

# **Place des recommandations dans l'optimisation de la prise en charge du patient diabétique algérien**

M.Belhadj

Médecine interne-diabétologie

E.H.U. Oran

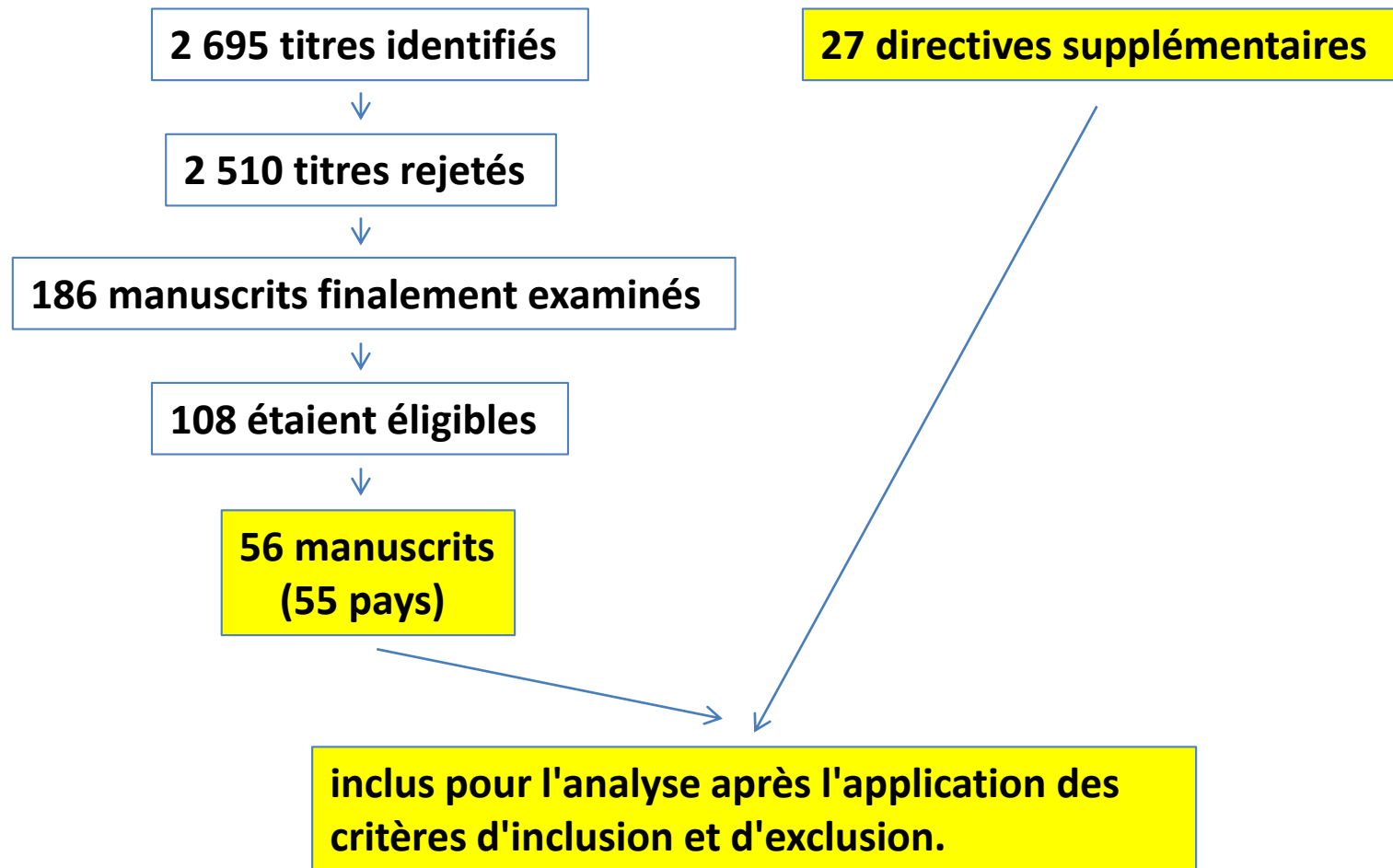


# Gaps in Guidelines for the Management of Diabetes in Low- and Middle-Income Versus High-Income Countries—A Systematic Review

*Diabetes Care* 2018;41:1097–1105 | <https://doi.org/10.2337/dc17-1795>

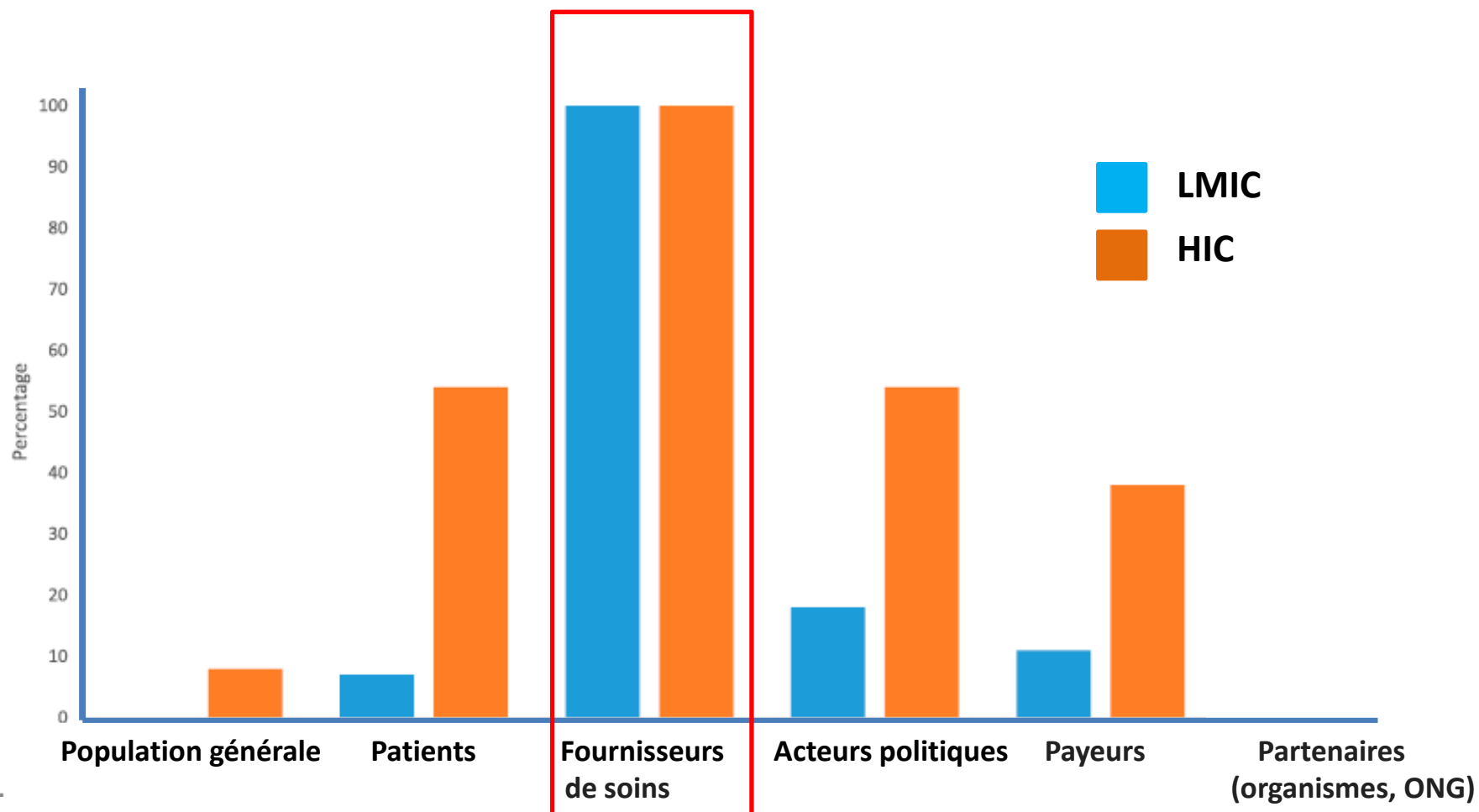
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# Revue systématique (2006-2016)

