Montpellier
et la région Occitanie - Méditerranée
LE CORUM, Montpellier
du lundi 30 août 2021
au mercredi 1er septembre 2021

22es Journées Nationales d'Infectiologie

Diabète et COVID-19 : que retenir de la pandémie ?

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Déclaration d'intérêts de 2014 à 2020

- **Intérêts financiers :**

- **Liens durables ou permanents : expertise Lilly, Novo, Amgen, Sanofi, MSD, Pfizer**

- **Interventions ponctuelles : Pfizer, Lilly, Sanofi, Novo-Nordisk, MSD, Sanofi, Amgen, Viatris**

- **Intérêts indirects :**

Diabète et pronostic du Covid

Etude rétrospective
201 patients Wuhan

Table 1. Demographic Characteristics of Patients With Coronavirus Disease 2019 Pneumonia

Study population	No. (%)
No. of patients	201
Age, median (IQR), y	51 (43-60)
≥65	40 (19.9)
<65	161 (80.1)
Highest patient temperature, median (IQR), °C	38.8 (38.3-39.0)
≥39 (high fever)	77 (38.3)
<39	93 (46.3)
Gender	
Male	128 (63.7)
Female	73 (36.3)
Wuhan seafood market exposure	99 (49.3)
Date of illness onset	
Before December 5, 2019	1 (0.5)
December 6-31, 2019	114 (56.7)
January 1-14, 2020	76 (37.8)
After January 15, 2020	10 (5.0)
Initial common symptoms	
Fever	188 (93.5)
Cough	163 (81.1)
Productive cough	83 (41.3)
Dyspnea	80 (39.8)
Fatigue or myalgia	65 (32.3)
Chest imaging, infiltrate[a]	
Unilateral	10 (5.0)
Bilateral	191 (95.0)
Comorbidities	
Hypertension	39 (19.4)
Diabetes	22 (10.9)
Cardiovascular disease	8 (4.0)
Liver disease	7 (3.5)
Nervous system disease	7 (3.5)
Chronic lung disease	5 (2.5)
Chronic kidney disease	2 (1.0)
Endocrine system disease[b]	2 (1.0)

Table 4. Bivariate Cox Regression of Factors Associated With ARDS Development or Progression From ARDS to Death

Patient characteristics and findings	ARDS		Death	
	HR (95% CI)	P value	HR (95% CI)	P value
Clinical characteristics				
Age (≥65 vs <65), y	3.26 (2.08-5.11)	<.001	6.17 (3.26-11.67)	<.001
Gender (male vs female)	1.47 (0.92-2.36)	.11	0.56 (0.30-1.05)	.07
Highest patient temperature (≥39 °C vs <39 °C)	1.77 (1.11-2.84)	.02	0.41 (0.21-0.82)	.01
Comorbidities				
Hypertension (yes vs no)	1.82 (1.13-2.95)	.01	1.70 (0.92-3.14)	.09
Diabetes (yes vs no)	2.34 (1.35-4.05)	.002	1.58 (0.80-3.13)	.19

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Diabète et pronostic du Covid

	Article type	Study population	Prevalence of diabetes	Outcome	Risk
Zhang et al[3]	Retrospective	258	24%	Mortality	3·64 (1·08–12·21)*
Kumar et al[4]	Meta-analysis	16 003	9·8%	Severe disease	2·75 (2·09–3·62)*
Kumar et al[4]	Meta-analysis	16 003	9·8%	Mortality	1·90 (1·37–2·64)*
Guan et al[10]	Retrospective	1590	NA	Composite†	1·59 (1·03–2·45)‡
Li et al[11]	Meta-analysis	1525	9·7%	ICU admission§	2·21 (0·88–5·57)¶
Fadini et al[12]	Meta-analysis	1687	NA	Severe disease	2·26 (0·98–4·82)‖
Fadini et al[12]	Meta-analysis	355	35·5%	Mortality	1·75‖
Petrilli et al[13]	Retrospective	5279	22·6%	Hospital admission	2·24 (1·84–2·73)*
Roncon et al[14]	Meta-analysis	1382	NA	ICU admission	2·79 (1·85–4·22)*
Roncon et al[14]	Meta-analysis	471	NA	Mortality	3·21 (1·82–5·64)*
Zhou et al[15]	Retrospective	191	19%	Mortality	2·85 (1·35–6·05)*
Zhu et al[16]	Retrospective	7337	13%	Mortality	1·49 (1·13–1·96)‡
Yan et al[17]	Retrospective	193	25%	Mortality	1·53 (1·02–2·3)‡
Sardu et al[18]	Retrospective	59	44%	Survival	0·172 (0·051–0·576)‡
Yang et al[19]	Meta-analysis	4648	NA	Severe disease	2·07 (0·88–4·82)*
Barron et al[20]	Cohort study	61 414 470	0·4% type 1 diabetes	Mortality	3·50 (3·15–3·89)*
Barron et al[20]	Cohort study	61 414 470	4·7% type 2 diabetes	Mortality	2·03 (1·97–2·09)*

