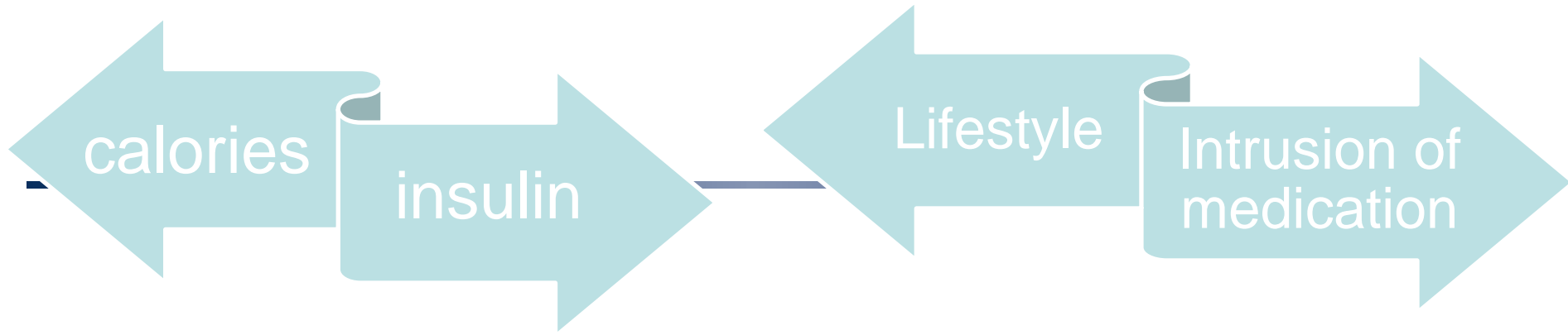
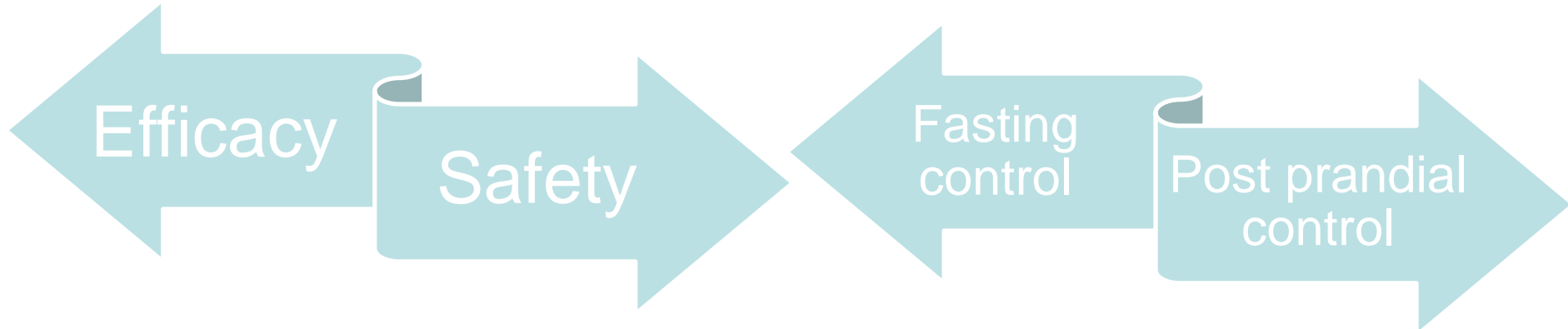


# **Insulin in developing countries**

**Sanjay Kalra**  
**Karnal, India**



finding a balance



## The middle path

---



alalatlan  
အလတ်လမ်း:

## The middle path



Mizzma Padipadar  
မေတ္တဗျာဓိ

အလတ်လမ်းတံဆိပ်: အ: ၆၆၆၁၁  
alalatlan sar phyt thaw

# Insulin: The 5 Ms that Matter

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## Editorial Diabetes

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Table 1: The five 'M's of Insulin therapy

---

1. Match: insulin to patient
2. Motivate: patient to accept insulin
3. Method: of injection technique
4. Monitor: glycemic and other parameters
5. Modify: dose, preparation, and regime as indicated

---

Table 2: Matching insulin to the patient

---

Regime	Basal	Premixed or basal plus	Basal-bolus
Frequency	Once daily	1–3 times daily	4–5 times daily
Glucophenotype	Fasting hyperglycemia	Fasting and postprandial hyperglycemia	Fasting and postprandial hyperglycemia
Risk of hypoglycemia	Low	Low-moderate	High
Ability/willingness to monitor	Low	Low-moderate	High

---

### Table 3: Motivational interviewing—the WATER approach

---

W: welcome with warmth

A: ask and assess complaints, medical status

T: tell the truth, while counselling

E: explain, with empathy, the need for insulin

R: reassure and ensure return

---

Table 4: Insulin technique—seven messages

---

1. Ensure clean injection site and hands
2. Prefer abdomen, upper thighs, and upper arms for injection
3. Prefer 4 mm pen needles, and 6 mm syringe needles
4. Encourage self-inspection of injection sites and screen for lipohypertrophy (LH)  
self insulin site examination (Self IE).
5. Inspect, palpate injection sites at least once a year, more often if LH is detected
6. Do not reuse needles, or share insulin pens, cartridges, and vials
7. Ensure safe disposal of needles and ancillary supplies



---

**Table 5: Monitoring of insulin therapy**

---

**Glucose monitoring**

- Laboratory-based blood glucose
- Self-monitoring blood glucose
- Ambulatory glucose monitoring
- Continuous glucose monitoring system (CGMS)
- Fructosamine
- 1,25-anhydroglucitol
- HbA<sub>1c</sub> (glycosylated hemoglobin)

**Patient-reported outcomes**

- Quality of life
- Treatment satisfaction

---

**Table 6: Modification of insulin**

---

Modification	Indication
Dose titration	<ul style="list-style-type: none"><li>• Mild deviation from glycemic target</li><li>• Newly begun regime</li></ul>
Change of preparation, e.g., <ul style="list-style-type: none"><li>• Human to analogue</li><li>• Long-acting to ultra-long acting</li><li>• Premixed to dual action co-formulation</li><li>• Low dose premix to high mix</li></ul>	<ul style="list-style-type: none"><li>• Mild deviation from glycemic target</li><li>• Patient unwilling to increase dose frequency</li><li>• Glycemic variability</li></ul>
Change of injection frequency, e.g., <ul style="list-style-type: none"><li>• Basal plus 1 to basal plus 2</li></ul>	<ul style="list-style-type: none"><li>• Gross deviation from glycemic target</li><li>• Isolated postprandial hyperglycemia</li></ul>
Change of regime, e.g., <ul style="list-style-type: none"><li>• Basal to basal plus</li><li>• Basal to premixed</li><li>• Premixed to basal plus</li></ul>	<ul style="list-style-type: none"><li>• Gross deviation from glycemic target</li><li>• Postprandial hyperglycemia</li></ul>

