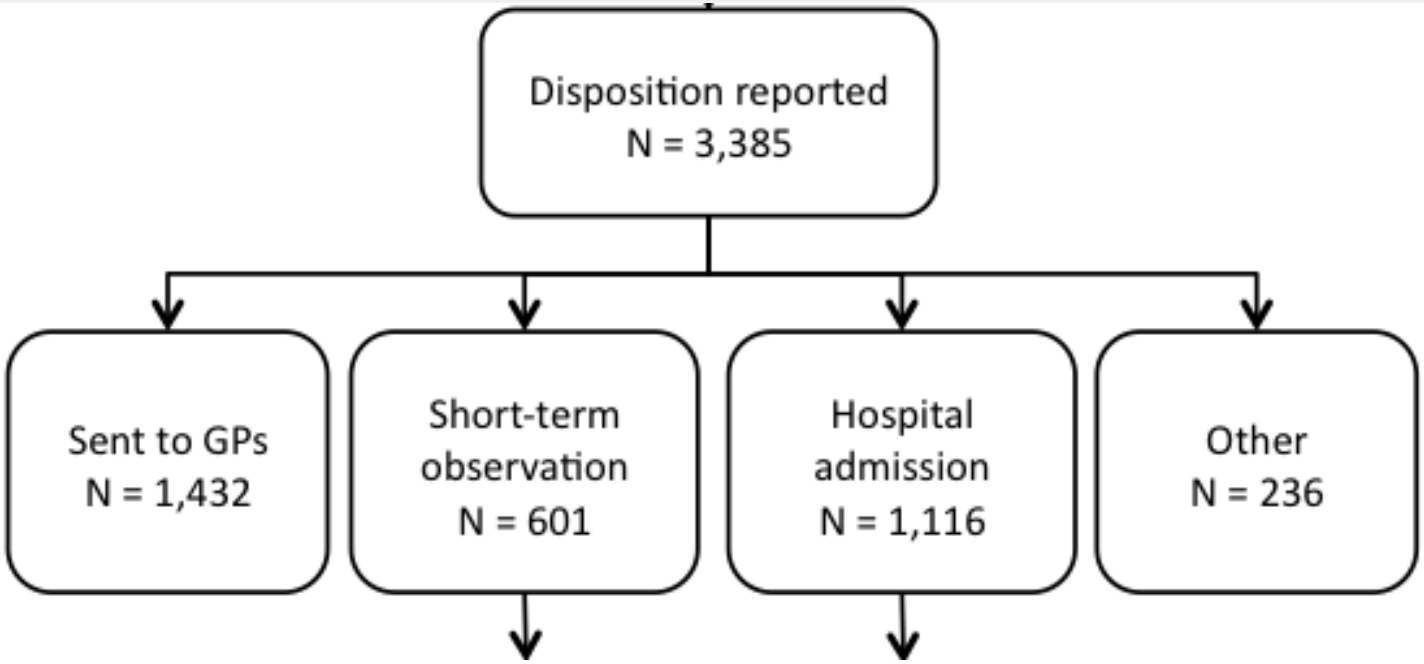
Disposition



- Admission according to specific conditions and/or local hospital organization (Internal Medicine or Pediatric or Geriatric Dept., 83.2%; ICU or Critical Care Dept., 4.1%; Endocrine/Metabolic Dept., 6.4%; other Dept., 6.2%).
- 5 pts died (no death occurred in subjects with traumatic injury or involved in traffic accidents).
- 236 pts. (9.0%) either refused admission to hospital or were referred to nursing homes (< 1% of total).

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Disposition of Subjects with Diabetes Attending the EDs According to the Reported Glucose-lowering Treatment.

Table 2 Disposition of subjects with diabetes attending the EDs according to the reported glucose-lowering treatment.

	Referred to GPs/diabetes units ($n = 1498$)	Short-term observation ($n = 604$)	Admission to hospital ($n = 1161$)	Refused admission/sent to nursing homes ($n = 239$)
Insulin-treated ($n = 1749$)	877 (50.1%)	280 (16.0%)	446 (25.5%)	146 (8.3%)
Treated by oral agents ($n = 1104$)[a]	330 (29.9%)	218 (19.7%)	499 (45.2%)	55 (5.0%)
Combination treatment ($n = 532$)[a]	238 (44.7%)	98 (18.4%)	161 (30.3%)	32 (6.0%)
No/undefined treatment ($n = 122$)	53 (43.4%)	8 (6.6%)	55 (45.1%)	6 (4.9%)
p Value				
Insulin vs. oral	<0.0001	0.012	<0.0001	0.0008
Insulin vs. combination	0.032	0.213	0.033	0.096
Oral vs. combination	<0.0001	0.569	<0.0001	0.450

[a] Five patients died in the ED; 2 cases were on oral agents and 3 cases on combination treatment.