ICU=intensive care unit. NA=not given. *Odds ratio (95% CI). †ICU admission, or invasive ventilation, or death. ‡Hazard ratio (95% CI). §Calculated for 1056 patients (in three of six studies). ¶Risk ratio (95% CI). ‖Rate ratio (95% CI not given).
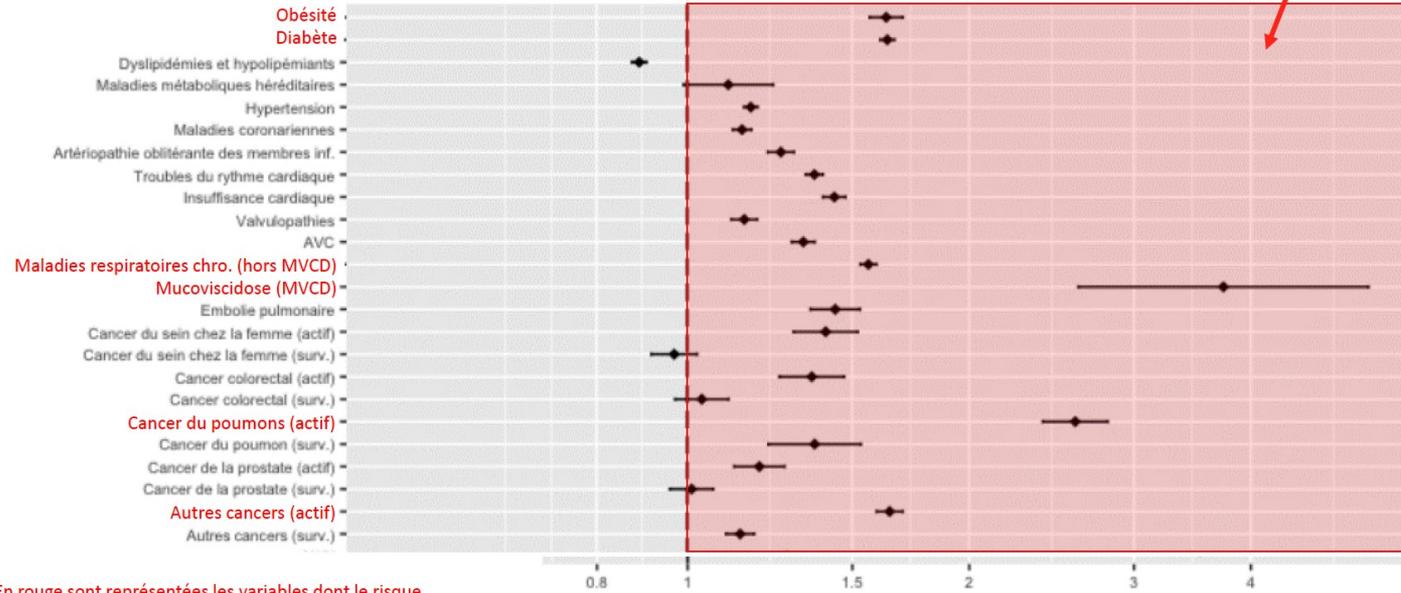
Table 1: COVID-19 outcomes according to pre-existing diabetes

Diabète associé au risque de Covid sévère,
d'admission en USI et
de Mté X2-3

Diabète et pronostic du Covid

Risques relatifs de décès pour COVID-19 en milieu hospitalier

Facteurs de risque

En rouge sont représentées les variables dont le risque relatif de décès est supérieur à 1,5 IC$_{95\%}$

Semenzato L *et al*. EPI-PHARE - Groupement d'intérêt scientifique (GIS) ANSM-CNAM 2021 Fev