# Conversation plan

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- Match the insulin to the patient

# Targets and strategies

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- Define a target
- Plan a strategy
- Pick your tools

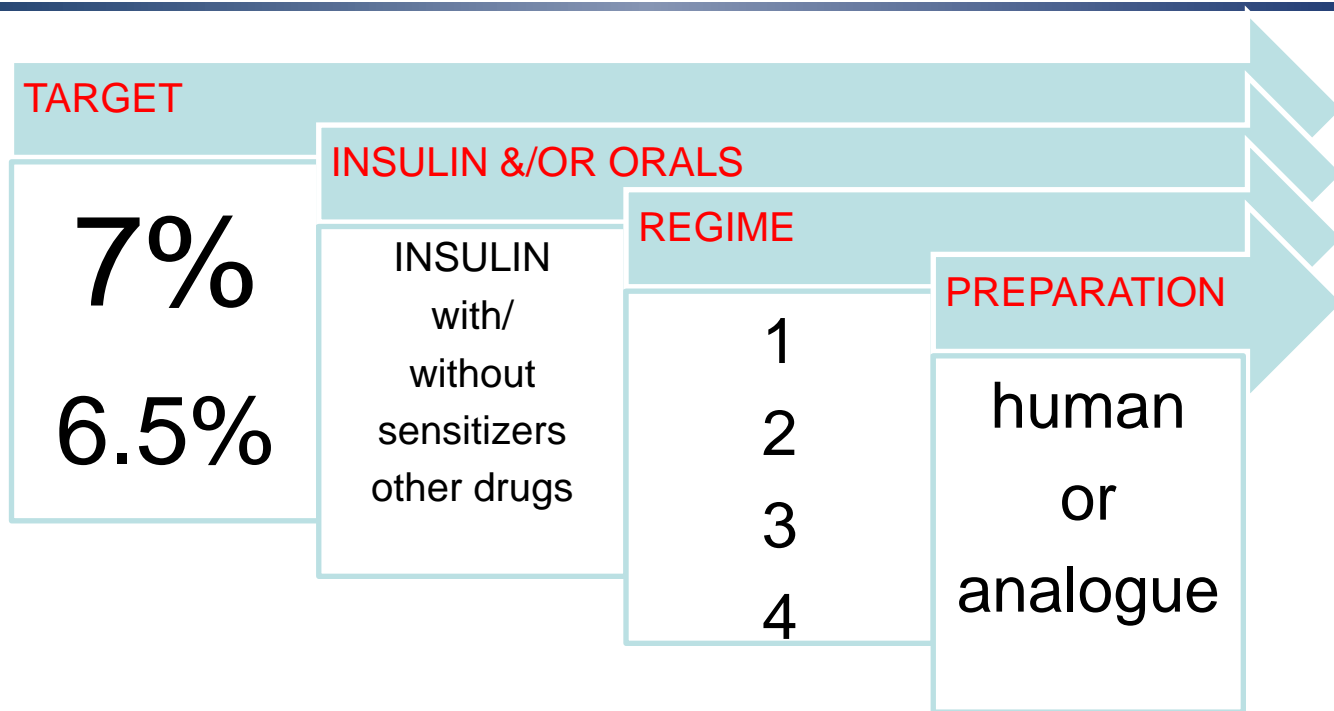
# Master strategist, master nation builder

---



# Targets and strategies

---



## Types of regimes

---

### basal

- Usually once daily
- May be twice daily

### premixed

- Usually twice daily
- May be once or thrice daily

### intensive

- Thrice daily or more often
- Usually four doses [basal bolus]



## Types of regimes

1

- Basal
- Premixed

2

- Premixed
- Basal
- Basal plus

3+

- Basal bolus
- Basal plus
- Rapid –rapid- premixed

REVIEW

## Number-Based Approach to Insulin Taxonomy

Sanjay Kalra · Yashdeep Gupta



# Number-based approach to insulin taxonomy

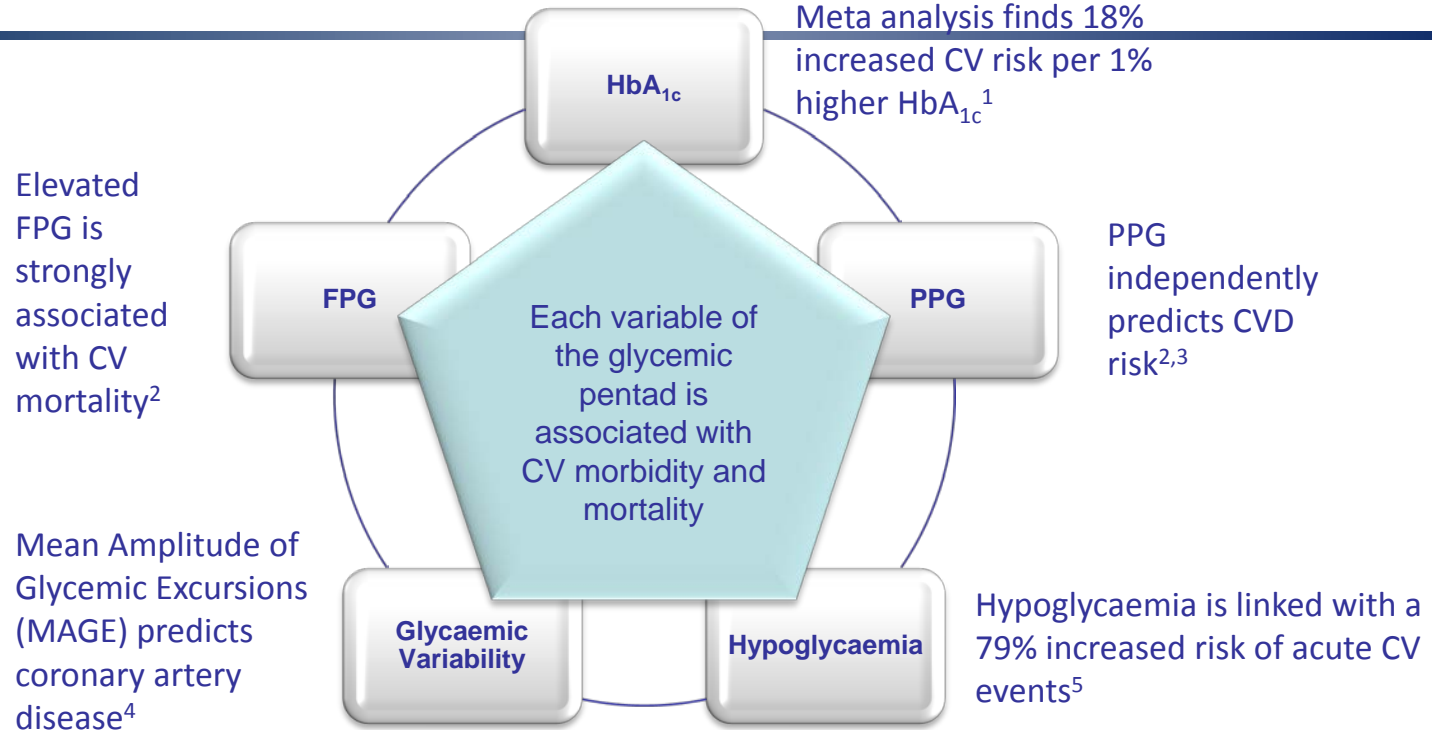
Frequency of injection	Name of regimen	Insulin preparations Used*	Timing of administration
1 x daily	Basal Basal Premixed Coformulation Basal+GLP1RA	NPH, IDet, Iglar, Iglar U300 IDeg BIAsp LisproMix IDegAsp Ideg + liraglutide Iglar + lixisenatide	At bedtime or same time everyday At any time of the day With major meal With major meal At any time of the day At any time of the day
2 x daily	Basal Premixed Coformulation Basal plus	NPH, IDet, Iglar BHI, BIAsp, LisproMix IDeg Asp Basal + prandial	At bedtime and in the morning With major meal <sup>a</sup> With major meal <sup>b</sup> At bedtime + with major meal
3 x daily	Prandial Bolus–bolus–premixed Premixed–bolus–premixed Bolus-bolus–coformulation	Regular, aspart, lispro, glulisine Prandial + premixed Prandial + premixed Aspart + IDegAsp	With meals With meals With meals With meals
4-5 x daily	Basal-bolus	Any combination of basal and bolus	With meals (3) and at bedtime or 2x daily
CSI (continuous insulin infusion pump)	Alternative to multiple injection		