Marchesini G, et al. ***Nutr Metab Cardiovasc Dis*** 2014 (in press)

Factors associated with disposition *vs.* GP referral

Variable	Short-term observation (N = 596)	Admittance to hospital (N = 1,116)
Age (years/10)	1.17 (1.10-1.23)	1.51 (1.43-1.60)
Female gender	1.20 (0.99-1.45)	1.10 (0.94-1.28)
*Glucose at event (mg/dL/10)^	0.97 (0.93-1.02)	0.92 (0.88-0.96)
*Insulin use	0.63 (0.51-0.78)	0.51 (0.42-0.61)
*Oral agents	1.55 (1.26-1.91)	1.54 (1.30-1.83)
*Traumatic injury	1.46 (1.04-2.07)	1.27 (0.94-1.73)
*Road accident	2.95 (1.39-6.26)	1.48 (0.64-3.41)
*Malnutrition	1.37 (0.83-2.27)	2.59 (1.76-3.08)
*Cardiovascular disease	0.94 (0.77-1.16)	1.60 (1.34-1.90)

*Data adjusted for age and gender.
^ N= 2,314

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Factors associated with Disposition *vs.* GP referral

Variable	Short-term observation (N = 596)	Admittance to hospital (N = 1,116)
*Chronic kidney disease	0.94 (0.68-1.30)	1.56 (1.22-1.98)
*End-stage renal disease (dialysis)	0.49 (0.14-1.69)	1.23 (0.57-2.66)
*Cancer	0.98 (0.67-1.41)	1.73 (1.31-2.27)
*Pancreatic disease	1.11 (0.54-2.26)	1.61 (0.91-2.86)
*Chronic liver disease	1.09 (0.64-1.87)	2.13 (1.43-3.17)
*Psychiatric disease	0.99 (0.58-1.68)	1.92 (1.28-2.87)
*Cognitive decline	0.86 (0.57-1.30)	1.45 (1.08-1.95)
*Chronic respiratory disease	0.67 (0.45-1.00)	1.45 (1.11-1.89)
*Parkinson's disease	1.10 (0.56-2.19)	1.79 (1.08-2.97)
*Number of associated complications	0.92 (0.82-1.04)	1.51 (1.38-1.66)

**Data adjusted for age and gender.*

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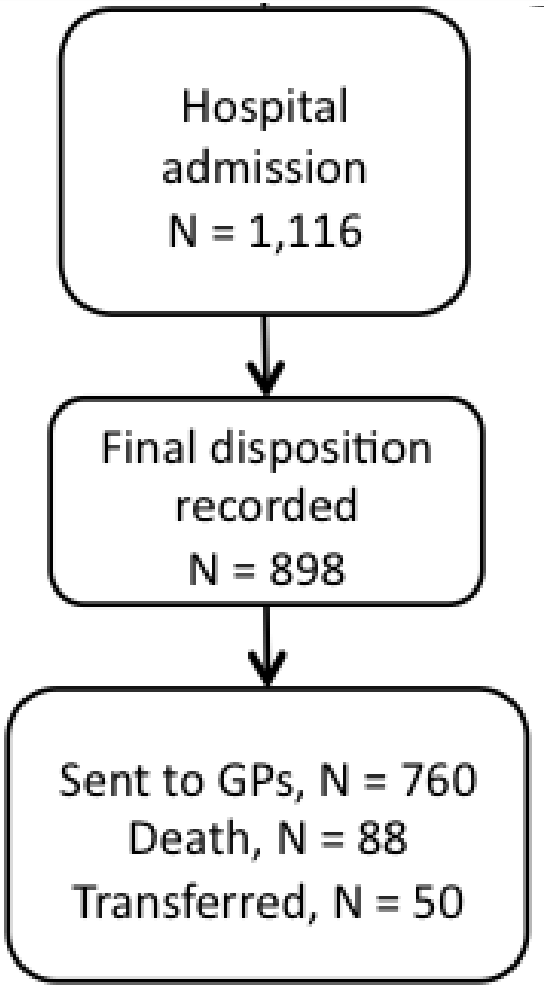
Final outcome



- Median length of stay, 6 days (interquartile range, 7; range 1-80);
- 88 cases (9.8%) died in hospital;
- 50 (5.7%) were transferred to other institutions or nursing homes.

After adjustment for age, in-hospital death was associated with:

- Cancer (OR, 1.94; 95% confidence interval (CI), 1.11-3.37; P = 0.019);
- Malnutrition (OR, 2.0; 95% CI, 1.02-3.87; P = 0.044), independent of cancer.

Marchesini G, et al. ***Nutr Metab Cardiovasc Dis*** 2014 (in press)