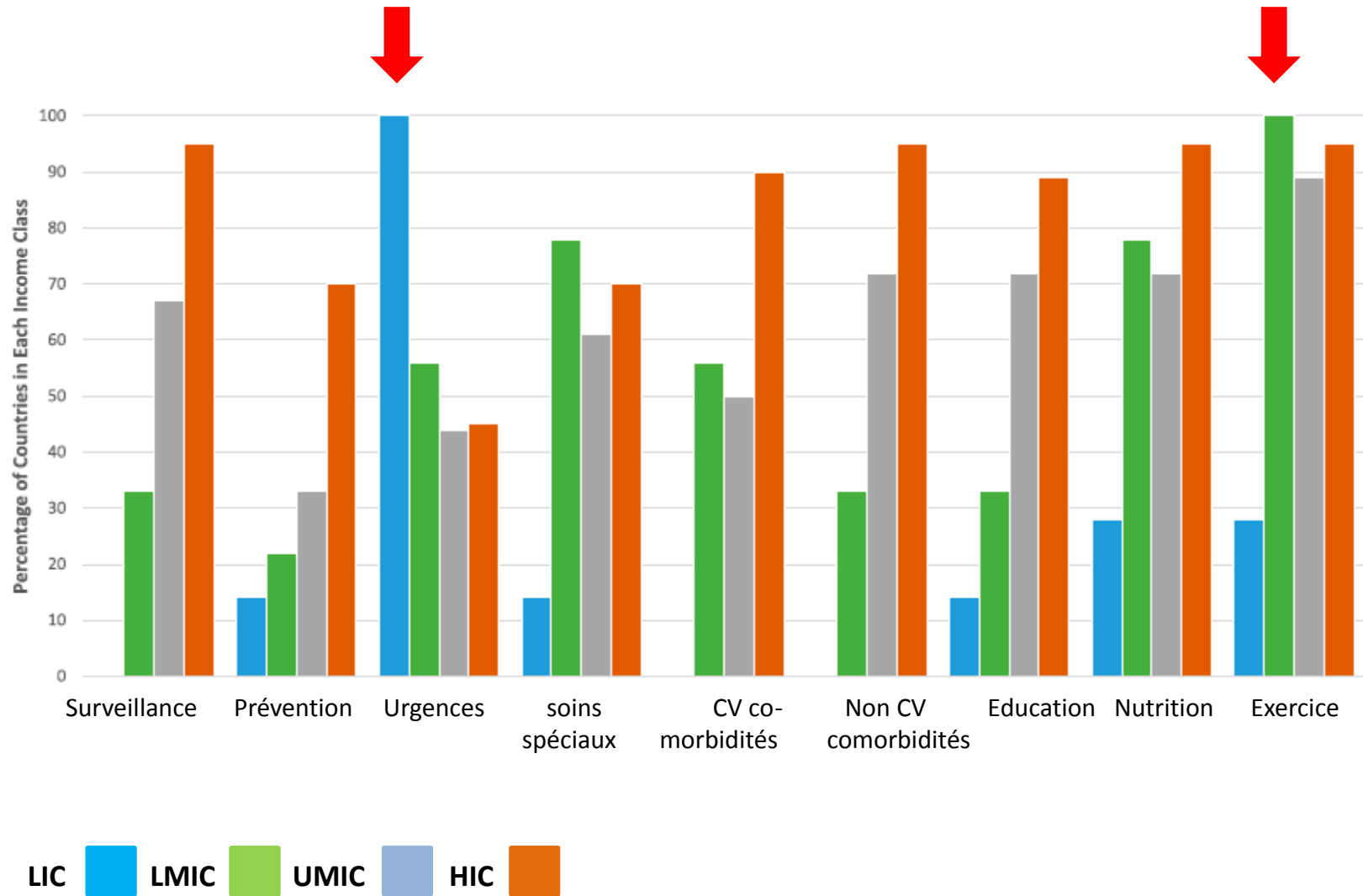


OMS → 126 pays ont un guideline national.

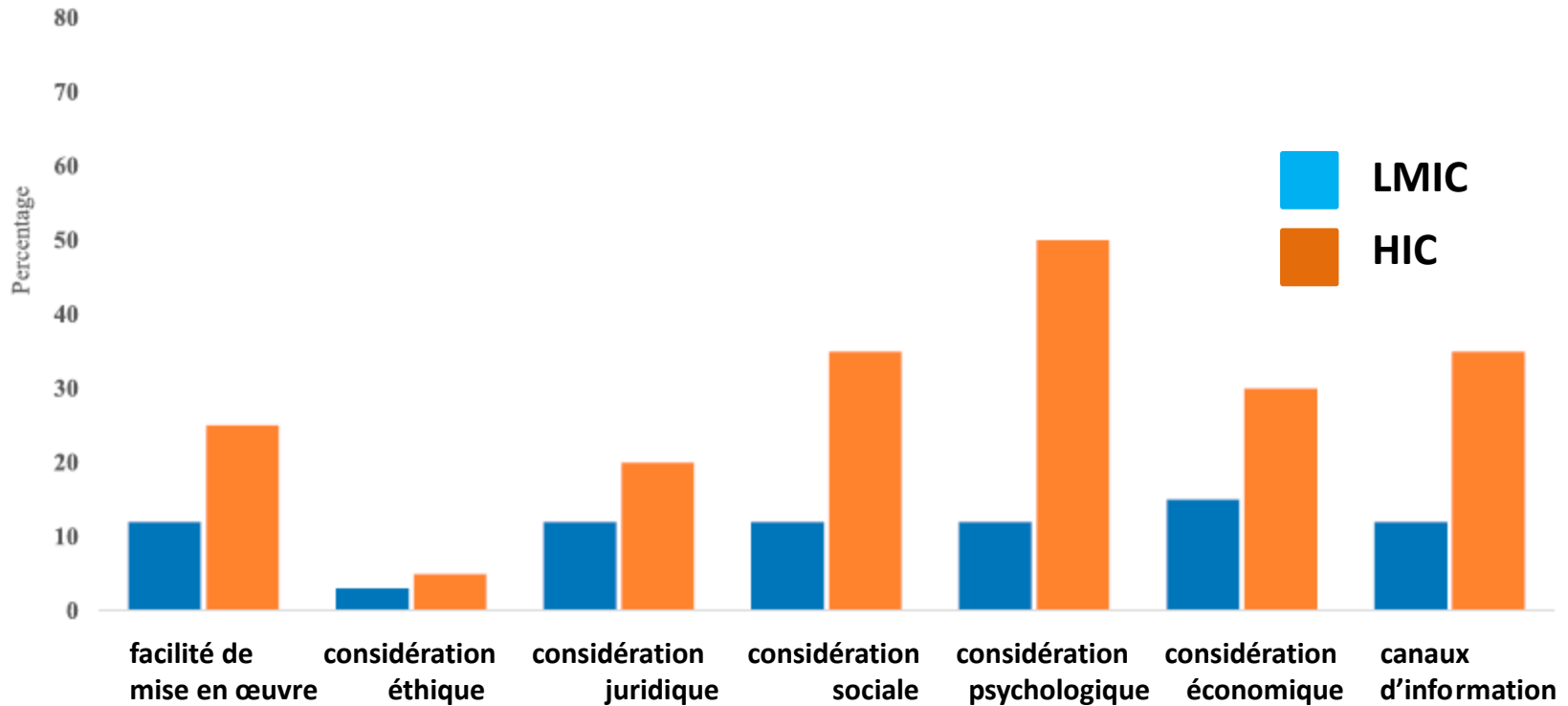
# Répartition du public cible indiqué dans les guidelines



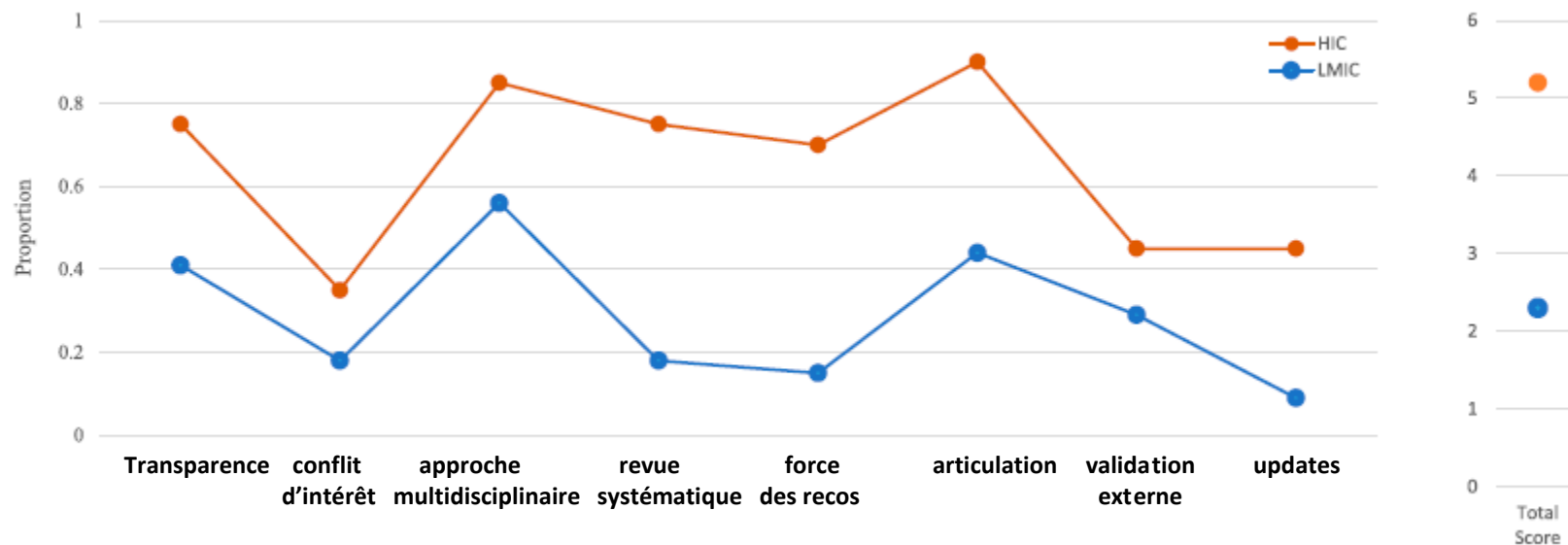
# Spectre des soins du diabète



# Aspects non médicaux abordés dans les guidelines



# Profil des autres scores



**HIC** **LMIC**

INTERNATIONAL DIABETES FEDERATION, 2012  
Clinical Guidelines Task Force

# Global Guideline for Type 2 Diabetes

**DIABETES  
CANADA**



Société  
francophone  
du  
diabète



**NICE** National Institute for  
Health and Care Excellence

**Objectif HbA1c 6,5%  
plus rigoureux**

**Objectif HbA1c 8%  
moins rigoureux**

Motivation du patient

très motivé

peu motivé

Risque d'hypoglycémie  
et autres effets indésirables

bas

élevé

Durée du diabète

diagnostic récent

ancien

Espérance de vie

élevée

courte

Comorbidités

absentes

sévères

Complications CV

absentes

sévères

Ressources

disponibles

limitées

1

At diagnosis, initiate lifestyle management, set A1C target, and initiate pharmacologic therapy based on A1C:

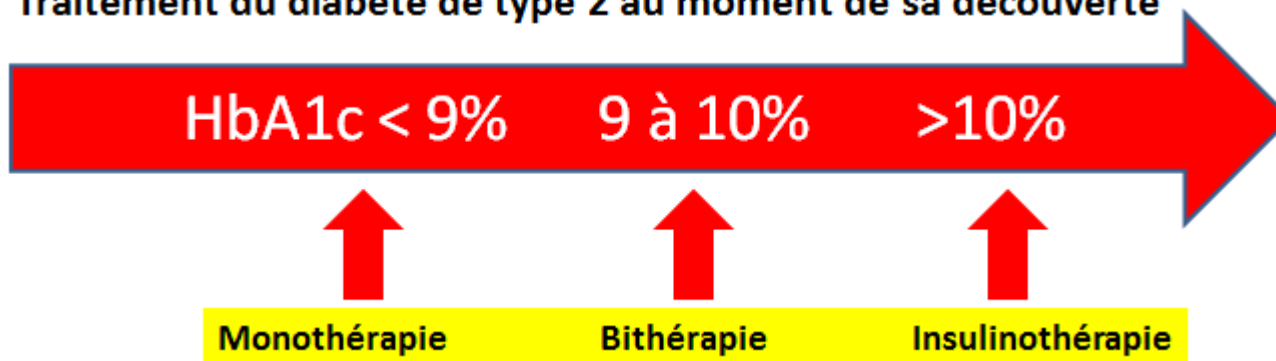
- A1C is less than 9%, consider **Monotherapy**.
- A1C is greater than or equal to 9%, consider **Dual Therapy**.
- A1C is greater than or equal to 10%, blood glucose is greater than or equal to 300 mg/dL, or patient is markedly symptomatic, consider **Combination Injectable Therapy** (See Figure 8.2).

**Monotherapy** Lifestyle Management + Metformin

Initiate metformin therapy if no contraindications\* (See Table 8.1)

<b>A1C at target after 3 months of monotherapy?</b>	<b>Yes:</b>	- Monitor A1C every 3–6 months
	<b>No:</b>	- Assess medication-taking behavior - Consider Dual Therapy

Traitement du diabète de type 2 au moment de sa découverte



At diagnosis, initiate lifestyle management, set A1C target, and initiate pharmacologic therapy based on A1C:

A1C is less than 9%, **consider Monotherapy.**

A1C is greater than or equal to 9%, **consider Dual Therapy.**

A1C is greater than or equal to 10%, blood glucose is greater than or equal to 300 mg/dL, or patient is markedly symptomatic, **consider Combination Injectable Therapy** (See Figure 8.2).

1

**Monotherapy** Lifestyle Management + Metformin

Initiate metformin therapy if no contraindications<sup>a</sup> (See Table 8.1)

A1C at target after 3 months of monotherapy? **Yes:** - Monitor A1C every 3–6 months  
**No:** - Assess medication-taking behavior  
 - Consider Dual Therapy

2

**Dual Therapy** Lifestyle Management + Metformin + Additional Agent

ASCVD? **Yes:** - Add agent proven to reduce major adverse cardiovascular events and/or cardiovascular mortality (see recommendations with <sup>b</sup> on p. 575 and Table 8.1)  
**No:** - Add second agent after consideration of drug-specific effects and patient factors (See Table 8.1)

**GLP1-RA, iSGLT2**

A1C at target after 3 months of dual therapy? **Yes:** - Monitor A1C every 3–6 months  
**No:** - Assess medication-taking behavior  
 - Consider Triple Therapy

3

**Triple Therapy** Lifestyle Management + Metformin + Two Additional Agents

Add third agent based on drug-specific effects and patient factors<sup>b</sup> (See Table 8.1)

A1C at target after 3 months of triple therapy? **Yes:** - Monitor A1C every 3–6 months  
**No:** - Assess medication-taking behavior  
 - Consider Combination Injectable Therapy (See Figure 8.2)

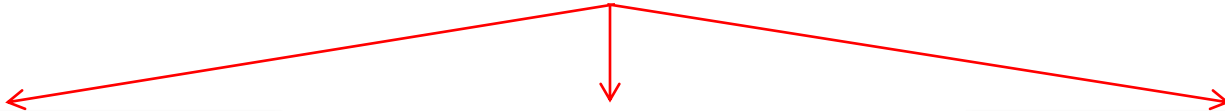
**GLP1-RA, iSGLT2**

**Combination Injectable Therapy** (See Figure 8.2)

**Insuline basale  
+ metformine + ADO**



**Si HbA1c non contrôlée**



**+ insuline rapide  
au repas le plus  
hyperglycémiant**

**+ GLP1-RA**

**Passez à 2 premix  
avant petit déjeuner  
et diner**

**Si HbA1c non contrôlée**

**Si objectif non  
atteint changer de  
schéma**

**Si HbA1c non contrôlée**

**+ 2 rapide  
→ basal-bolus**

**Si objectif non  
atteint changer de  
schéma**

**3 premix  
matin, midi et soir**



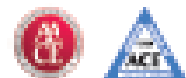


## AAACE/ACE Consensus Statement

# **CONSENSUS STATEMENT BY THE AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS AND AMERICAN COLLEGE OF ENDOCRINOLOGY ON THE COMPREHENSIVE TYPE 2 DIABETES MANAGEMENT ALGORITHM – *2018 EXECUTIVE SUMMARY***

**ENDOCRINE PRACTICE Vol 24 No. 1 January 2018. 91**

# Glycemic Control Algorithm



## INDIVIDUALIZE GOALS

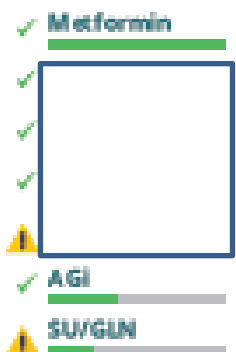
**A1C ≤ 6.5%** For patients without concurrent serious illness and at low hypoglycemic risk