Impact du Covid sur la mortalité des personnes diabétiques

Angleterre

Ecosse
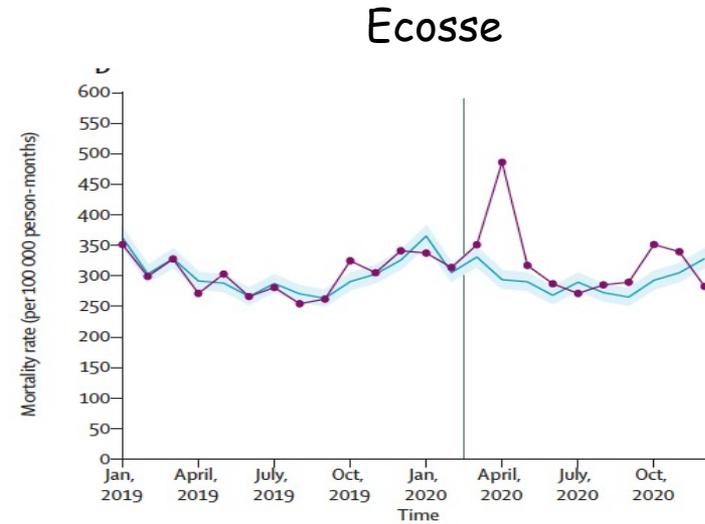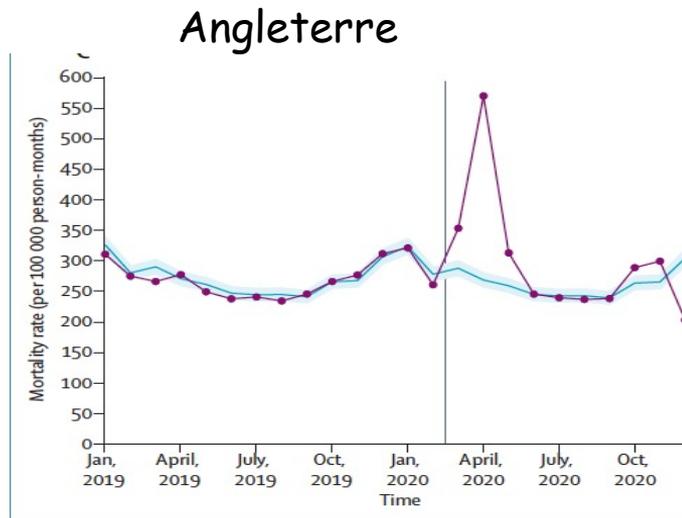
Phénotype des patients diabétiques Covid: Coronado

- La majorité des sujets hospitalisés présentent:
  - **Un diabète de type 2** (89%) et une minorité
  - **un diabète de type 1** (<3%) **Un diabète découvert** au moment de l'hospitalisation (3%)

- **L'âge moyen** est de 70 ans

- 35% sont des femmes et **65% sont des hommes**

Clinical features		Number of people with available data	Whole population
Sex (female)		1317	462/1317 (35.1%)
Age (yrs)*		1317	69.8 ± 13.0
Age class (yrs)		1317	
	< 55		159/1317 (12.1%)
	55-64		266/1317 (20.2%)
	65-74		394/1317 (29.9%)
	≥75		498/1317 (37.8%)
Type of diabetes		1317	
	Type 2		1166/1317 (88.5%)
	Type 1		39/1317 (2.9%)
	Other		71/1317 (5.4%)
	Diagnosed on admission		41/1317 (3.1%)
Ethnicity		1035	
	EU		641/1035 (61.9%)
	MENA		196/1035 (18.9%)
	AC		174/1035 (16.8%)
	AS		24/1035 (2.3%)
BMI (kg/m²)*		1117	28.4 [25.0; 32.7]
BMI class		1117	
	< 25 kg/m²		279/1117 (25%)
	25-29.9 kg/m²		410/1117 (36.7%)
	30-39.9 kg/m²		359/1117 (32.1%)
	≥40 kg/m²		69/1117 (6.2%)

Cariou B et al. Diabetologia. 2020 May 29:1-16.

Phénotype des patients diabétiques Covid: Coronado

- Le taux moyen d'HbA1c est de **8,1%** (>8% chez **44%** des sujets)

- Les complications microvasculaires (œil, rein et nerfs) sont présentes chez **47%** des sujets analysés

- Les complications macrovasculaires (artères du cœur, du cerveau, des jambes) sont présentes chez **41%** des sujets analysés

Clinical features	Number of people with available data	Whole population
Diabetes duration (yrs)	772	13.6 ± 10.9
HbA1c (mmol/mol)*	846	65.4 ± 21.2
HbA1c (%)*	846	8.1 ± 1.9
HbA1c (categories)	846	
< 53 mmol/mol (7 %)		245/846 (29.0%)
53-63 mmol/mol (7-7.9 %)		228/846 (27.0%)
64-74 mmol/mol (8-8.9 %)		164/846 (19.4%)
≥ 75 mmol/mol (9 %)		209/846 (24.7%)
Hypertension	1299	1003/1299 (**77.2%**)
Dyslipidemia	1255	640/1255 (51.0%)
Tobacco use	1029	
Never		582/1029 (56.6%)
Former		390/1029 (37.9%)
Current		57/1029 (5.5%)
Long-term diabetes complications		
Microvascular complications	883	413/883 (**46.8%**)
Severe diabetic retinopathy	954	66/954 (6.9%)
Diabetic kidney disease	1066	355/1066 (33.3%)
History of diabetic foot ulcer	1232	76/1232 (6.2%)
Macrovascular complications	1189	485/1189 (**40.8%**)
Ischemic heart disease (ACS/CAR)	1251	336/1251 (26.9%)
Cerebrovascular disease (stroke or TIA)	1267	163/1267 (12.9%)
Peripheral artery disease	1285	145/1285 (11.3%)

Cariou B et al. Diabetologia. 2020 May 29:1-16.