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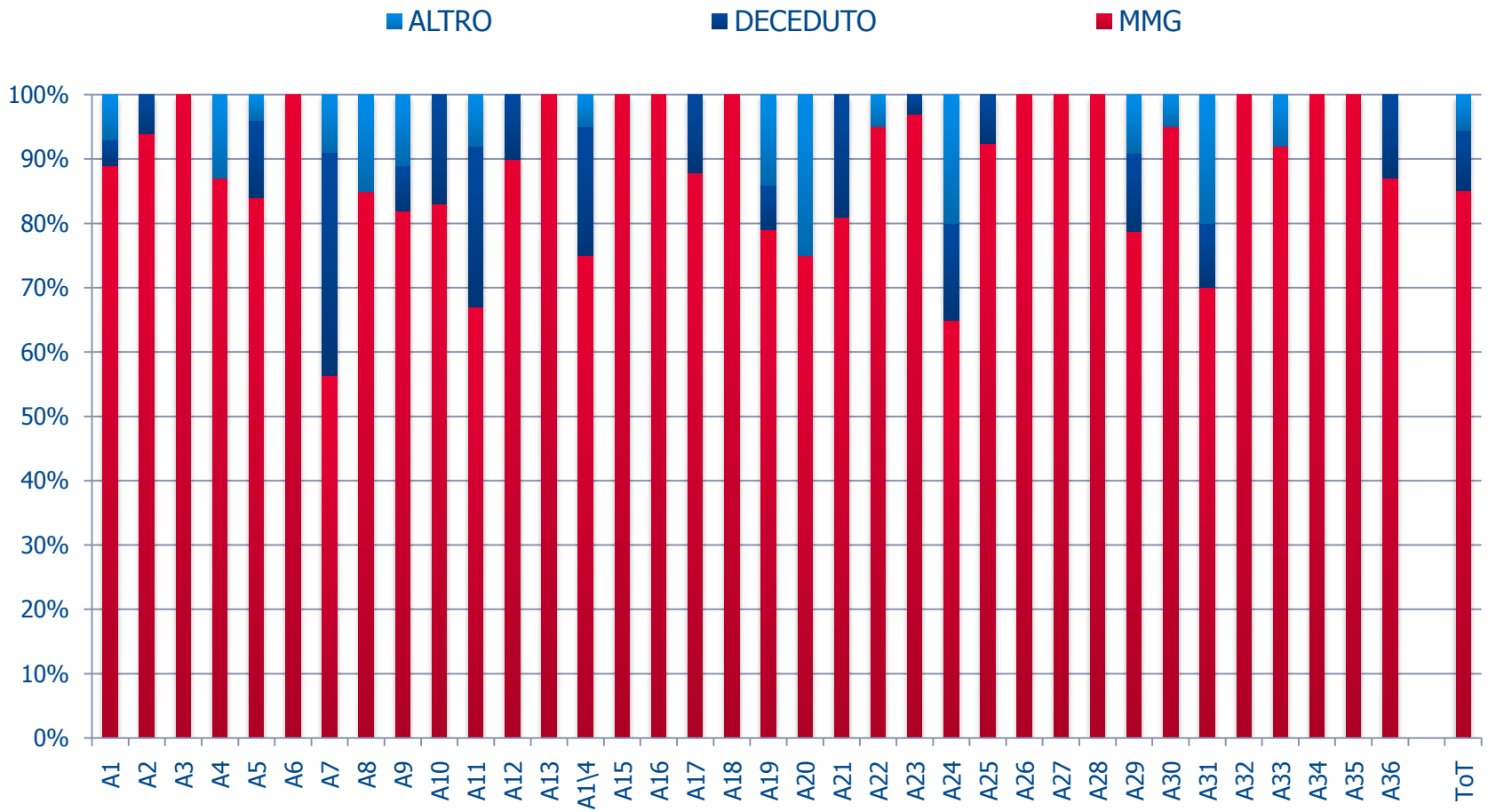
Mortalità



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Event rates

- **Type of event**: hypoglycemia severe enough to indicate immediate attendance to ED or intervention of the out-of-hospital Emergency service (52% of cases) and referral to hospital
- **Study area**: 12 million inhabitants. The attendance rate for hypoglycemia may thus be estimated around 0.21/1000 inhabitants-year, i.e., 0.6/1000 individuals attending the ED in the same period.
- **In Italy** (60 million people), nearly 12,000 individuals with diabetes are expected to attend the EDs for severe hypoglycemic events, which require the intervention of out-of-hospital Emergency services in nearly 6,000 cases.

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Outcome after hospital admission

- Follow-up data after admission was available in 898 of 1,161 cases (77.3%).
- A total of 760 cases (84.6%) were discharged after a median length of stay of 6 days (range, 1–80), without differences in relation to diabetes treatment.
- A total of 88 cases (9.8%) died in hospital; 50 (5.7%) were transferred to other institutions/nursing homes. No differences in death rate were observed in relation to the type of glucose-lowering drugs associated with hypoglycemia (insulin, 33/334 = 9.9%; oral agents, 39/396 = 9.8%; combination treatment, 13/144 = 9%).
- After adjusting for covariates, in-hospital death was associated with the number of comorbidities (OR, 1.28; 95% CI, 1.01–1.63).

Limitations & Strengths

Limitations

- Retrospective nature of the study;
- Possible underestimation of cases with diabetes, of co-morbidities or drug use (particularly for new drugs – DPP4 inhibitors or GLP1 RA, with trade names less known by general physicians operating in EDs
- No possibility to dissect the type of insulin (basal *vs.* IIT).

Strengths

- Large population covering the whole country;
- Use of hospital-based resources
- Involvement of physicians actively participating in ED research.