<sup>a</sup> Antipodal meal (meals spaced roughly 12 hours apart)

<sup>b</sup> Minimum 8-hour gap between 2 doses

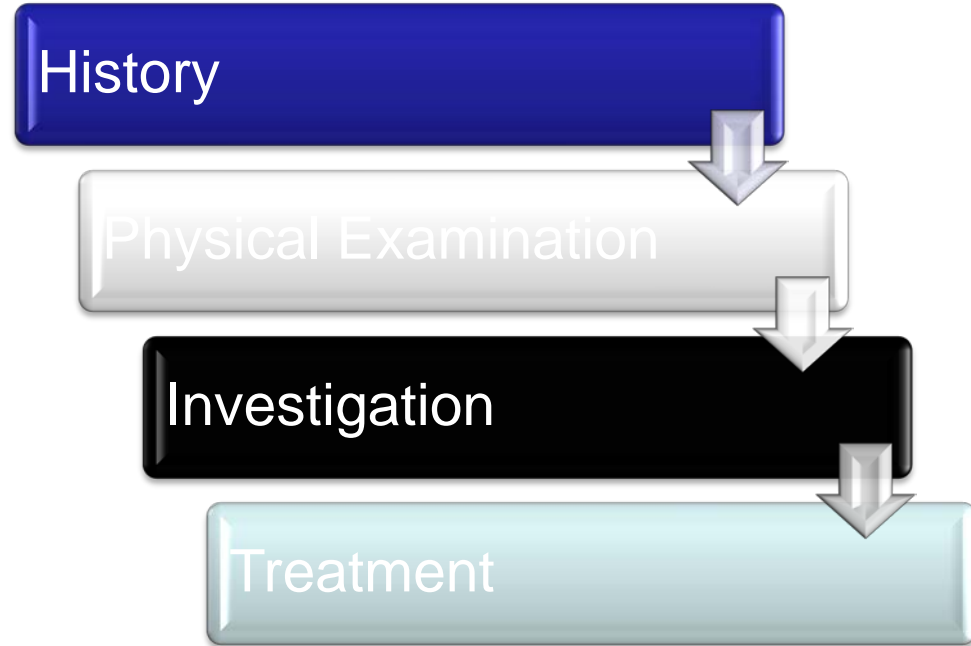
\* Supported by RCTs

# Glycaemic pentad



# Hierarchy of Management

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# Gluco-phenotype

History

Age/  
Duration

Diet  
Pattern

Physical  
Activity

Physical  
Examination

Weight

Co-  
morbidities

Hypo-  
glycemia  
Risk

Investigation

FPG

PPG

A1c

Treatment

Basal  
Insulin

Premixed  
Insulin

Intensive  
Insulin

Clinical factor/choice of regime	Basal <sup>1</sup>	Premixed <sup>2</sup>	Intensive <sup>3</sup>
Fasting hyperglycaemia alone	++	+	++
Postprandial hyperglycaemia alone	—	+	++
Both fasting and postprandial hyperglycaemia	—	++	++
High HbA <sub>1c</sub> at presentation (>8.5%)	—	++	++
Low HbA <sub>1c</sub> at presentation (<8.5%)	+	++	—
Acute comorbidity requiring euglycaemia for management, e.g. infection, trauma	—	+	++
High risk of hypoglycaemia	+	+	—

# Choosing an insulin regime: a developing country perspective

S Kalra and Y Gupta

Insulin is a frequently prescribed drug in diabetes practice. Considered the most effective glucose-lowering intervention, insulin replacement therapy is a key component of effective diabetes management, irrespective of the stage of the condition.<sup>1</sup> Used as monotherapy, in combination with oral anti-diabetic drugs, and with incretin-based therapy, insulin is the most potent glycaemia-lowering therapy available.<sup>1</sup>

Insulin is available in a range of preparations and delivery devices, and can be used to craft a variety of combinations and regimes.<sup>2</sup> All these regimes are backed by evidence in the form of randomised controlled trials

Association of Clinical Endocrinologists guidelines, for example, reinforce the validity of this assumption when they classify persons seeking anti-diabetic therapy in to three categories, based upon their initial HbA<sub>1c</sub>. The mid-range HbA<sub>1c</sub> of 7.5% to 9.0% is perhaps thought to be the glycaemic status of the average person presenting for treatment in the United States.<sup>9</sup>

## The developing world: diabetes as an acute or chronic disease

Most of the world's population, however, live in developing countries. So too, do 80% of the world's people



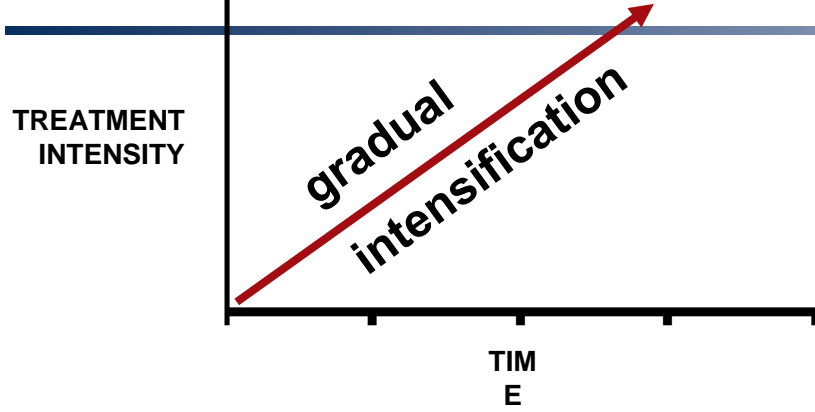
patient-centred care in diabetology  
strategy for improving diabetes care in Nigeria  
management for diabetic patients with kidney disease  
choosing an insulin regime in developing countries  
diabetic peripheral neuropathy in diabetic amputees