Phénotype des patients diabétiques Covid: Coronado

Parmi les comorbidités :
- Insuffisance cardiaque (12%)
- Hépatopathie métabolique (11%)
- Bronchite chronique (10%)
- SAOS appareillé (12%)

A l'admission, **38%** des sujets analysés sont sous insuline, **57%** sous metformine, **22%** sous DPP4i

A l'admission, **56%** des sujets reçoivent un IEC ou un Sartan

Clinical features	Number of people with available data	Whole population
Comorbidities		
Heart failure	1206	140/1206 (11.6%)
NAFLD or liver cirrhosis	1107	119/1107 (10.7%)
Active cancer	1282	194/1282 (15.1%)
COPD	1278	133/1278 (10.4%)
Treated OSA	1189	144/1189 (12.1%)
Organ graft	1302	38/1302 (2.9%)
End stage renal failure	831	60/831 (7.2%)
Routine treatment before admission		
Metformin	1317	746/1317 (56.6%)
Sulfonylurea/glinides	1317	367/1317 (27.9%)
DPP4-inhibitors	1317	285/1317 (21.6%)
GLP1-RA	1317	123/1317 (9.3%)
Insulin	1317	504/1317 (38.3%)
Loop diuretics	1317	252/1317 (19.1%)
Thiazide diuretics	1317	267/1317 (20.3%)
Potassium-sparing diuretics	1317	59/1317 (4.5%)
ACE inhibitors	1317	354/1317 (26.9%)
MRA	1317	53/1317 (4.0%)
Beta blockers	1317	442/1317 (33.6%)
ARBs	1317	389/1317 (29.5%)
ARBs and/or ACE inhibitors	1317	737/1317 (56.0%)
Statins	1317	627/1317 (47.6%)

Cariou B et al. Diabetologia. 2020 May 29:1-16.

Coronado: Facteurs associés survenue DC J7

Patient characteristics	Model 'prior to admission': fully adjusted		Model 'prior to admission': stepwise selection with age and sex forced	
	OR (95% CI)	p value	OR (95% CI)	p value
Age (+1 SD)	2.39 (1.67, 3.42)	<0.0001	2.48 (1.74, 3.53)	<0.0001
Sex (female/male)	0.78 (0.43, 1.40)	0.4023	0.78 (0.44, 1.38)	0.4007
Hypertension	0.76 (0.34, 1.70)	0.5087		
Microvascular complications	1.78 (0.92, 3.44)	0.0846	2.14 (1.16, 3.94)	0.0153
Macrovascular complications	2.26 (1.25, 4.08)	0.0069	2.54 (1.44, 4.50)	0.0013
Heart failure	1.08 (0.54, 2.15)	0.8249	–	–
Active cancer	1.45 (0.77, 2.73)	0.2458	–	–
Treated OSA	2.65 (1.36, 5.19)	0.0044	2.80 (1.46, 5.38)	0.0020
β-Blockers	1.19 (0.69, 2.06)	0.5321	–	–
Metformin	0.80 (0.45, 1.43)	0.4532	–	–
Insulin	1.26 (0.72, 2.22)	0.4130	–	–
Loop diuretics	1.39 (0.76, 2.55)	0.2806	–	–
ARBs and/or ACE inhibitors and/or MRAs	1.22 (0.68, 2.20)	0.5069	–	–

Models were applied to 758 participants yielding 74 deaths (9.8%)

The OR for age corresponds to an increase of 1 SD after standardisation

MRAs include spironolactone and eplerenone

Cariou B et al. Diabetologia. 2020 May 29:1-16.

COVID-19 Severity Is Tripled in the Diabetes Community: A Prospective Analysis of the Pandemic's Impact in Type 1 and Type 2 Diabetes