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Conclusions

- The study identifies a large number of hypoglycemic events requiring hospital treatment in the diabetes population.
- They were associated with a significant work-up of the Emergency services, both out- and in-hospital.
- The presence, number and severity of co-morbidities dictated the disposition and hospital admission, not death rate (very high in the population), probably unrelated to hypoglycemia *per se* but as the result of patients' frailty;

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Conclusions

- Nearly 50% of cases were treated with insulin, but oral agents were associated in nearly 25% of cases.
- Nearly 30% of cases occurred in non-insulin treated subjects, and in most cases in subject using insulin secretagogues.
- The event was associated with a traumatic injury or a road accident in several cases. No inference can be found on a possible relationship between hypoglycemia and trauma of road accident on a retrospective analysis

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Other participants: A Billeci, M Pesenti Compagnoni (**Aosta**); P Caporaletti, F Stea (**Bari**); D Manganaro, C Menon (**Bassano del Grappa**); C Arici, E Belotti, E Margutti (**Bergamo**); M Cavazza, A Venturi (**Bologna**); A Arru, B Usai (**Cagliari**); M Barozzi (**Cesena**); G Rastelli (**Fidenza**); S Grifoni, P Nazerian (**Firenze**); A Fabbri (**Forlì**); P Cremonesi, M Corbo, P Moscatelli, G Sacchi (**Genova**); F Dalmonte, T Lenzi (**Imola**); F Deiaco, C Gervasoni **(Imperia**); P Iannone (**Lavagna**); E Daghini, MA Di Sarli, M Pratesi (**Livorno**); A Brambilla, D Coen, R Cosentini (**Milano**); G Bandiera **(Modena**); A Barillari, E Lubini (**Monfalcone**); G Abbate, M Guarino **(Napoli**); G Berti, A Bettella, M Chiesa (**Padova**); A Magnacavallo, A Vercelli (**Piacenza**); A Bertini (**Pisa**); M Pazzaglia, AG Taglioli (**Ravenna**); A Ferrari (**Reggio Emilia**); M Galletti, C Pesci (**Rimini)**; C Barletta, S Beniamino, G Bertazzoni, G Carlotti, L Cipollone, E Guglielmelli, M Mazzone, L Pietropaolo, G Pignataro, GM Ricciuto, MP Ruggeri, C Sighieri (**Roma**), P Groff, L Mattucci (**San Benedetto del Tronto**), G Marras **(Sassari**), M Pastorelli, S Sartini **(Siena**), P Balzaretti, G Carbone, F Molinaro, E Paschetta (**Torino**), GA Cibinel (**Pinerolo**), P Faes, C Ramponi (**Trento**), L Scaldaferri (**Treviso**), R Petrino (**Vercelli**), V Natale (**Vibo Valenzia**).

and the **Italian Society of Emergency Medicine**

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- Potter, ***BMJ*** *1982*: 3.0 /1000 ED visits per year
- Feher, ***Arch Emerg Med*** *1989*: 1.8 /1000 ED visits per year
- Anderson, ***Acta Anestesiol. Scand***. 2002:. 5.0% incidence of all Emergency call
- Leese, ***Diab. Care*** 2003; 1.15 and 1.18 /1000 visits per years for type 1 and type 2 (primary care, ambulance services, hospital ED, inpatient care)
- Brackenridge, **EMJ** 2006: 1.3% incidence of all SAS Emergency call per year.
- Brudnitz, ***Ann Intern Med*** 2007: 11.5% event rate per 100 pts. hospitalized
- Ginde, ***Diab. Care*** 2008: 2.8 - 4.9 /1000 ED visits per year
- Brudnitz, ***NEJM*** 2011: 18 (insulin) and 4 (oral antidiabetics) hospitalization 10.000 out-patients medication visits per year.
- Farmer, ***Diabet Med*** 2012: 1.02% / all Emergency call per year.
- Lombardo, ***PLOS ONE*** 2013: 0.4% – 0.8% / 1000 discharged pts. 1.7 – 3.1 events / 100.000 residents.
- Geller AI, ***JAMA Intern Med*** 2014**;**
- *Marchesini G, et al.* ***Nutr Metab Cardiovasc Dis*** 2014: 0.6 /1000 ED visits per year