# Health care-seeking behaviour

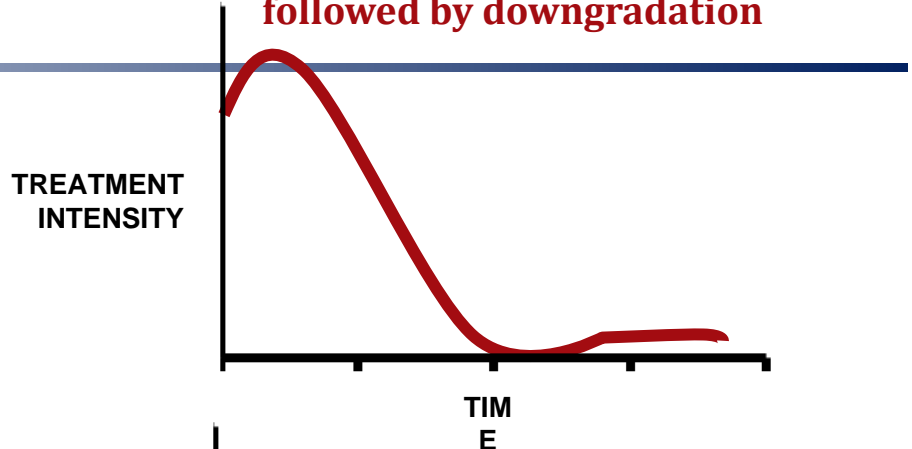
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- Escalation
- De-escalation
- Yo-yo
- Linear

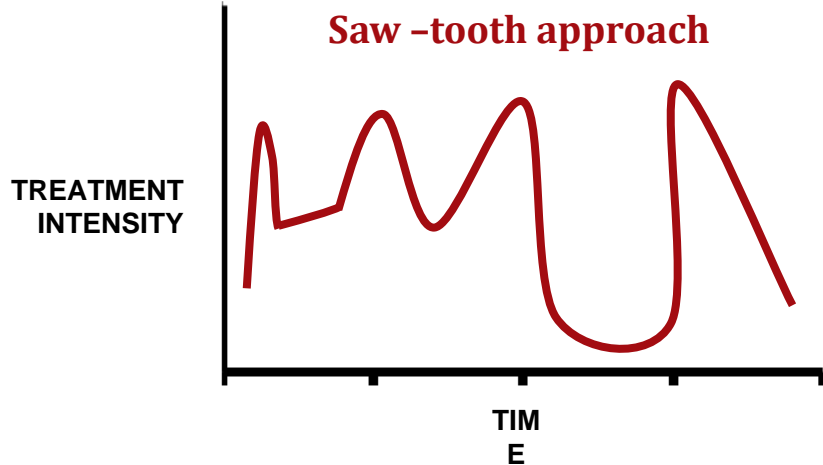
**Gradual upgradation/intensification**



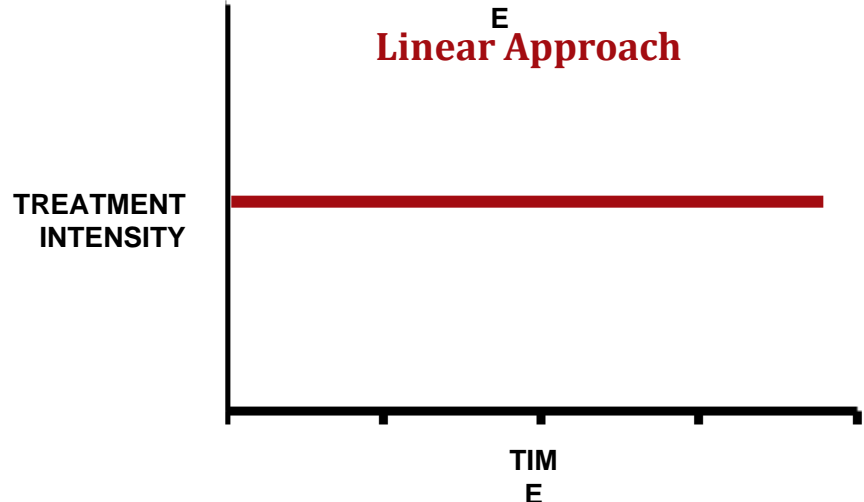
**Initial intensive therapy, followed by downgradation**



**Saw-tooth approach**



**Linear Approach**





# Ethnopharmacy

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Racial and ethnic differences in

- insulin resistance,
- dietary pattern,
- glucose metabolism, and
- genetic variation



Contents lists available at ScienceDirect

## Medical Hypotheses

journal homepage: [www.elsevier.com/locate/mehy](http://www.elsevier.com/locate/mehy)



### Recommendations for insulin initiation based on ethnicity

M. John <sup>a,\*</sup>, S. Kalra <sup>b</sup>, A.G. Unnikrishnan <sup>c</sup>, B. Ganapathy <sup>d</sup>, M.P. Baruah <sup>e</sup>, R.K. Sahay <sup>f</sup>

<sup>a</sup> Providence Endocrine & Diabetes Specialty Centre, Trivandrum, India

<sup>b</sup> Bharti Hospital, Karnal, India

<sup>c</sup> Amrita Institute of Medical Sciences, Cochin, India

<sup>d</sup> St. John's Medical College, Bangalore, India

<sup>e</sup> Excel Care Hospital, Guwahati, India

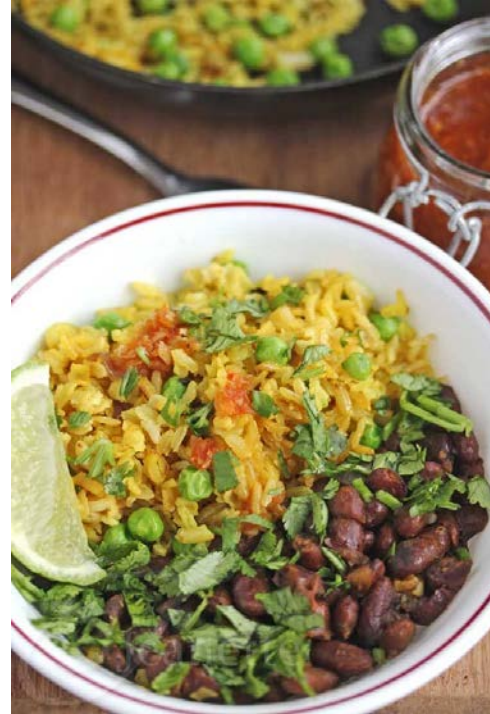
<sup>f</sup> Osmania Medical College, Hyderabad, India