**A1C > 6.5%** For patients with concurrent serious illness and at risk for hypoglycemia

## LIFESTYLE THERAPY (Including Medically Assisted Weight Loss)

A1c < 7,5%

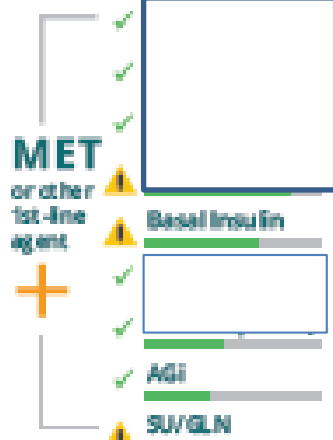
### monothérapie



If not at goal in 3 months proceed to Dual Therapy

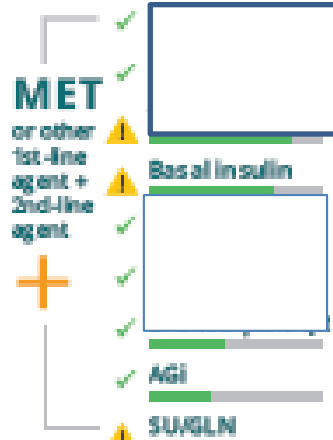
A1c > 7,5%

### bithérapie



If not at goal in 3 months proceed to Triple Therapy

### trithérapie



If not at goal in 3 months proceed to or intensify insulin therapy

A1c > 9%

### SYMPTOMS

NO YES

Dual therapy  
OR

Insulin ± other agents

Triple therapy

### ADD OR INTENSIFY INSULIN

Refer to Insulin Algorithm

### LEGEND

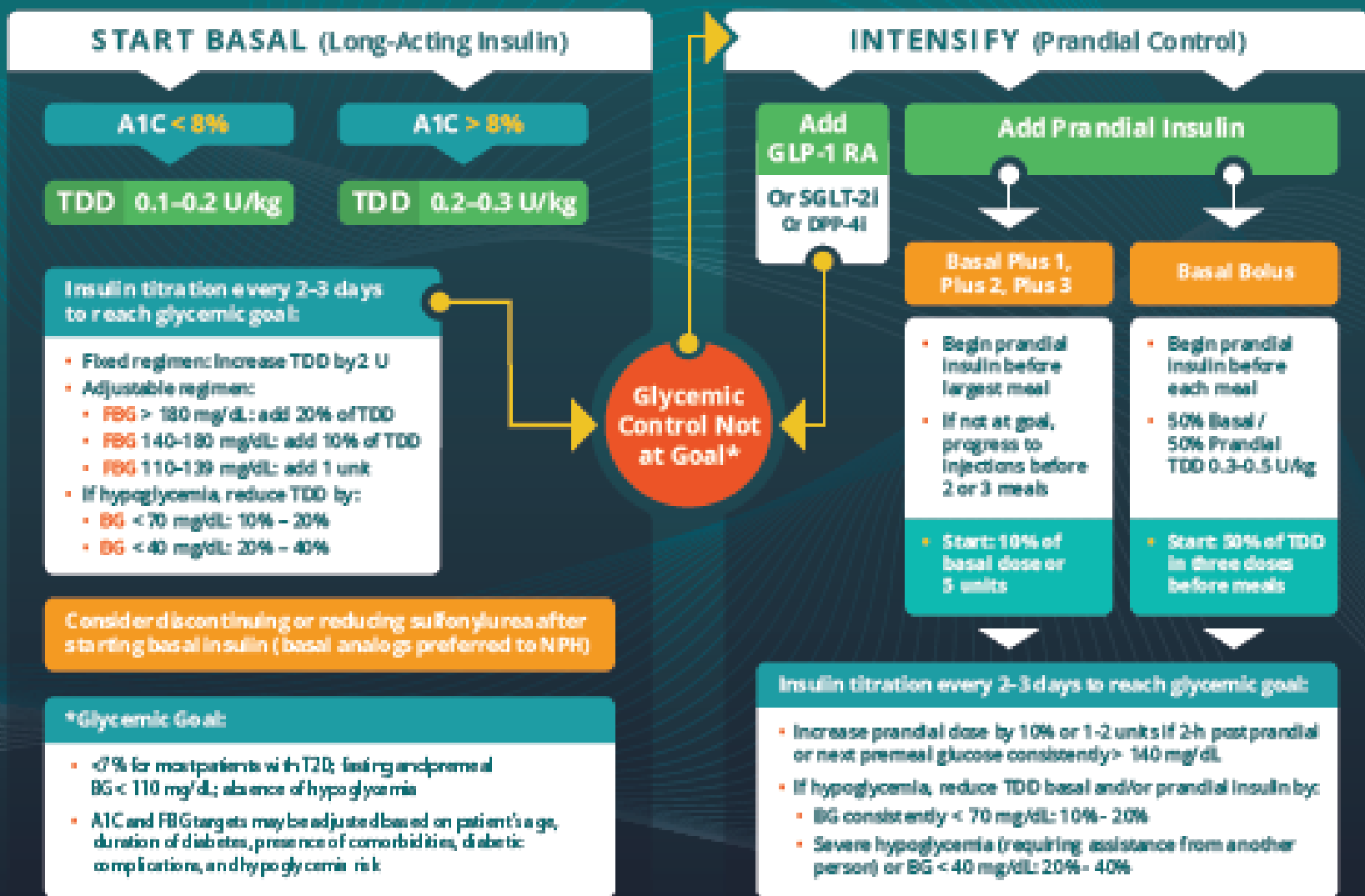
✓ Few adverse events and/or possible benefits

⚠ Use with caution

\* Order of medications represents a suggested hierarchy of usage; length of fill near effects strength of recommendation

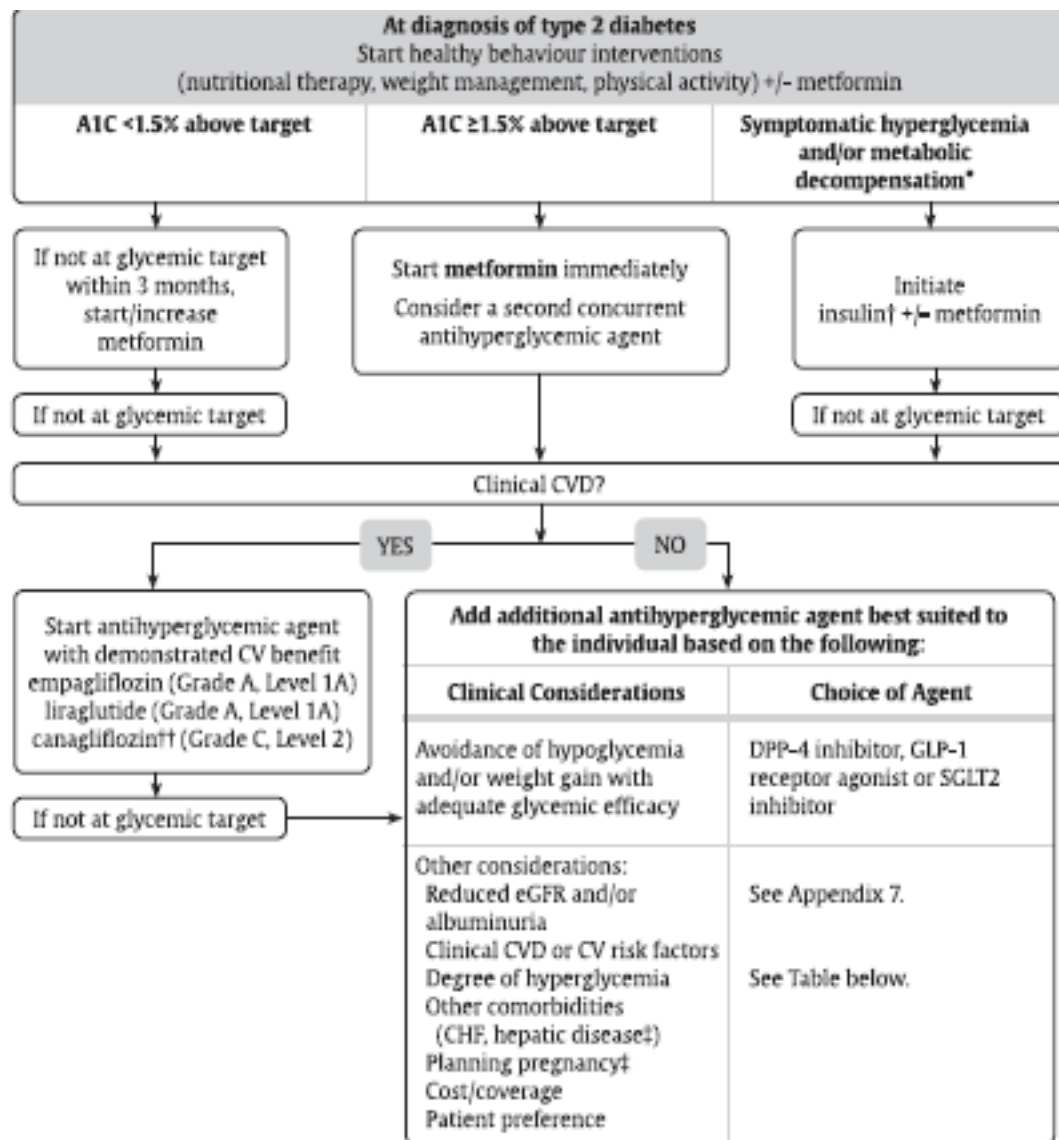
## PROGRESSION OF DISEASE

# Algorithm for Adding/Intensifying Insulin



## 2018 Clinical Practice Guidelines

HEALTHY BEHAVIOUR INTERVENTIONS





oui

non

- Empaglifozin
- Liraglutide
- Canaglifozin

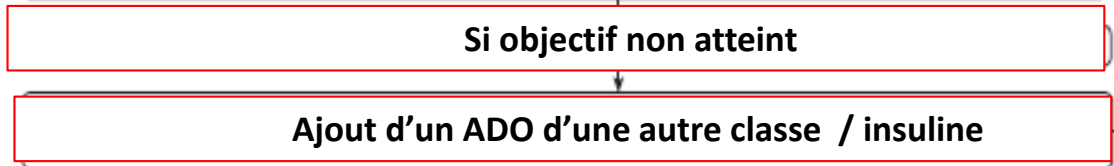
**+ ADO en fonction du profil du malade**

Considérations cliniques	Choix du médicament
Hypo. /poids/	<b>iDPP4, Analogue GLP1</b> <b>iSGLT2</b>

**Add additional antihyperglycemic agent best suited to the individual by prioritizing patient characteristics** (Classes listed in alphabetical order)