HYPOTHESIS – 2

Nr.	Age	Hb A1c	ICD9-CM
1	86	7.1	250.02 - DIABETE MELLITO, TIPO II O NON SPECIFICATO, SCOMPENSATO, SENZA MENZIONE DI COMPLICAZIONI
2	80	8.7	250.80 - DIABETE TIPO II O NON SPECIFICATO, NON DEFINITO SE SCOMPENSATO, CON ALTRE COMPLICAZIONI SPECIFICATE
3	76	6.9	250.80 - DIABETE TIPO II O NON SPECIFICATO, NON DEFINITO SE SCOMPENSATO, CON ALTRE COMPLICAZIONI SPECIFICAT
4	86	7.4	250.00 - DIABETE MELLITO, TIPO II O NON SPECIFICATO, NON DEFINITO SE SCOMPENSATO, SENZA MENZIONE DI COMPLICAZIONI
5	77	--	276.51 - DISIDRATAZIONE
6	68	5.7	250.42 - DIABETE TIPO II O NON SPECIFICATO, SCOMPENSATO, CON COMPLICAZIONI RENALI
7	89	5.9	**250.32 -** DIABETE CON ALTRI TIPI DI COMA, TIPO II O NON SPECIFICATO, SCOMPENSATO
8	55	8.0	250.03 - DIABETE MELLITO, TIPO I (DIABETE GIOVANILE), SCOMPENSATO, SENZA MENZIONE DI COMPLICAZIONI
9	55	7.4	250.80 - DIABETE TIPO II O NON SPECIFICATO, NON DEFINITO SE SCOMPENSATO, CON ALTRE COMPLICAZIONI SPECIFICATE
10	91	6.3	250.82 - DIABETE TIPO II O NON SPECIFICATO, SCOMPENSATO, CON ALTRE COMPLICAZIONI SPECIFICATE
11	79	6.2	250.00 - DIABETE MELLITO, TIPO II O NON SPECIFICATO, NON DEFINITO SE SCOMPENSATO, SENZA MENZIONE DI COMPLICAZIONI
12	86	7.3	**250.02 -** DIABETE MELLITO, TIPO II O NON SPECIFICATO, SCOMPENSATO, SENZA MENZIONE DI COMPLICAZIONI
13	91	6.8	250.00 - DIABETE MELLITO, TIPO II O NON SPECIFICATO, NON DEFINITO SE SCOMPENSATO, SENZA MENZIONE DI COMPLICAZIONI
14	80	7.4	250.00 - DIABETE MELLITO, TIPO II O NON SPECIFICATO, NON DEFINITO SE SCOMPENSATO, SENZA MENZIONE DI COMPLICAZIONI
15	90	6.1	250.32 - DIABETE CON ALTRI TIPI DI COMA, TIPO II O NON SPECIFICATO, SCOMPENSATO
16	85	5.5	402.91 - CARDIOPATIA IPERTENSIVA NON SPECIFICATA CON INSUFFICIENZA CARDIACA
17	74	7.8	250.32 - DIABETE CON ALTRI TIPI DI COMA, TIPO II O NON SPECIFICATO, SCOMPENSATO
18	59	6.6	250.02 - DIABETE MELLITO, TIPO II O NON SPECIFICATO, SCOMPENSATO, SENZA MENZIONE DI COMPLICAZIONI
19	80	8.7	250.80 - DIABETE TIPO II O NON SPECIFICATO, NON DEFINITO SE SCOMPENSATO, CON ALTRE COMPLICAZIONI SPECIFICATE
20	80	5.8	518.84 - INSUFFICIENZA RESPIRATORIA ACUTA E CRONICA
21	90	6.4	402.11 - CARDIOPATIA IPERTENSIVA BENIGNA CON INSUFFICIENZA CARDIACA
22	96	--	250.02 - DIABETE MELLITO, TIPO II O NON SPECIFICATO, SCOMPENSATO, SENZA MENZIONE DI COMPLICAZIONI
23	83	6.9	**250.80 -** DIABETE TIPO II O NON SPECIFICATO, NON DEFINITO SE SCOMPENSATO, CON ALTRE COMPLICAZIONI SPECIFICATE
	80	6.9	
	11	0.92	

Trends and Disparities in U.S. Emergency Department Visits for Hypoglycemia, 1993-2005

Epidemiologic data from National Hospital Ambulatory Medical Care Survey

	N. of cases	Estimated N. cases (95% CI)	Rate per 1,000 of the diabetic Pts. (95% CI)	Rate per 1,000 ED visits (95% CI)
Years				
1993–1995	215	773 (578–969)	30 (23–38)	2.8 (2.1–3.5)
1996–1997	152	672 (524–820)	43 (32–54)	3.6 (2.8–4.4)
1998–1999	141	740 (543–937)	26 (19–33)	3.6 (2.7–4.6)
2000–2001	222	897 (663–1,130)	40 (30–50)	4.2 (3.1–5.2)
2002–2003	262	776 (633–920)	32 (24–39)	3.5 (2.8–4.1)
2004–2005	311	1,100 (864–1,340)	33 (26–39)	4.9 (3.8–5.9)
Age (years)				
≤45	401	1,550 (1,330–1,780)	62 (53–71)	1.7 (1.5–2.0)
0–19	78	359 (229–489)	—	0.9 (0.6–1.2)
20–44	323	1,200 (1,020–1,370)	—	2.3 (2.0–2.7)
45–64	364	1,230 (1,060–1,400)	19 (17–22)	5.5 (4.7–6.2)
65–74	219	845 (698–991)	25 (20–29)	10 (8.5–12)
≥75	319	1,330 (1,090–1,580)	54 (44–64)	12 (9.4–14

Ginde AA, **Diab. Care** 2008

Trends and Disparities in U.S. Emergency Department Visits for Hypoglycemia, 1993–2005

	N. of cases	Estimated N. cases (95% CI)	Rate per 1,000 of the diabetic Pts. (95% CI)	Rate per 1,000 ED visits (95% CI)
Race				
White	829	3,270 (2,910–3,640)	28 (25–31)	3.6 (3.2–4.0)
Black	326	1,210 (970–1,450)	50 (40–60)	4.8 (3.9–5.8)
Other	36	104 (50–159)	14 (6.5–21)	3.4 (1.6–5.1)
Ethnicity				
Hispanic	100	329 (241–416)	21 (15–27)*	2.5 (1.8–3.2)
Non-Hispanic	985	3,720 (3,290–4,150)	12 (10–13)*	3.9 (3.5–4.4)
Insurance				
Private	285	1,140 (963–1,300)	NA	2.6 (2.2–3.0)
Public	643	2,430 (2,090–2,760)	NA	5.8 (5.0–6.6)
Self-pay	111	414 (316–513)	NA	2.2 (1.7–2.7)
Other/unknown	124	416 (316–515)	NA	2.4 (1.8–3.0)