*“We postulate that certain ethnic characteristics of populations will decide the best form of insulin therapy rather than blanket recommendations on starting every patient on basal insulin.”*

# Myanmar cuisine

---

- Rice based
- Post prandial load
- Match the medicine to the meal pattern, and to the meal



---

Match the medicine to the meal,  
not the meal to the medicine

Match the insulin regime to the lifestyle,  
not the lifestyle to the regime

# Conversation plan

---

- Motivate the patient

# Attributes of a good diabetologist

---

- Confident Competence
- Authentic Accessibility
- Reciprocal Respect
- Expressive Empathy
- Straightforward Simplicity

---

### Table 3: Motivational interviewing—the WATER approach

---

W: welcome with warmth

A: ask and assess complaints, medical status

T: tell the truth, while counselling

E: explain, with empathy, the need for insulin

R: reassure and ensure return

## 3I Approach

---

- Inform
- Incubate
- Initiate



# Conversation plan

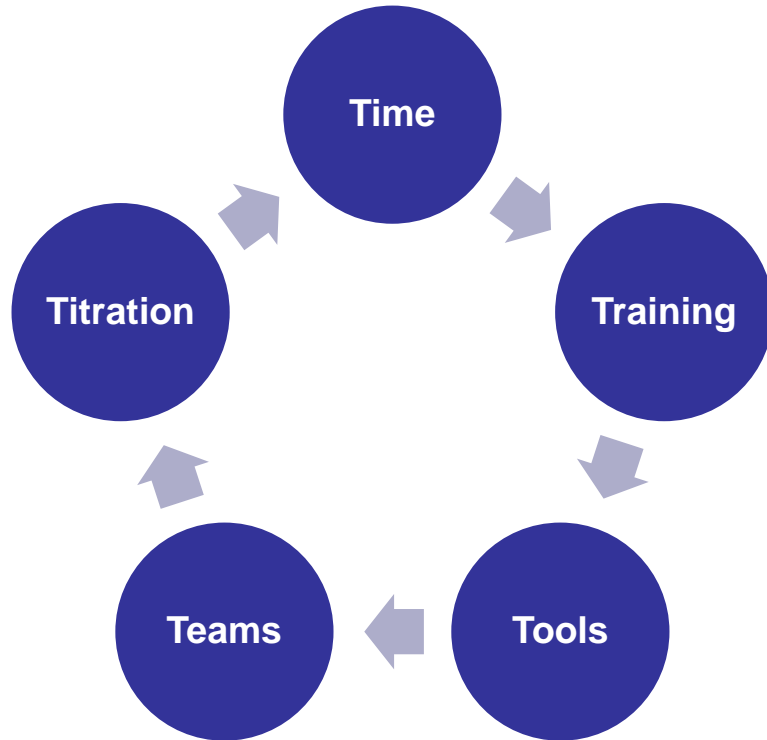
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- Method of injection technique

# Issues with insulin therapy in Asia

## Absence of 5 "T"s

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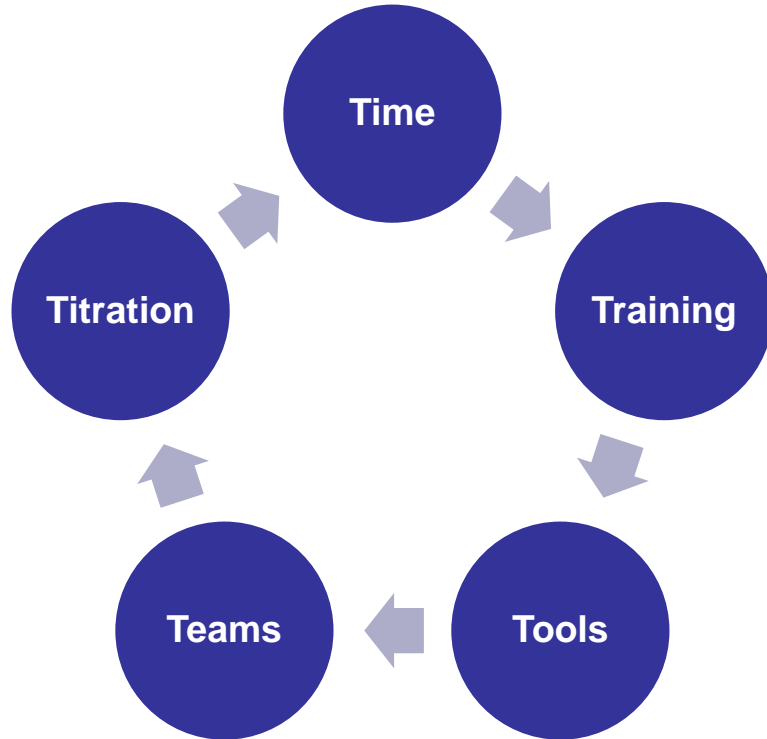


# Issues with insulin therapy in Asia

## Absence of 5 "T"s

**5T = Time Taken To Teach Technique**

---



**Convenience offered  
by premixed insulin  
regimens can  
probably address  
these issues**

# Flexibility in insulin prescription

Sanjay Kalra, Yashdeep Gupta<sup>1</sup>, Ambika Gopalakrishnan Unnikrishnan<sup>2</sup>

*Department of Endocrinology, Bharti Hospital, Karnal, Haryana, <sup>1</sup>Department of Endocrinology, All India Institute of Medical Sciences, New Delhi, <sup>2</sup>Department of Endocrinology, Chellaram Diabetes Institute, Pune, Maharashtra, India*

## A B S T R A C T

This communication explores the concept of flexibility, a propos insulin preparations and insulin regimes used in the management of type 2 diabetes. The flexibility of an insulin regime or preparation is defined as their ability to be injected at variable times, with variable injection-meal time gaps, in a dose frequency and quantum determined by shared decision making, with a minimal requirement of glucose monitoring and health professional consultation, with no compromise on safety, efficiency and tolerability. The relative flexibility of various basal, prandial and dual action insulins, as well as intensive regimes, is compared. The biopsychosocial model of health is used to assess the utility of different insulins while encouraging a philosophy of flexible insulin usage.