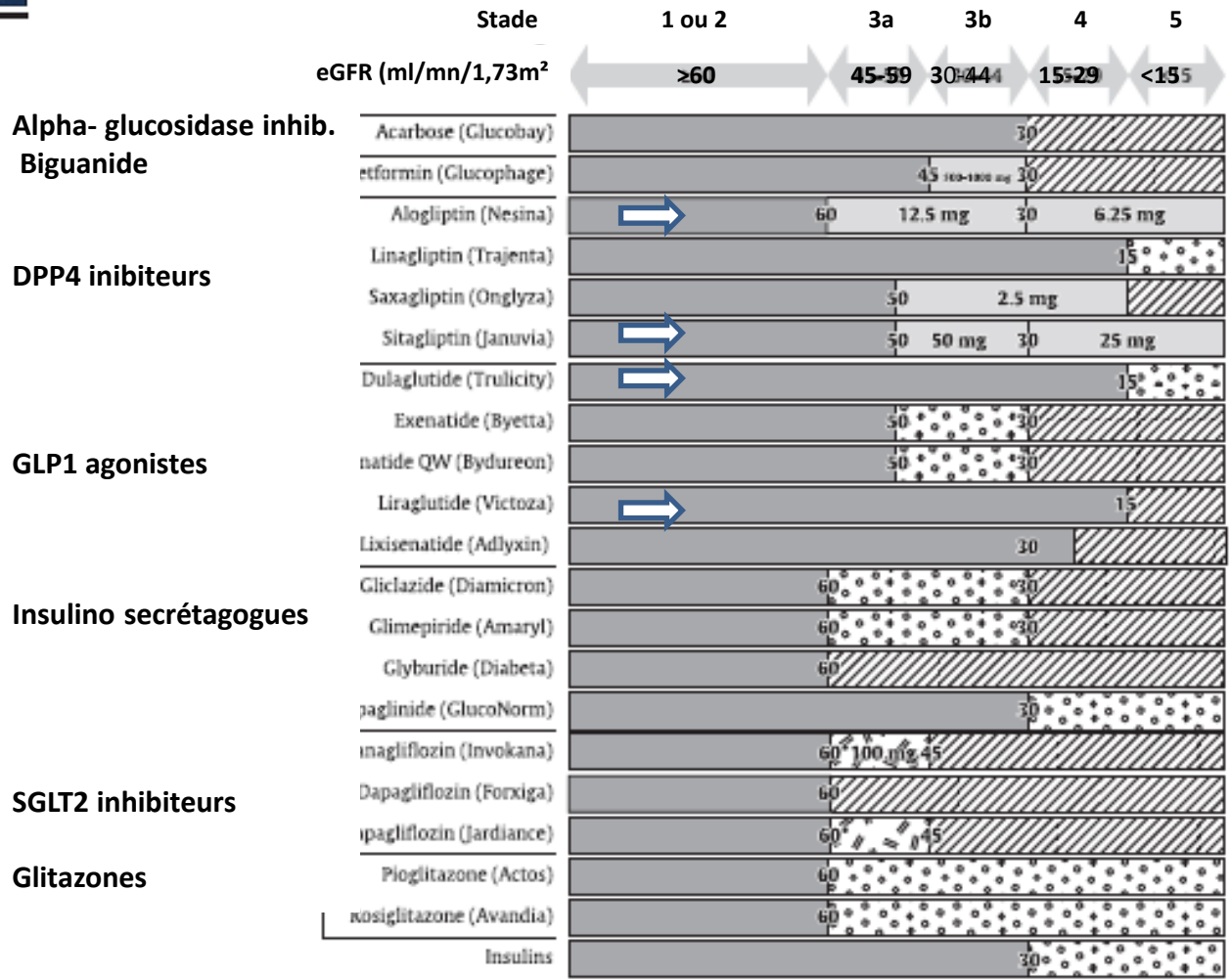
Class*	Effect on CVD outcomes	Hypo-glycemia	Weight	Relative A1C lowering when added to metformin	Other therapeutic considerations	Cost
<b>insuline</b>	glar: Neutral degludec: noninferior to glar	Yes	↑↑	↓↓ to ↑↑↑	No dose ceiling, flexible regimens Requires subcutaneous injection	\$- \$\$\$\$
<b>IAG</b>		Rare	Neutral	↓	GI side-effects common Requires 3 times daily dosing	\$\$
<b>Glinides</b>		Yes	↑	↓↓	More rapid BG-lowering response Reduced postprandial glycemia with meglitinides but usually requires 3 to 4 times daily dosing	\$\$
<b>SU</b>		Yes	↑	↓↓	Gliclazide and glimepiride associated with less hypoglycemia than glyburide Poor durability	\$

*alo*, alogliptin; *can*, canagliflozin; *emp*, empagliflozin; *glar*, glargine; *lir*, liraglutide; *ex* *LAR*, exenatide long-acting release; *lix*, lixisenatide; *sax*, saxagliptin; *sit*, sitagliptin.



\* Listed by CV outcome data

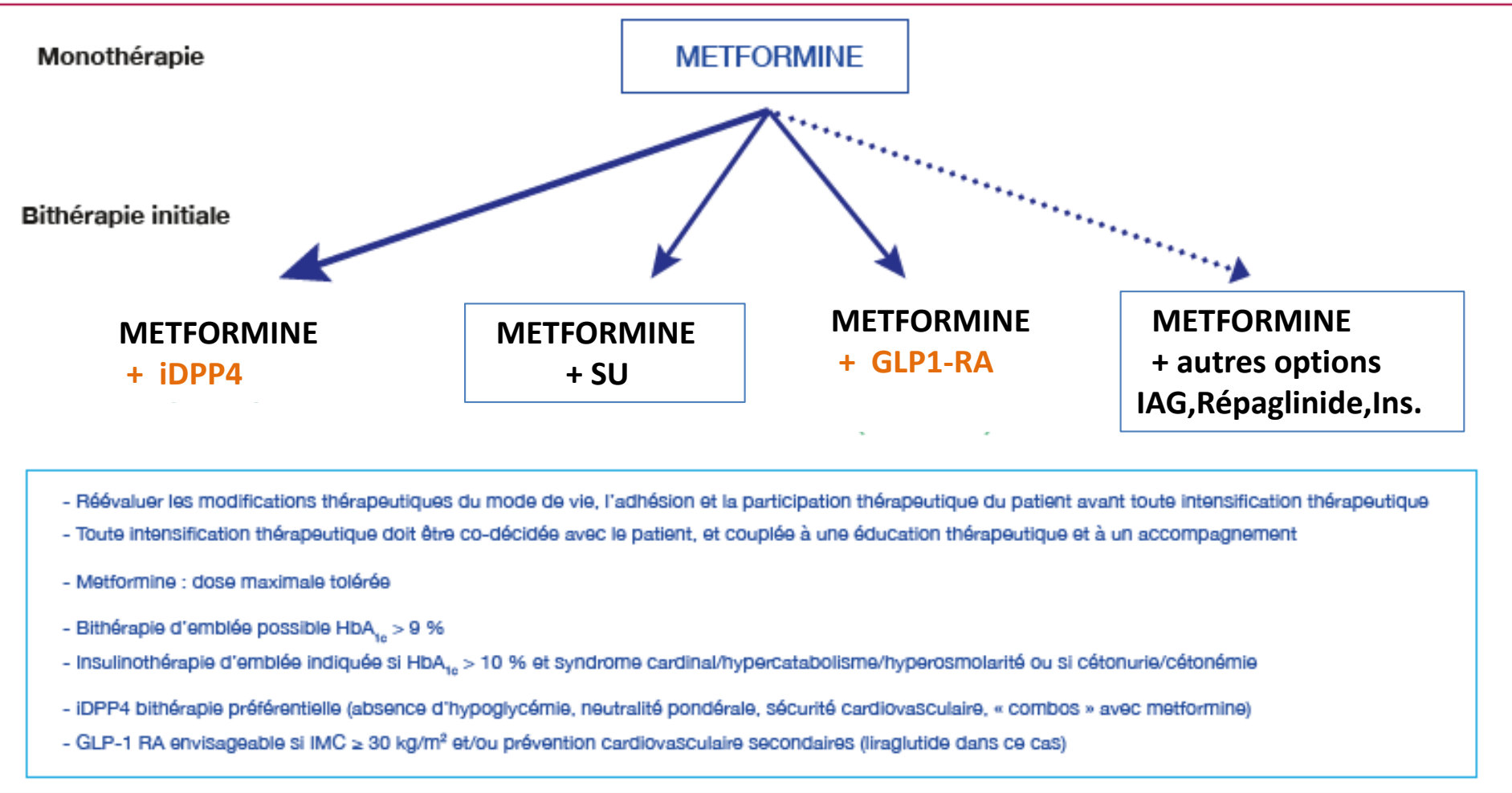
# Hypoglycémiants et fonction rénale



use alternative agent   
  dose adjustment required   
  caution  
 do not initiate   
  dose adjustment not required

\*May be considered when indicated for CV and renal protection with eGFR <60 but >30 mL/min/1.73m<sup>2</sup>

CKD, chronic kidney disease; CV, cardiovascular; GFR, glomerular filtration rate; TZD, thiazolidinedione.



**Figure 1.** Stratégie thérapeutique si  $HbA_{1c} >$  objectif personnalisé malgré modifications thérapeutiques du mode de vie et monothérapie par metformine à dose maximale tolérée bien observée.