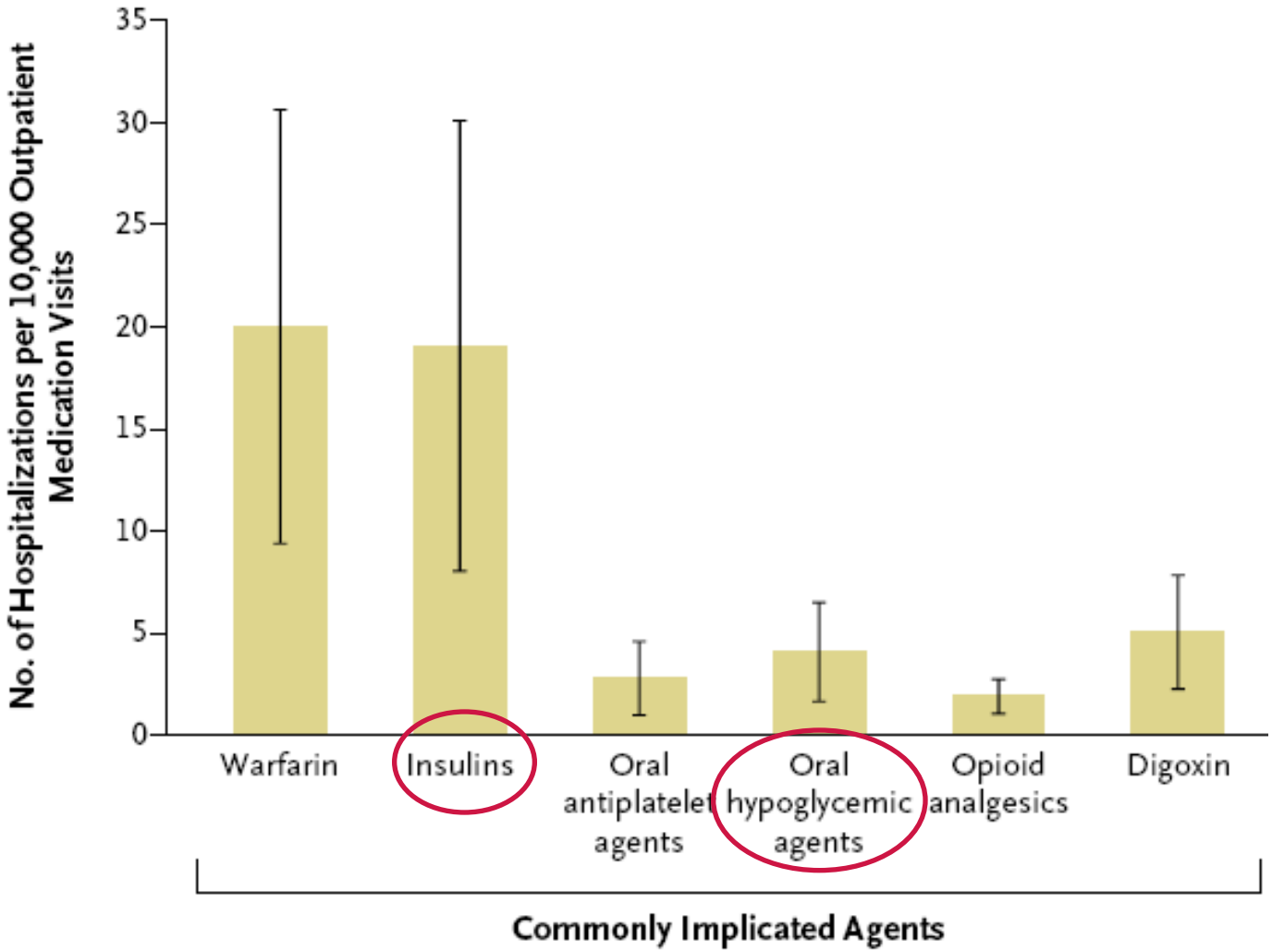
Ginde AA, **Diab. Care** 2008

Emergency Hospitalizations for Adverse Drug Events in Older Americans

	Annual National Hospitalizations (N = 99,628)		Proportion of ED Visits Resulting in Hospitalization
	No	% (95%CI)	%
Most commonly implicated medications			
Warfarin	33,171	33.3 (28.0–38.5)	46.2
Insulins	3,854	13.9 (9.8–18.0)	40.6
Oral antiplatelet agents	13,263‡	13.3 (7.5–19.1)	41.5
Oral hypoglycemic agents	10,656	10.7 (8.1–13.3)	51.8
Opioid analgesics	4,778	4.8 (3.5–6.1)	32.4
Antibiotics	4,205	4.2 (2.9–5.5)	18.3
Digoxin	3,465	3.5 (1.9–5.0)	80.5
Antineoplastic agents	3,329‡	3.3 (0.9–5.8)‡	51.5
Antiadrenergic agents	2,899	2.9 (2.1–3.7)	35.7
Renin–angiotensin inhibitors	2,870	2.9 (1.7–4.1)	32.6
Sedative or hypnotic agents	2,469	2.5 (1.6–3.3)	35.2
Anticonvulsants	1,653	1.7 (0.9–2.4)	40.0
Diuretics	1,071‡	1.1 (0.4–1.8)‡	42.4