Justin M. Gregory,[1] James C. Slaughter,[2] Sara H. Duffus,[1] T. Jordan Smith,[1] Lauren M. LeStourgeon,[3] Sarah S. Jaser,[1] Allison B. McCoy,[4] James M. Luther,[5] Erin R. Giovannetti,[6] Schafer Boeder,[6] Jeremy H. Pettus,[6] and Daniel J. Moore[1]
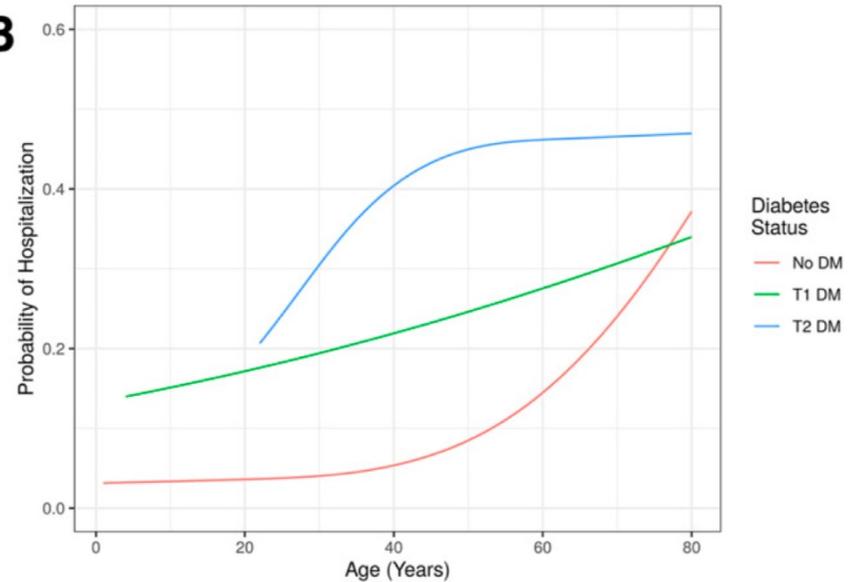
Sévérité Covid et type de diabète

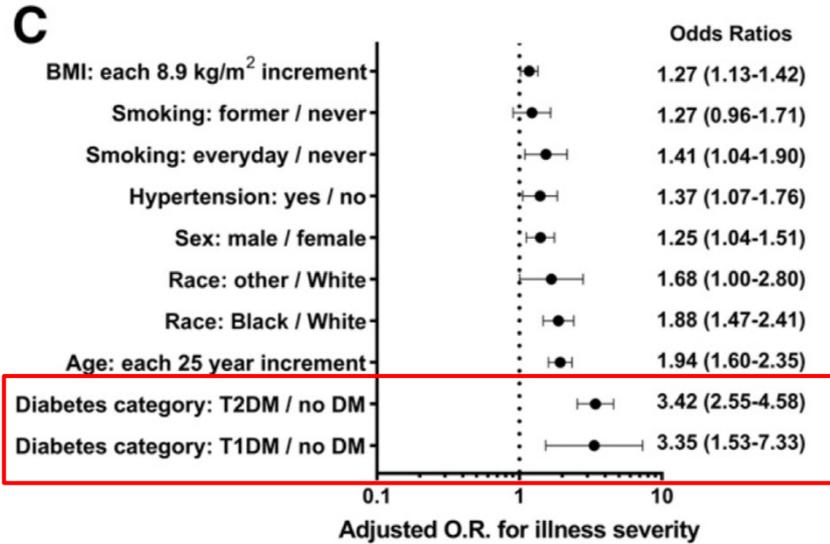Gregory et al. Diabetes Care 2021 Feb; 44(2): 526-532
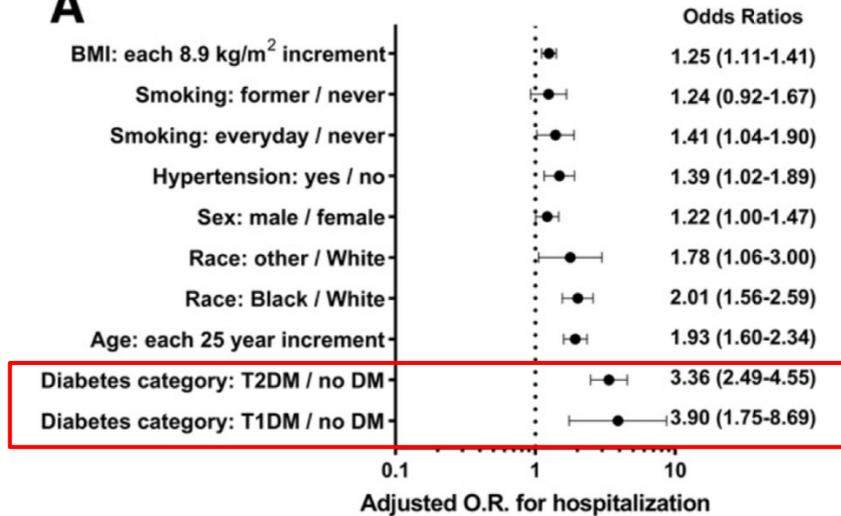
Sévérité Covid et type de diabète
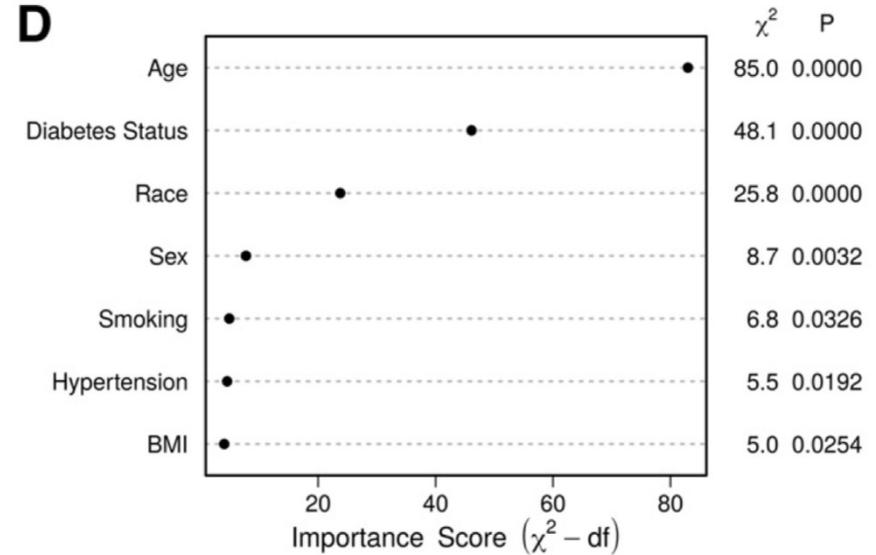
Impact de l'équilibre glycémique sur le pronostic Covid