Monothérapie

METFORMINE

Bithérapie initiale

METFORMINE  
+ i DPP4

METFORMINE  
+ SU

METFORMINE  
+ analog. GLP1

METFORMINE  
+ autres options  
(IAG, répaglinide, insuline)

METFORMINE  
GLP1-RA  
+/- SU

METFORMINE  
GLP1-RA  
+/- SU

METFORMINE  
Insuline basale  
+/- iDPP4 ou SU

OU

OU

OU

METFORMINE  
+ iDPP4  
+ SU

METFORMINE  
+ iDPP4  
+ SU

METFORMINE  
GLP1-RA  
+/- SU

OU

OU

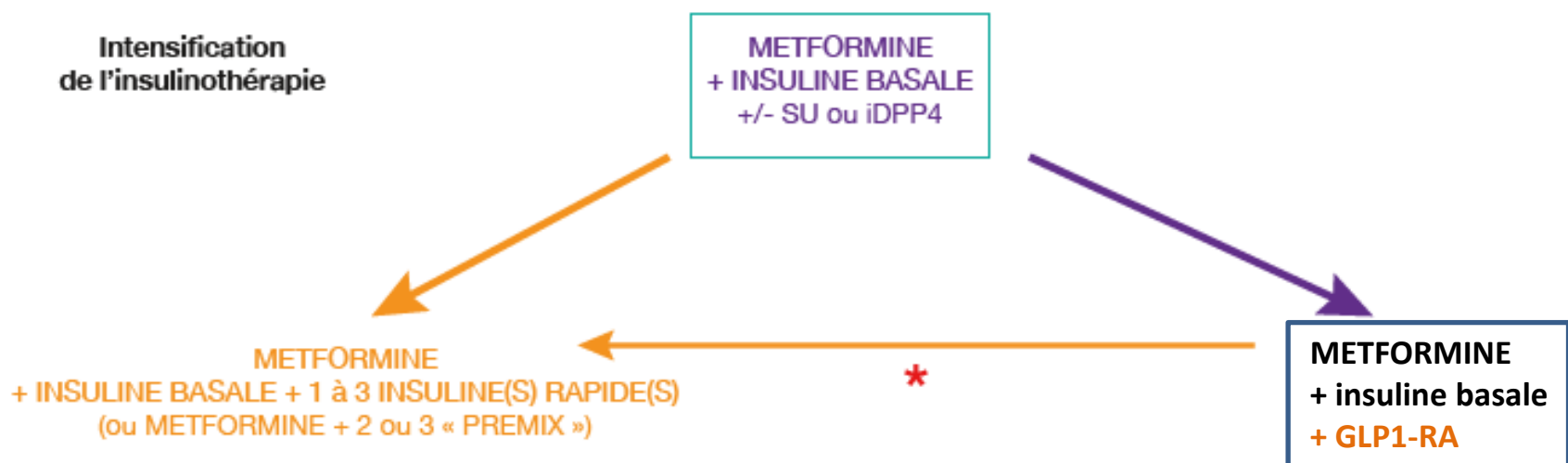
OU

METFORMINE  
Insuline basale  
+/- iDPP4 ou SU

METFORMINE  
Insuline basale  
+/- iDPP4 ou SU

METFORMINE  
GLP1-RA  
Insuline basale

METFORMINE  
+ SU  
Insuline basale

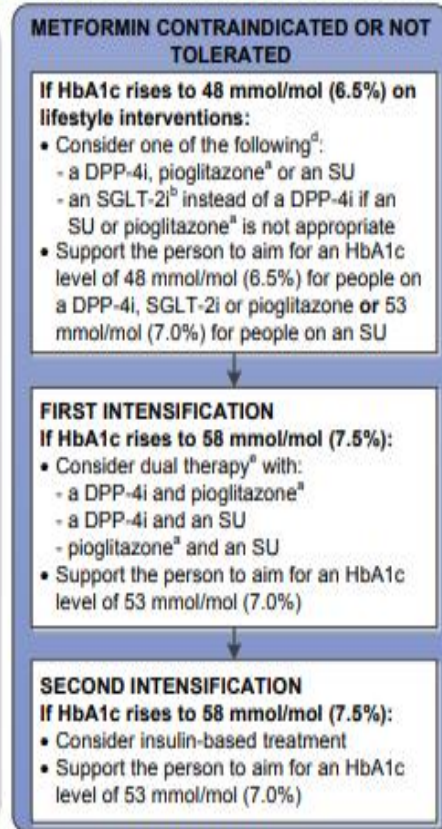
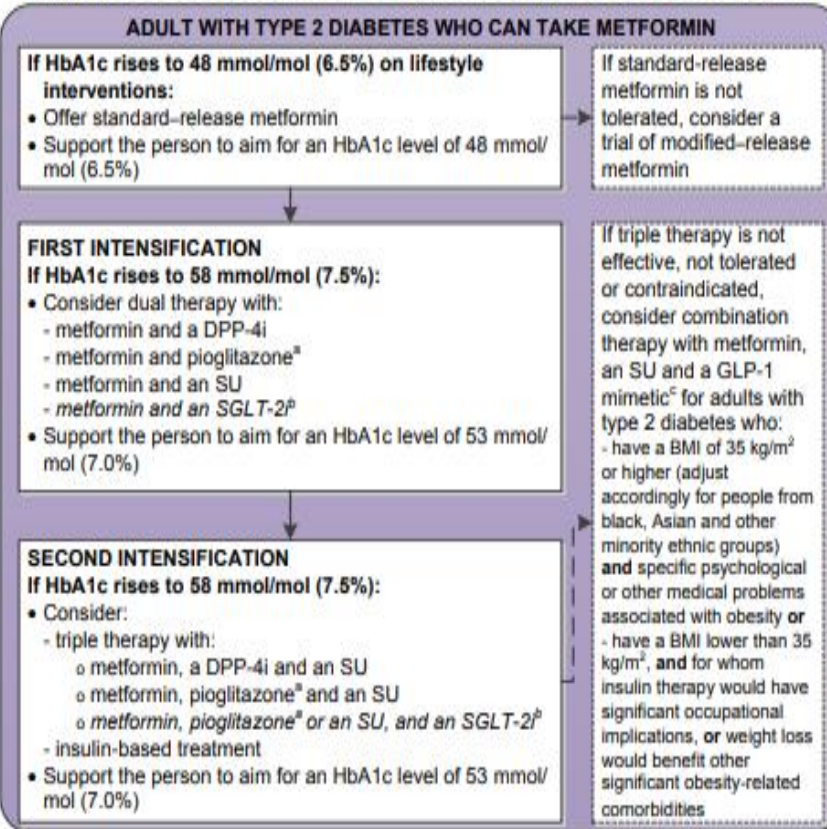


- Réévaluer les modifications thérapeutiques du mode de vie, l'adhésion et la participation thérapeutique du patient avant toute intensification thérapeutique
  - Toute intensification thérapeutique doit être co-décidée avec le patient, et couplée à une éducation thérapeutique et à un accompagnement
  - Préférer un GLP1-RA si IMC  $\geq 30$  kg/m<sup>2</sup> et/ou prévention cardiovasculaire secondaire (liraglutide dans ce dernier cas)
  - Préférer un GLP1-RA chez les patients qui pourraient avoir des réticences ou des difficultés (adaptation des doses par exemple) avec les schémas d'insulinothérapie en multi-injections
- L'association fixe liraglutide + degludec pourra alors être utilisée chez certains patients (remboursement uniquement en relais d'une association libre liraglutide + insuline basale, prescription initiale spécialisée)
- \* Règle d'arrêt GLP-1 RA : baisse d'HbA<sub>1c</sub> < 0,5 % et HbA<sub>1c</sub> > objectif 3 à 6 mois après l'initiation du traitement (à condition que l'adhésion au traitement soit jugée satisfaisante et en l'absence de facteur bien identifié de déséquilibre glycémique)
  - Préférer un schéma d'insulinothérapie intensifiée par multi-injections en cas de signes d'hypercatabolisme

**Figure 5. Stratégie thérapeutique si HbA<sub>1c</sub> > objectif personnalisé malgré modifications thérapeutiques du mode de vie + insuline basale bien titrée bien observée.**

- Reinforce advice on diet, lifestyle and adherence to drug treatment.
- Agree an individualised HbA1c target based on: the person's needs and circumstances including preferences, comorbidities, risks from polypharmacy and tight blood glucose control and ability to achieve longer-term risk-reduction benefits. Where appropriate, support the person to aim for the HbA1c levels in the algorithm. Measure HbA1c levels at 3/6 monthly intervals, as appropriate. If the person achieves an HbA1c target lower than target with no hypoglycaemia, encourage them to maintain it. Be aware that there are other possible reasons for a low HbA1c level.
- Base choice of drug treatment on: effectiveness, safety (see MHRA guidance), tolerability, the person's individual clinical circumstances, preferences and needs, available licensed indications or combinations, and cost (if 2 drugs in the same class are appropriate, choose the option with the lowest acquisition cost).
- Do not routinely offer self-monitoring of blood glucose levels unless the person is on insulin, on oral medication that may increase their risk of hypoglycaemia while driving or operating machinery, is pregnant or planning to become pregnant or if there is evidence of hypoglycaemic episodes.

If the person is symptomatically hyperglycaemic, consider insulin or an SU. Review treatment when blood glucose control has been achieved.



**Insulin-based treatment**

- When starting insulin, use a structured programme and continue metformin for people without contraindications or intolerance. Review the continued need for other blood glucose lowering therapies<sup>f</sup>.
- Offer NPH insulin once or twice daily according to need.
- Consider starting both NPH and short-acting insulin either separately or as pre-mixed (biphasic) human insulin (particularly if HbA1c is 75 mmol/mol (9.0%) or higher).
- Consider, as an alternative to NPH insulin, using insulin detemir or glargine<sup>g</sup> if the person: needs assistance to inject insulin, lifestyle is restricted by recurrent symptomatic hypoglycaemic episodes **or** would otherwise need twice-daily NPH insulin in combination with oral blood glucose lowering drugs.
- Consider pre-mixed (biphasic) preparations that include short-acting insulin analogues, rather than pre-mixed (biphasic) preparations that include short-acting human insulin preparations, if the person prefers injecting insulin immediately before a meal, hypoglycaemia is a problem **or** blood glucose levels rise markedly after meals.
- Only offer a GLP-1 mimetic<sup>c</sup> in combination with insulin with specialist care advice and ongoing support from a consultant-led multidisciplinary team<sup>h</sup>.
- Monitor people on insulin for the need to change the regimen.
- An SGLT-2i in combination with insulin with or without other antidiabetic drugs is an option<sup>i</sup>.