Budnitz DS, **NEJM** 2011

Emergency Hospitalizations for Adverse Drug Events in Older Americans



Budnitz DS, **NEJM** 2011

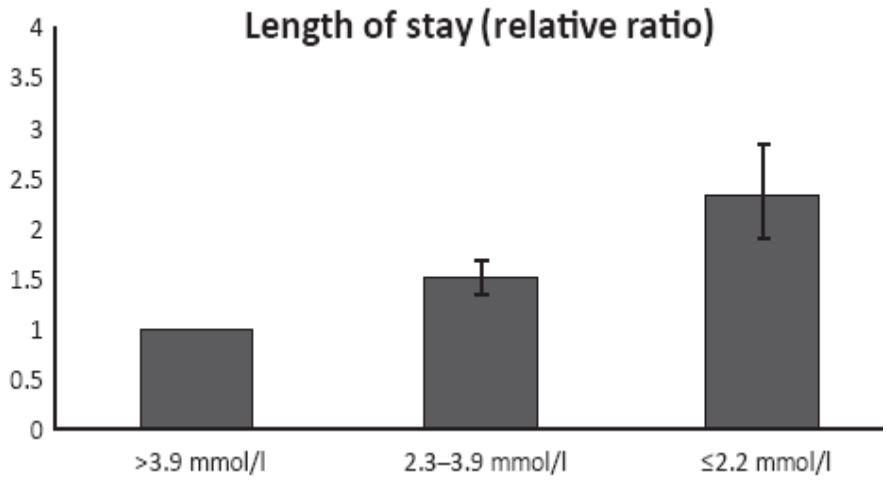
Emergency Hospitalizations for Adverse Drug Events in Older Americans

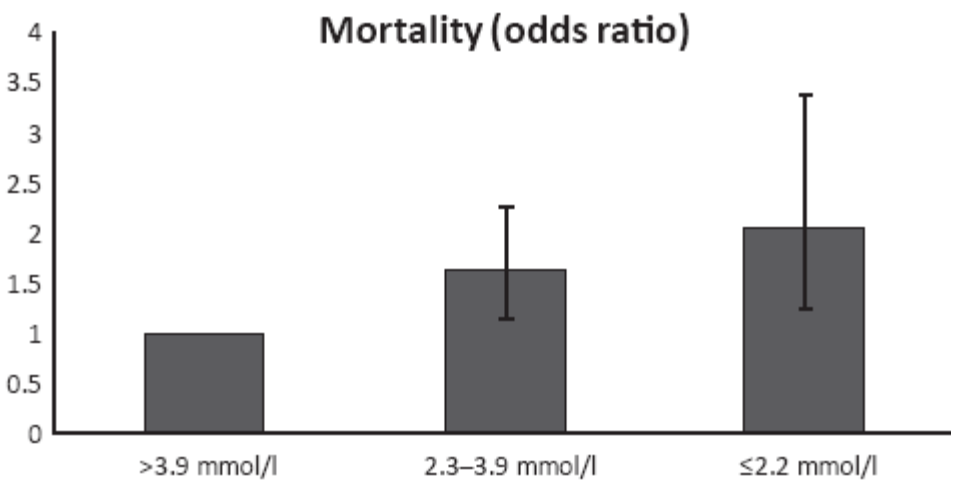
Table 3. National Estimates of Emergency Hospitalizations for Common Manifestations of Adverse Drug Events in Older U.S. Adults, 2007–2009.*

Therapeutic Category and Adverse-Event Manifestation†	Annual National Estimate of Hospitalizations	Proportion of Emergency Department Visits Resulting in Hospitalization
	% (95% CI)	%
Endocrine agents		
Hypoglycemia with loss of consciousness or seizure	26.0 (13.5–38.4)	57.5
Hypoglycemia with altered mental status or other neurologic sequelae	40.7 (31.8–49.5)	42.4
Hypoglycemia with cardiovascular sequelae	8.3 (6.1–10.4)	49.6
Hypoglycemia with weakness, dyspnea, or respiratory distress	5.7 (3.0–8.5)	47.5
Hypoglycemia with other or unspecified sequelae	14.0 (6.2–21.8)	37.3

Budnitz DS, **NEJM** 2011

Hypoglycaemia is associated with increased length of stay and mortality in people with diabetes who are hospitalized





Severity of hypoglycaemia vs. inpatient mortality and length of stay (adjusted odds ratio for mortality and adjusted relative ratio for length of stay). Relative ratio here is the exponential of regression coefficient obtained from the analysis of log transformed length-of-stay data.
Covariates adjusted for are age, gender, ethnicity, social class, admission type, insulin use and Charlsonc comorbidity score. Bars indicate the confidence intervals.