	Study population	Number of patients (n)	Parameter of glycemic control	Outcome	Risk HR/OR (95% CI)
a. Glycemic control before hospitalization					
Holman et al. (10)	United Kingdom, nationwide population-based cohort *March 1st – May 11th 2020*	T1D: 265,090 T2D: 2,889,210	HbA1c 59 – 74 mmol/mol (7.6 – 8.9%)	Mortality	T1D: HR 1.16 (0.81 – 1.67)* T2D: HR 1.22 (1.15 – 1.30)*
			HbA1c 75 – 85 mmol/mol (9.0 – 9.9%)		T1D: HR 1.37 (0.90 – 2.07)* T2D: HR 1.36 (1.24 – 1.50)*
			HbA1c ≥ 86 mmol/mol (10.0%)		T1D: HR 2.23 (1.50 – 3.30)* T2D: HR 1.61 (1.47 – 1.77)*
Williamson et al. (58)	United Kingdom, nationwide population-based cohort *January 1st – May 6th 2020*	17,278,392	HbA1c ≥ 58 mmol/mol (7.5%)	Mortality	HR 2.61 (2.46 – 2.77)[#] HR 1.95 (1.83 – 2.08)[$]
Cariou et al. (60)	France, multi-center cohort *March 10th – March 31st 2020*	846	HbA1c 53 – 63 mmol/mol (7.0 – 7.9%) HbA1c 64 – 74 mmol/mol (8.0 – 8.9%) HbA1c ≥ 75 mmol/mol (9.0%)	Mortality	OR 1.55 (0.82 – 2.93)[&] OR 1.09 (0.52 – 2.28)[&] OR 0.84 (0.40 – 1.75)[&]
Gregory et al. (51, 52)[Φ]	USA, single-center cohort *March 17th – December 24th 2020*	T1D: 102	1st HbA1c quartile 2nd HbA1c quartile 3rd HbA1c quartile 4th HbA1c quartile	Hospitalization	OR 2.96 (1.11 – 7.86)[€] OR 2.96 (1.11 – 7.86)[€] OR 5.12 (2.12 – 12.35)[€] OR 9.76 (4.42 – 21.54)[€]
c. Glycemic control during in-hospital stay					
Bode et al. (20)	USA, multi-center retrospective *March 1st – April 6th 2020*	1,122	Diabetes and/or uncontrolled hyperglycemia (≥ 2 measurements > 10.0 mmol/l (180 mg/dL) within 24h)	Mortality	OR 6.12 (3.63 – 10.31)[&φ]
Zhu et al. (19)	China, multi-center retrospective *December 30th 2019 – March 20th 2020*	Total: 7,337 T2D: 952	Normoglycemia (glycemic variability during hospital stay 3.9 – 10.0 mmol/l (70 – 180 mg/dL) versus hyperglycemia (> 10.0 mmol/l (180 mg/dL)	Mortality	HR 0.14 (0.03 – 0.60)[ω]

Impact des traitements du diabète sur le pronostic Covid

Association Between Glucagon-Like Peptide 1 Receptor Agonist and Sodium–Glucose Cotransporter 2 Inhibitor Use and COVID-19 Outcomes

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Hemalkumar Mehta,[3,4]
Joshua D. Miller,[10] Richard A. Moffitt,[11]
Til Stürmer,[12] Kajsa Kvist,[2]
John B. Buse,[9,13] and N3C Consortium