**Key words:** Biphasic aspart, biphasic lispro, degludec, degludec aspart, detemir, glargine, glulisine, hypoglycemia, insulin aspart, lispro, neutral protamine Hagedorn, type 2 diabetes

# Flexibility

The ability of an insulin regime/preparation to be injected:  
at variable times  
with variable injection-meal time gaps  
in a dose frequency and quantum determined by shared decision  
making  
with minimal requirement of glucose monitoring and HCP consultation  
with no compromise on safety, efficiency and tolerability

---

Table 4: Insulin technique—seven messages

---

1. Ensure clean injection site and hands
2. Prefer abdomen, upper thighs, and upper arms for injection
3. Prefer 4 mm pen needles, and 6 mm syringe needles
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self insulin site examination (Self IE).
5. Inspect, palpate injection sites at least once a year, more often if LH is detected
6. Do not reuse needles, or share insulin pens, cartridges, and vials
7. Ensure safe disposal of needles and ancillary supplies

# Conversation plan

---

- Monitoring of insulin therapy

## Hypoglycemia

---

1. In the past week, did you ever have morning headaches?

- ☐ No  
☐ Yes  
☐ Don't know

### Items (using the same format as above):

1. In the past week, did you ever have morning headaches?
2. In the past week, did you ever have nightmares?
3. In the past week, did you ever have night sweats?
4. In the past week, did you ever have lightheadedness?
5. In the past week, did you ever have shakiness or weakness?
6. In the past week, did you ever have intense hunger?
7. In the past week, did you ever have times when you passed out, fainted, or lost consciousness, even for a short time?

### Scoring

Code as follows: No="0", Yes="1", Don't know=blank. Score is the sum of the seven items, higher score indicating more hypoglycemia symptoms.

### Characteristics

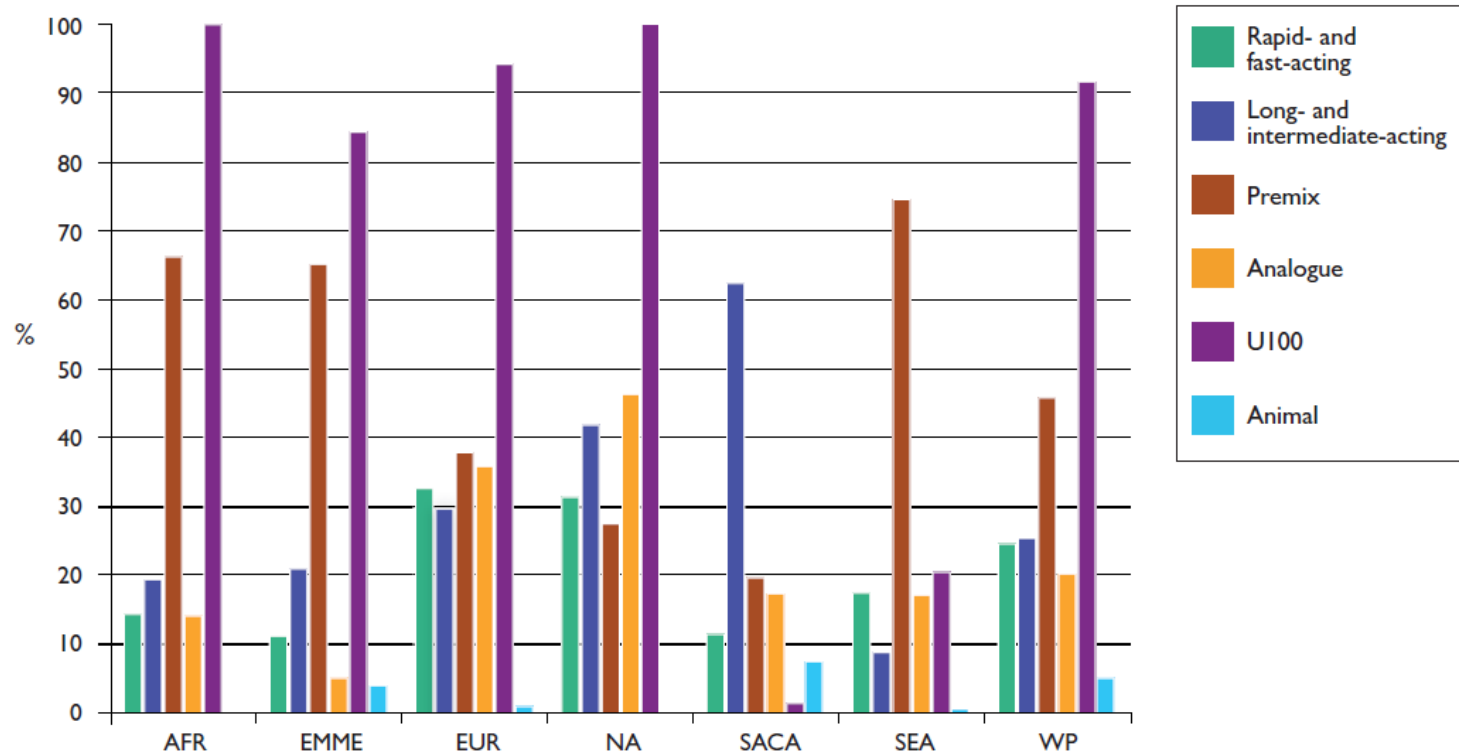


# Conversation plan

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- Guidelines and suggestions

# Usage of insulin type by IDF Regions



Source: IDF, Diabetes Voice, 2006



**MMD** Myanmar Diabetes Association

## MYANMAR GUIDELINE FOR INSULIN THERAPY

1<sup>st</sup> Edition  
2014

### CHAPTER (5)

#### INSULIN REGIMENS FOR NON-EMERGENCY CONDITION

The choice of insulin regimens should be individualized based on the patient's glycemic profile, dietary pattern, personal lifestyle as well as desired flexibility.

The two basic insulin regimens are:

- Supplementary therapy
- Substitution therapy

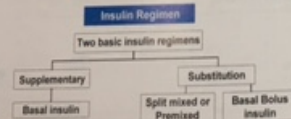
Supplementary therapy is given as basal insulin and Substitution therapy which is given as basal bolus insulin or pre-mixed insulin therapy (Fig 2).

In patients with T2DM, insulin is commonly initiated as supplementary treatment to OAD therapy. Less commonly it is initiated as complete substitution of OAD. Rapid improvement in glycemic control can be associated with adverse outcomes, especially related to frequent hypoglycemia; therefore, the mantra, "Start low, and go slow" is pertinent while using insulin.

These regimens require individualization which is carried out in phases of initiation, optimization and intensification.

**Initiation:** entails the selection of the appropriate type of insulin, regimen and starting dose for the patient. This ensures that the patient's individual need based on the glycemic status is appropriately addressed.