Nirantharakumar K, **Diabet Med** 2012

Temporal Trend in Hospitalizations for Acute Diabetic Complications: A Nationwide Study, Italy, 2001–2010

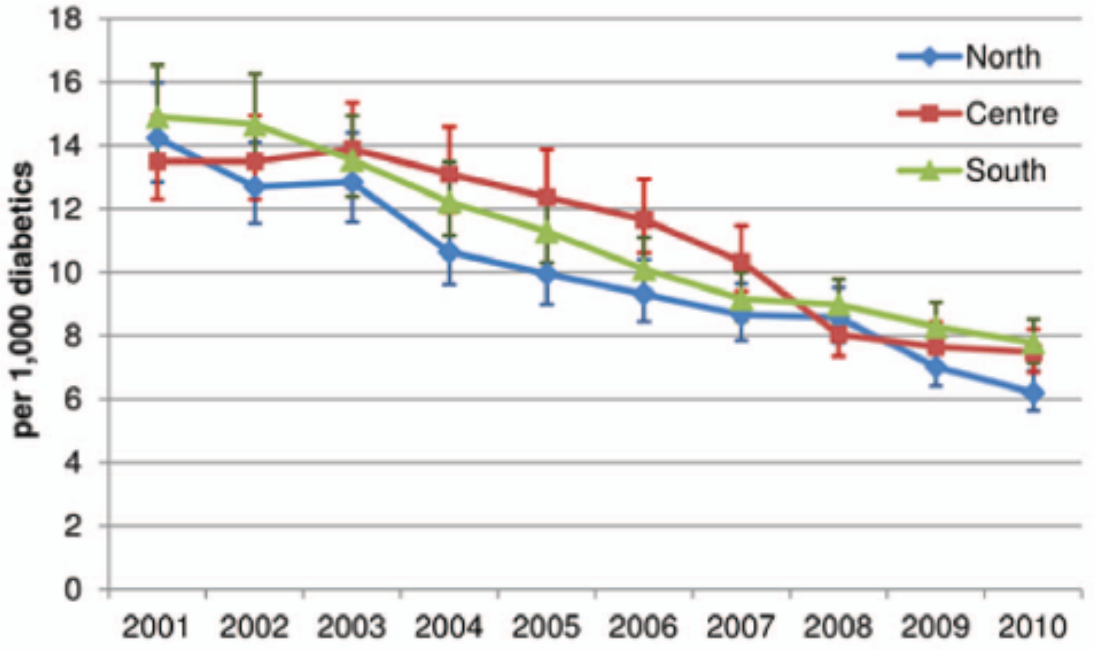


Figure 1. Temporal trend in hospitalization rates/1,000 diabetic people for acute diabetic complications, by North, Center and South of Italy, 2001–2010. Vertical bars indicate 95% CIs.
doi:10.1371/journal.pone.0063675.g001

Lombardo F, **PLOS ONE** 2013; 8 (5): e63675. doi:10.1371/journal.pone.0063675

Temporal Trend in Hospitalizations for Acute Diabetic Complications: A Nationwide Study, Italy, 2001–2010

Discharges	Acute Diabetic Complications	Acute Hyperglycemic Complications	Hypoglycemic Coma
N. of cases	266,374	251,528	14,846
Complications	110,033 (41.3%)	98,133 (39.0%)	11,900 (80.2%)
Duration of stay in days	9.2 (11.1)	9.3 (11.3)	6.9 (6.8)
Age distribution (years)			
0–19	8.3%	8.7%	1.1%
20–44	9.0%	9.2%	6.0%
45–64	20.6%	21.0%	14.0%
≥65	62.1%	61.1%	78.9%
Patients			
N	214,899	203,273	13,764
Female, n (%)	111,917 (52.1%)	105,321 (51.8%)	7724 (56.1%)
Age*, mean (SD)	65.8 (20.4)	65.3 (20.6)	72.8 (15.4)
Re-hospitalizations	26,552 (12.4%)	24,629 (12.1%)	543 (3.9%)
In-hospital deaths, n (%)	16,402 (7.6%)	16,117 (7.9%)	285 (2.1%)

- Lombardo F, **PLOS ONE** 8 (5): e63675. doi:10.1371/journal.pone.0063675

Temporal Trend in Hospitalizations for Acute Diabetic Complications: A Nationwide Study, Italy, 2001–2010

Hospital admission rates for acute diabetic complications in Italy, 2001–2010.

	Acute Diabetic Complications			Hypoglycemic coma		
	N	Rate /100,000 Residents	Rate / 1000 Diabetics	N	Rate /100,000 Residents	Rate / 1000 Diabetics
2001	32,096	56.3	14.4 (13.8–15.1)	1,794	3.1	0.81 (0.84–0.77)
2002	30,304	53.1	13.7 (13.1–14.3)	1,758	3.1	0.80 (0.76–0.83)
2003	30,072	51.7	13.5 (12.9–14.1)	1,615	2.8	0.72 (0.69–0.76)
2004	27,694	46.9	11.9 (11.3–12.4)	1,492	2.5	0.64 (0.61–0.67)
2005	26,861	44.7	11.0 (10.5–11.6)	1,466	2.4	0.60 (0.57–0.63)
2006	26,512	43.5	10.2 (9.7–10.7)	1,445	2.3	0.56 (0.53–0.58)
2007	25,177	40.7	9.3 (8.9–9.7)	1,463	2.3	0.54 (0.52–0.56)
2008	24,732	39.3	8.6 (8.3–9.0)	1,371	2.1	0.48 (0.46–0.50)
2009	22,052	34.5	7.7 (7.3–8.0)	1,275	1.9	0.44 (0.42–0.46)
2010	20,874	32.4	7.1 (6.8–7.4)	1,167	1.7	0.39 (0.38–0.41)

Lombardo F, **PLOS ONE** 8 (5): e63675. doi:10.1371/journal.pone.0063675