Si HbA1c monte à 6.5% sous MHD  
→ metformin → 6.5%.



Si metformine non tolérée essayer  
modified-release metformine



**FIRST INTENSIFICATION** si HbA1c monte à 7,5%  
- metformin + DPP-4i  
- metformin + pioglitazone  
- metformin + SU  
- metformin + iSGLT-2i b  
→ 7.0%



**SECOND INTENSIFICATION** si HbA1c monte à  
7.5% → triple therapy :  
metformin + DPP-4i + SU  
metformin + pioglitazone + SU  
metformin + pioglitazone + SGLT-2i b  
metformine + SU + SGLT2  
→ insulin- based treatment  
Objectif = 7%



Metformin + SU + **GLP-1 mimetic** si  
BMI  
≥ 35 kg/m<sup>2</sup> (ou BMI ≤ 35 kg/m<sup>2</sup> avec  
Pb insuline)

Si HbA1c monte à 6.5% sous MHD  
→ metformin → 6.5%.



Si metformine non tolérée essayer  
modified-release metformine



**FIRST INTENSIFICATION** si HbA1c monte à 7,5%  
- metformin + DPP-4i  
- metformin + pioglitazone  
- metformin + SU  
- metformin + SGLT-2i b  
→ 7.0%



**SECOND INTENSIFICATION** si HbA1c monte à  
7.5% → triple therapy :  
metformin + DPP-4i + SU  
metformin + pioglitazone + SU  
metformin + pioglitazone + SGLT-2i b  
metformine + SU + SGLT2  
→ insulin- based treatment  
Objectif = 7%



Metformin + SU + GLP-1 mimetic si  
BMI  
≥ 35 kg/m<sup>2</sup> (ou BMI ≤ 35 kg/m<sup>2</sup> avec  
Pb insuline)

# Australian NHMRC, National Evidence Based Guideline for Blood Glycemic Control in T2DM, 2017



# Guideline for Blood Glycemic Control in T2DM

**First line: Metformin is the usual first-line therapy unless contraindicated or not tolerated**

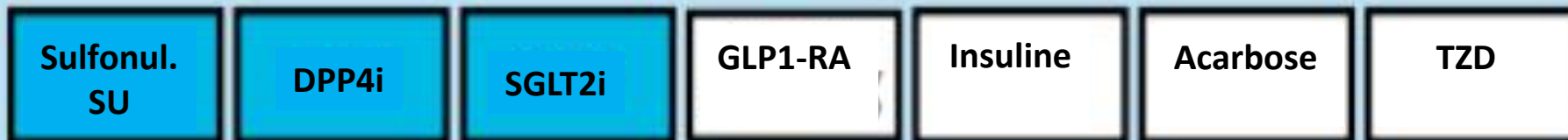


**If glycated haemoglobin (HbA1c) target not achieved in three months:**

- check and review current therapies, stop any that fail to improve glycaemic control
- check patient's understanding and self-management
- review use of therapies
- exclude other comorbidities/therapies impacting on glycaemic control

**Second line: If metformin was not used first line, add it now, if not contraindicated**

SU are the usual initial agent to add to metformin. If SU are contraindicated or not tolerated, another agent may be used



**If HbA1c target not achieved in three months:**

- check and review current therapies, stop any that fail to improve glycaemic control
- check patient understanding and self-management
- review use of therapies
- exclude other comorbidities/therapies impacting on glycaemic control



# Australian NHMRC, National Evidence Based Guideline for Blood Glycemic Control in T2DM, 2017

**Third line : consider triple oral therapy or addition of GLP1-RA or insulin**



**If HbA1c target not achieved in three months:**

- check and review current therapies, stop any that fail to improve glycaemic control
- check patient understanding and self-management
- review use of therapies
- exclude other comorbidities/therapies impacting on glycaemic control