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Impact des traitements du diabète sur le pronostic Covid

Table 2—Crude primary and secondary outcomes according to premorbid medication use

	All ($N = 12,446$)	GLP1-RA users ($N = 6,692$)	SGLT2i users ($N = 3,665$)	DPP4i users ($N = 3,511$)
60-day mortality, E (%)	387 (3.11)	138 (2.06)	85 (2.32)	199 (5.67)
Total mortality, E (%)*	423 (3.40)	153 (2.29)	91 (2.48)	217 (6.18)
Emergency room visit, E (%)†	3,878 (31.16)	1,930 (28.84)	1,074 (29.30)	1,285 (36.60)
Hospitalization, E (%)†	3,163 (25.41)	1,465 (21.89)	851 (23.22)	1,172 (33.38)
Mechanical ventilation (intubation or ventilation), E (%)†	827 (6.64)	387 (5.78)	226 (6.17)	300 (8.54)

E, number of outcome events (first event only); N, total number of individuals; %, proportion of individuals with the outcome. *During the observation period. †Within 14 days after a positive SARS-CoV-2 test.

Obésité ou diabète associé au pronostic?

Risque de décès ou intubation à J7:

Patient characteristics	Model 'prior to admission': fully adjusted		Model 'prior to admission': stepwise selection with age and sex forced	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Age (+1 SD)	1.05 (0.90, 1.21)	0.5495	1.06 (0.92, 1.22)	0.4448
Sex (female/male)	0.76 (0.57, 1.03)	0.0777	0.75 (0.56, 1.01)	0.0559
BMI (+1 SD)	1.24 (1.06, 1.44)	0.0064	1.28 (1.10, 1.47)	0.0010
Treated OSA	1.15 (0.76, 1.73)	0.5036	–	–
ARBs and/or ACE inhibitors and/or MRAs	1.15 (0.86, 1.54)	0.3493	–	–

Obésité ou diabète associé au pronostic?

Diabetes and Overweight/Obesity
Are Independent, Nonadditive
Risk Factors for In-Hospital
Severity of COVID-19: An
International, Multicenter
Retrospective Meta-analysis

https://doi.org/10.2337/dc20-2676

Diabetes and COVID-19–Related Mortality in Women and Men in the UK Biobank: Comparisons With Influenza/ Pneumonia and Coronary Heart Disease

Marit de Jong,[1] Mark Woodward,[2,3,4] and Sanne A.E. Peters[1,2,3]

Impact du diabète sur le pronostic des infections et mal CV

	Death from COVID-19			Death from influenza/pneumonia			Death from CHD		
	Women	Men	RHR	Women	Men	RHR	Women	Men	RHR
Previously diagnosed diabetes vs. not	1.52 (0.82; 2.82)	1.73 (1.19; 2.52)	0.88 (0.43; 1.81)	2.06 (1.30; 3.28)	1.80 (1.32; 2.44)	1.15 (0.66; 2.00)	3.17 (2.51; 3.99)	1.93 (1.73; 2.15)	1.64 (1.27; 2.12)
Diabetes status									
No diabetes	1.00 (0.77; 1.30)	1.00 (0.82; 1.22)	1.00 (0.72; 1.39)	1.00 (0.79; 1.26)	1.00 (0.84; 1.19)	1.00 (0.75; 1.34)	1.00 (0.87; 1.15)	1.00 (0.94; 1.07)	1.00 (0.86; 1.16)
Prediabetes	0.93 (0.64; 1.35)	0.94 (0.67; 1.31)	0.99 (0.60; 1.63)	1.15 (0.85; 1.57)	1.11 (0.85; 1.45)	1.04 (0.69; 1.57)	1.55 (1.32; 1.82)	1.26 (1.15; 1.37)	1.23 (1.03; 1.48)
Undiagnosed diabetes	1.27 (0.32; 5.08)	3.51 (1.82; 6.78)	0.36 (0.08; 1.68)	0.73 (0.10; 5.15)	1.71 (0.71; 4.12)	0.42 (0.05; 3.64)	1.68 (0.80; 3.53)	2.17 (1.69; 2.80)	0.77 (0.35; 1.70)
Previously diagnosed diabetes	1.51 (0.85; 2.69)	1.80 (1.29; 2.52)	0.84 (0.43; 1.64)	2.17 (1.42; 3.31)	1.89 (1.44; 2.47)	1.15 (0.69; 1.89)	3.76 (3.07; 4.61)	2.12 (1.93; 2.33)	1.78 (1.42; 2.22)
HbA_{1c} levels									
No previously diagnosed diabetes	1.00 (0.45; 2.21)	1.00 (0.62; 1.61)	1.00 (0.39; 2.53)	1.00 (0.49; 2.05)	1.00 (0.66; 1.51)	1.00 (0.44; 2.30)	1.00 (0.75; 1.33)	1.00 (0.87; 1.15)	1.00 (0.73; 1.38)
≤6.5%	0.82 (0.28; 2.39)	1.38 (0.85; 2.23)	0.60 (0.18; 1.92)	1.01 (0.52; 1.96)	1.27 (0.86; 1.87)	0.80 (0.37; 1.71)	2.18 (1.62; 2.94)	1.48 (1.29; 1.69)	1.48 (1.06; 2.05)
>6.5% to ≤7.5%	1.10 (0.35; 3.45)	1.69 (0.93; 3.07)	0.65 (0.18; 2.36)	1.42 (0.77; 2.62)	1.26 (0.78; 2.03)	1.13 (0.52; 2.46)	2.18 (1.53; 3.10)	1.62 (1.38; 1.89)	1.35 (0.92; 1.99)
>7.5%	2.67 (0.98; 7.22)	2.25 (1.20; 4.24)	1.18 (0.36; 3.85)	0.94 (0.43; 2.07)	1.69 (1.04; 2.74)	0.56 (0.22; 1.40)	3.70 (2.65; 5.15)	2.08 (1.77; 2.45)	1.77 (1.22; 2.57)
Per 1% HbA_{1c} change	1.04 (0.76; 1.42)	1.10 (0.98; 1.22)	0.95 (0.68; 1.32)	1.06 (0.83; 1.35)	1.09 (1.00; 1.19)	0.97 (0.75; 1.25)	1.21 (1.14; 1.29)	1.12 (1.09; 1.14)	1.09 (1.02; 1.16)