**Optimization:** entails gradual titration/ adjustment of the dose of insulin to obtain an optimal dose which is adequate to achieve the desired level of glycemic control with minimal or no adverse effects for the patient. Dose adjustments are carried out on the basis of blood glucose monitoring (usually self-monitoring of blood glucose, SMBG). SMBG should be carried out three or more times daily for patients using multiple insulin injections.<sup>14</sup>



(Fig 2)

Table 4  
Insulin Regimens & Frequency of Injections per day

No. of injections per day	Insulin regimen	Type of Insulin and Timing
	Basal	Intermediate acting (NPH) insulin bed time
	Basal	Long acting analogue once daily
	Premixed CO	Premixed insulin pre-dinner/pre-breakfast
	Premixed BO	Premixed insulin pre-breakfast & pre-dinner
	Premixed analogue	Premixed insulin pre-breakfast, pre-lunch TID & pre-dinner
	Basal-Bolus	Basal insulin once/twice daily + prandial insulin pre-breakfast, pre-lunch & pre-dinner

Intensification: entails modification/ switching from one insulin regimen to another in order to achieve better glycemic control. The dose and regimen is individualized based on patient's blood glucose profile, patient's lifestyle and preference.

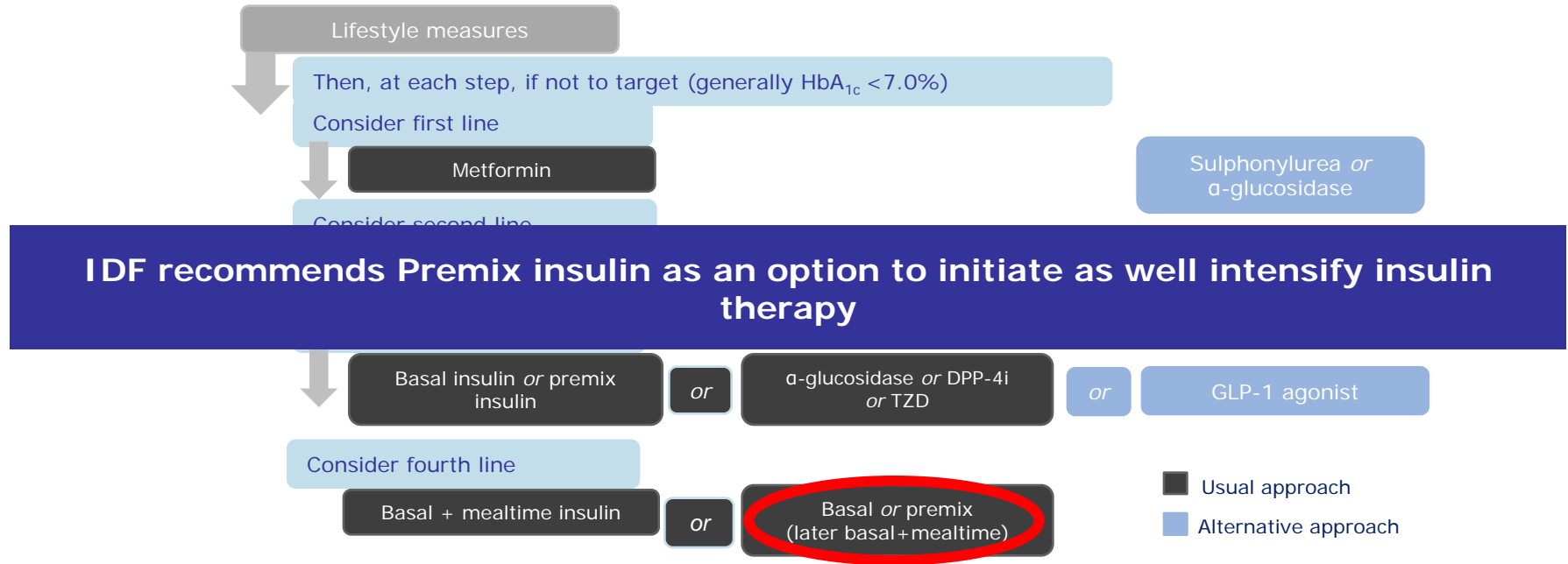
Table 5  
Choice of insulin regimen according the blood sugar profile

Blood Glucose Profile		Preferred insulin regimen
Pre-breakfast	Daytime	
High	Normal/Near Normal	Basal (Bed time) or Premixed CO (Pre dinner)
High	High	1. Basal → Basal Plus → Basal Bolus 2. Premixed Insulin, BID
Normal	High	Prandial insulin and later add on basal insulin



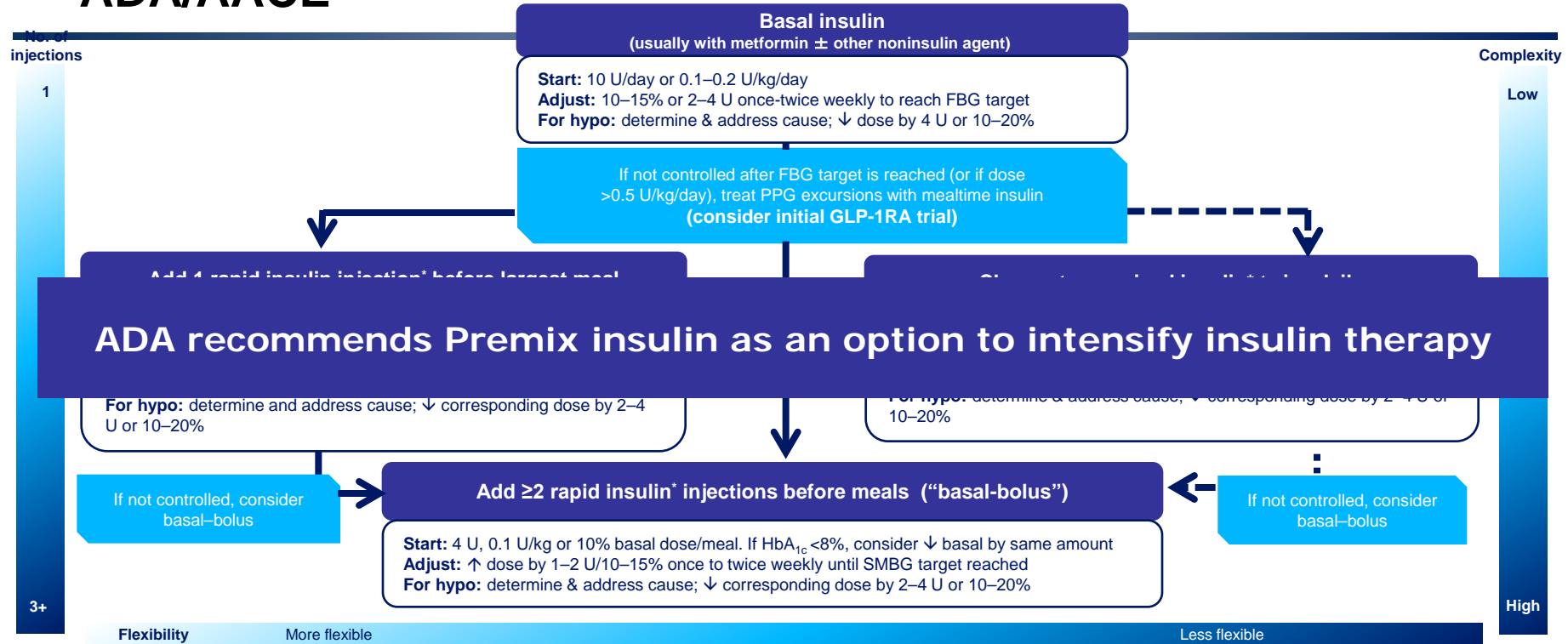
# Guidelines and Intensifying Insulin therapy