**THEN**

**If on triple oral therapy**

**If on GLP-1RA**

**If on basal insulin**

Switch ≥ oral agent  
GLP1-RA or insulin  
or another oral agent

**OU**


Change to basal  
or premixed  
insulin

Add basal  
or premixed  
insulin


**OU**

Add SGLT2 inhibitor or  
GLP1-RA or basal bolus  
or basal plus insulin




 Recommendations:  
Monotherapy

**Metformine**  
Sinon SU (sauf glibenclamide,  
Glyburide) ou autres ADO


 Recommendations:  
Initial combination therapy

**Si HbA1C + 1 ou 2%**  
**Bithérapie : metformine +**  
**SU //iDPP4 // iSGLT2**

 Recommendations:  
Initial insulin therapy

**Hyperglycémie , décompensation**  
**aigüe → insuline basale**




 Recommendations:  
Dual therapy

**Echec monothérapie → bithérapie**  
**SU//iDPP4//iSGLT2//AGI//GLP1RA**

**Profil patient → choix**



 Recommendations:  
Triple therapy

**Bithérapie → trithérapie**  
**Bithérapie + insuline ou GLP1-RA**  
**ou 3 ADO**

# L'initiation de l'insulinothérapie selon les différentes recommandations

## IDF

Insuline basale en 1 inj/j

Insuline premix en 1 inj/j

Insuline premix en 2 inj/j

## NICE

Insuline NPH en 1 ou 2 inj

Insuline basale en 1 inj/j

Insuline premix en 1 inj/j

Insuline premix en 2 inj/j

## Association Canadienne

Insuline basale en 1 inj/j

Insuline premix en 1 inj/j

Insuline premix en 2 inj/j

Insuline NPH en 1 inj/j

## Guide de Bonnes pratiques Algérie 20015

Insuline basale en 1 inj/j

Insuline premix en 1 inj/j

Insuline premix en 2 inj/j

Insuline NPH en 1 inj/j  
Insuline NPH en 1 inj/j

## Recommandations Australiennes

Insuline basale en 1 inj/j

Insuline premix en 1 inj/j

## ADA

Insuline basale en 1 inj/j

## AACE

Insuline basale en 1 inj/j

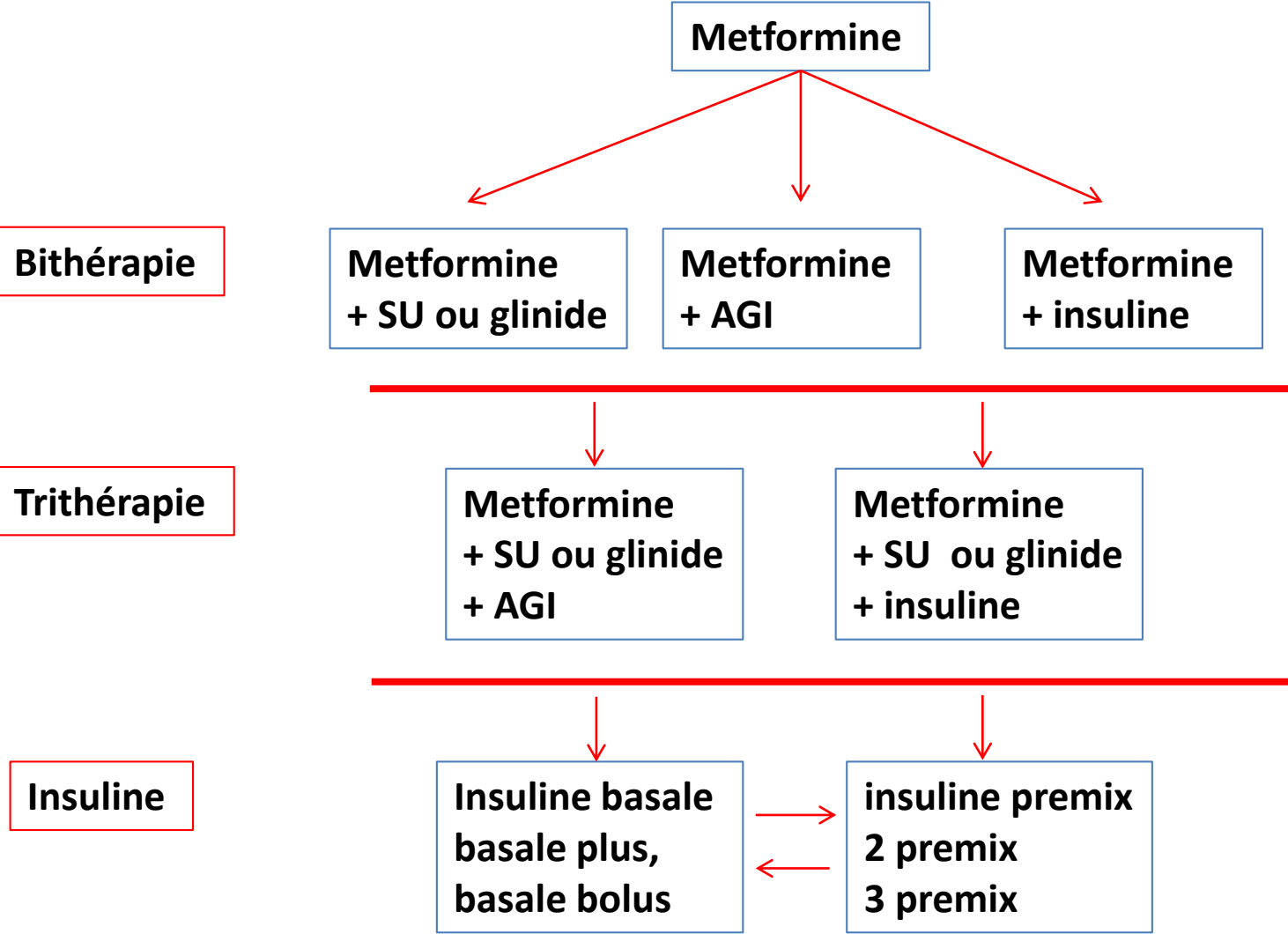
## SFD

Insuline basale en 1 inj/j





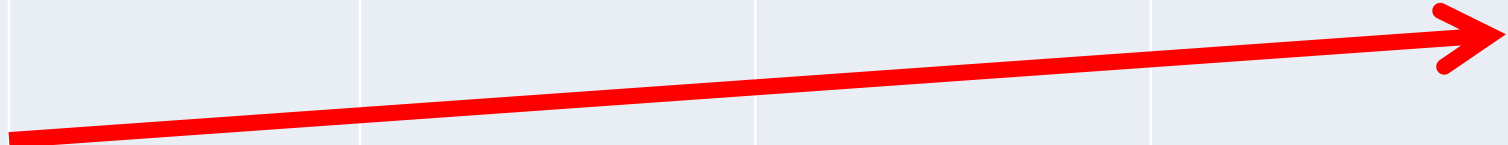
# Intensification de l'insulinothérapie selon les différentes recommandations

	Basale plus	Basale + GLP1-RA	Basale + SGLT2	Basale bolus	2premix	3 premix
A.D.A.	+	+		+	+	+
A.A.C.E.	+	+	+	+		
I.D.F.	+	+	+	+	+	+
NICE	+	+	+	+	+	+
SFD	+	+		+	+	+
Canada	+	+	+	+	+	+
Australie	+	+	+	+	+	+
Algérie	+			+	+	+

# Quelle prise en charge thérapeutique en Algérie avec les hypoglycémiantes existants et remboursés ?

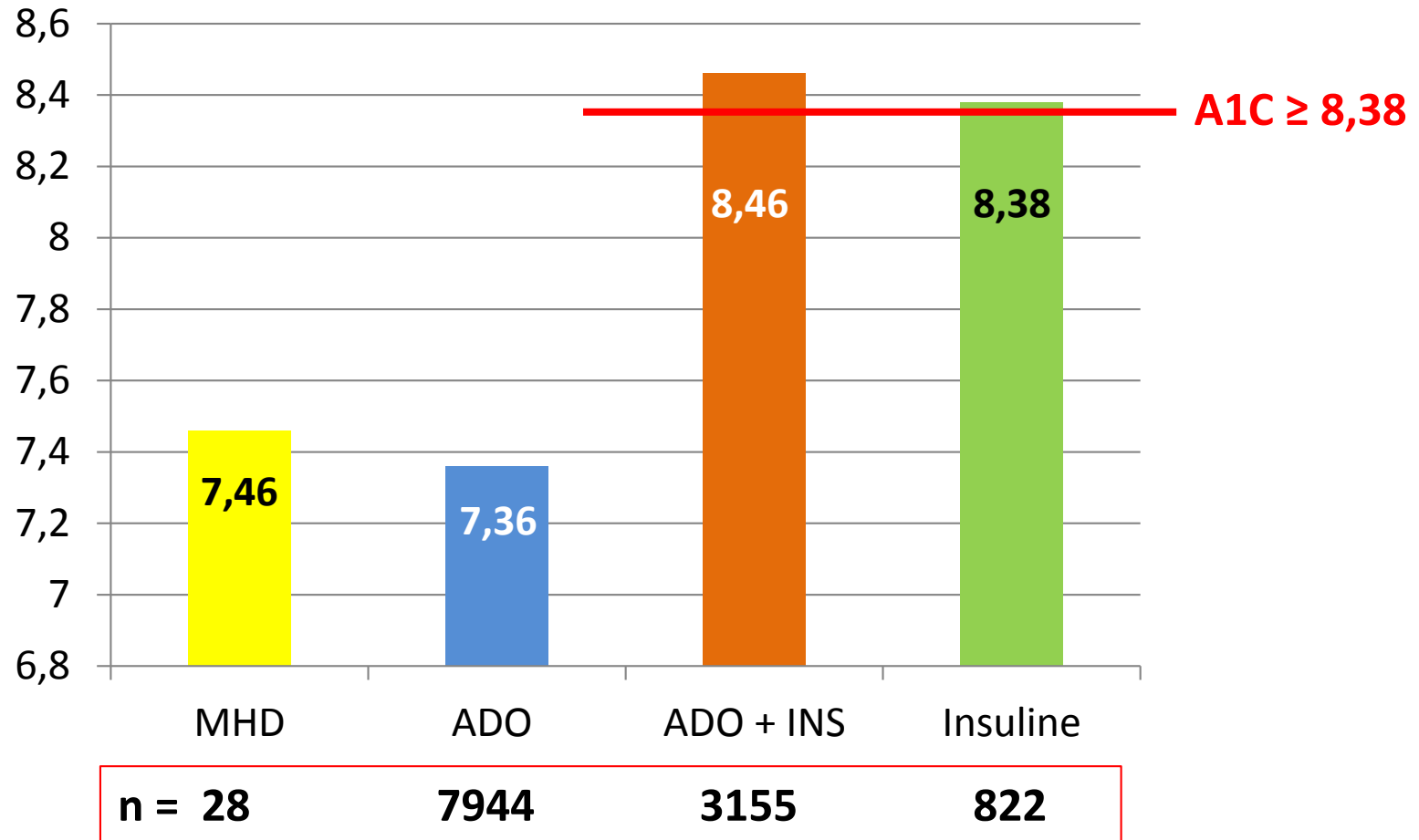


# Baromètre : hypoglycémiant oraux, HbA1c et durée du diabète (patients non insulinés)

	< 5 ans	10-14 ans	15-19 ans	> 20 ans
n	1147	873	698	632
Big. %	97,03	95,87	95,55	96,04
Sulf %	47,42	52,46	56,01	64,71
Autre %	2,70	4,58	4,15	4,27
				
A1c %	7,42 ± 1,67	8,03 ± 1,69	8,18 ± 1,63	8,25 ± 1,63
				

Les limites de l'association metformine + sulfonylurées

# Baromètre. Taux d'HbA1c par schéma thérapeutique



# Clinique mobile : indicateurs de qualité par wilaya

Variable	Batna n=614 A1c%	Bejaia n=996 A1c%	Biskra n=1021 A1c%	Tlemcen n=810 A1c%	Skikda n=1120 A1c%	BBA n=686 A1c%	Relizane n=527 A1c%	Sétif n=979 A1c%
<b>A1c &lt; 7,0%</b>	<b>32,1</b>	<b>40,2</b>	<b>23,7</b>	<b>22,5</b>	<b>28,1</b>	<b>39,8</b>	<b>20,0</b>	<b>35,4</b>
<b>A1c ≥ 9,0%</b>	<b>28,2</b>	<b>20,4</b>	<b>35,4</b>	<b>36,7</b>	<b>32,4</b>	<b>24,1</b>	<b>47,7</b>	<b>41,6</b>
<b>DT2 non insuliné A1c ≥ 9%</b>	<b>42,4</b>	<b>57,2</b>	<b>55,9</b>	<b>46,2</b>	<b>58,4</b>	<b>55,9</b>	<b>62,0</b>	<b>50,6</b>

MHD : mesures hygiéno diététiques

# Taux d'HbA1c par schéma d'insulinothérapie et dose moyenne d'insuline

n = 4352

Schéma insulinique	n	Moyenne de l'HbA1c %	Dose d'insuline (Moyenne ± Ecart type) unités
Basale seule	1675	8,19 ±1,67	22,6 ± 11,4
Premix 1,2,3	1127	8,46 ±1,80	50,1 ± 23,2
Rapide seule	37	8,24 ±1,58	39,7 ± 26,0
Basal + ≥ 1rapide	1325	8,55 ±1,76	68,7 ± 29,9
Premix + rapide	188	8,68 ±1,82	61,8 ± 23,6

# Etude IDEALS

Initiation de l'insuline detemir chez des patients diabétiques de type 2 insulino-naïfs en échec aux antidiabétiques oraux : étude de tolérance d'efficacité en pratique courante en Algérie (Etude IDEALS)

- n = 1974 DT2 sous ADO
- 40,3 % → HbA1c ≤ 7 % en 24 semaines
- dose d'insuline detemir **21,7 U/jour** correspondant à **0,35 U/kg** seulement,
- **titration insuffisante** en pratique courante

# Conclusion

- Niveaux d'intervention (taux HbA1C) différents
- Mesures hygiéno-diététiques
- Metformine unanimité
- Bithérapie → divergences
- Trithérapie suit la logique de la bithérapie
- Initiation insuline : 1 basale ou 1 premix ou 2 premix
- Intensification insuline : basal bolus ou 3 premix

**→ Il est toujours possible d'améliorer nos résultats avec les moyens disponibles.**