« La 5ème vague.. »??
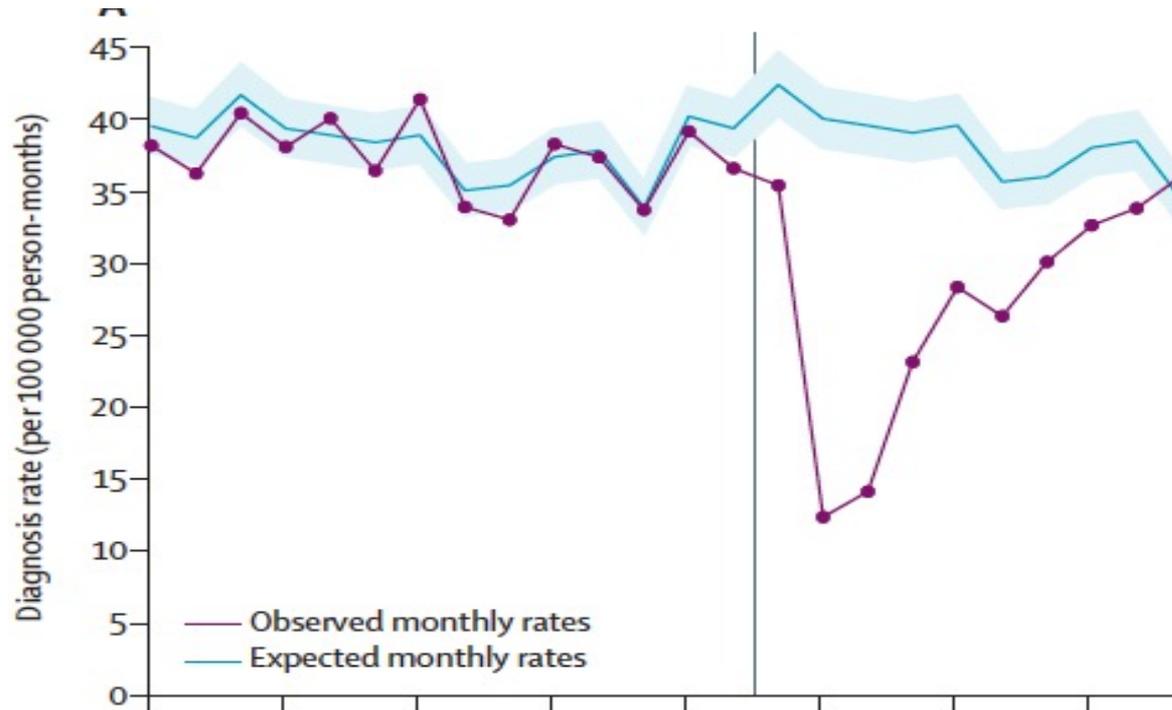
En conclusion, diabète et Covid

- Diabète associé à la sévérité du Covid/obésité

- Type 1 et type 2

- Identification d'un phénotype associé au pronostic dans le type 2

- Impact de l'hyperglycémie chronique…

- Message pour le diabétologue: Risque infectieux dans le diabète!!