## IDF

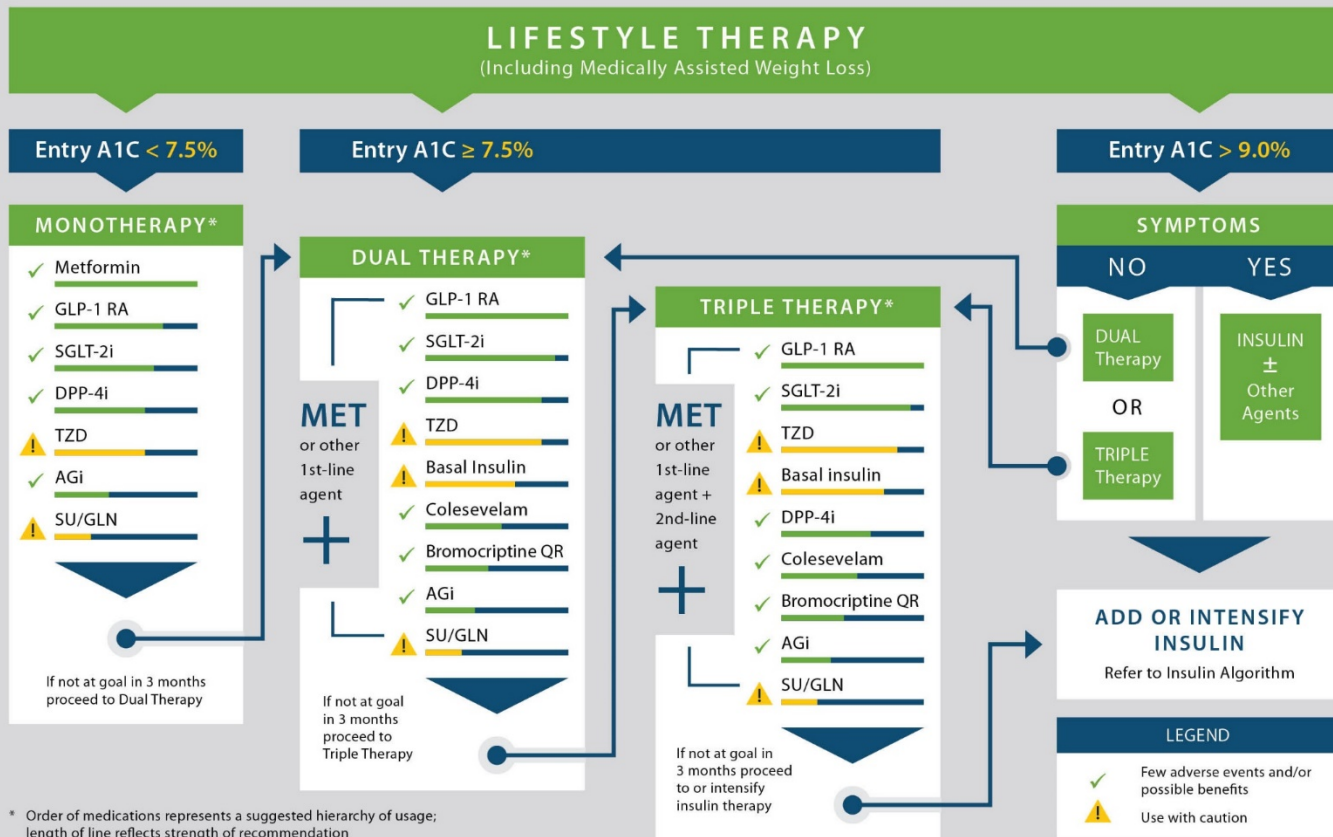


# Guidelines and Intensifying Insulin therapy

## ADA/AACE



\*Regular human insulin and human NPH-regular premixed formulations (70/30) are less costly alternatives to rapid-acting insulin analogues and premixed insulin analogues, but their pharmacodynamic profiles make them suboptimal for the coverage of postprandial glucose excursions. ADA, American Diabetes Association; EASD, European Association for the Study of Diabetes; FBG, fasting blood glucose; GLP-1RA, glucagon-like peptide-1 receptor agonist; PPG, postprandial glucose; SMBG, self-monitoring of blood glucose



PROGRESSION OF DISEASE



# Guidelines and Intensifying Insulin therapy

## Summary

Guideline	Initiation	Intensification
ADA/EASD 2015 position statement update <sup>1</sup>	<ul style="list-style-type: none"><li>Basal</li></ul>	<ul style="list-style-type: none"><li>Add GLP-1RA</li><li>Basal-plus then basal-bolus</li><li>Premix BID then basal-bolus</li></ul>
IDF <sup>2</sup>	<ul style="list-style-type: none"><li>Basal OD</li><li>Premix OD/BID</li></ul>	<ul style="list-style-type: none"><li>Basal-plus or basal-bolus</li></ul>
<b>International guidelines recommend both initiation as well a intensification with Premixed Insulins</b>		
Association <sup>4</sup>	<ul style="list-style-type: none"><li>Premix OD/BID</li></ul>	<ul style="list-style-type: none"><li>Premix BID</li></ul>
NICE <sup>5</sup>	<ul style="list-style-type: none"><li>Basal insulin OD or BID</li><li>Basal insulin + prandial</li><li>Premixed insulin</li></ul>	<ul style="list-style-type: none"><li>Basal-plus</li><li>Basal-bolus or premix</li><li>Add GLP-1RA or SGLT-2i</li></ul>
AACE <sup>6</sup>	<ul style="list-style-type: none"><li>Basal</li></ul>	<ul style="list-style-type: none"><li>Add GLP-1RA or prandial insulin</li><li>(premix among other options)</li></ul>

AACE, American Association of Clinical Endocrinologists; ADA, American Diabetes Association; BID, twice daily; EASD, European Association for the Study of Diabetes; GLP-1RA, glucagon-like peptide 1 receptor agonist; IDF, International Diabetes Federation; NICE, UK National Institute for Health and Care Excellence; OD, once daily; SGLT-2i, sodium-glucose cotransporter 2 inhibitor; TID, three times daily; T2D, type 2 diabetes

1. Inzucchi *et al. Diabetes Care* 2015;38:140–9; 2. IDF Clinical Guidelines Task Force. Global Guideline for Type 2 Diabetes, 2012. [www.idf.org/sites/default/files/IDF-Guideline-for-Type-2-Diabetes.pdf](http://www.idf.org/sites/default/files/IDF-Guideline-for-Type-2-Diabetes.pdf); 3. General practice management of type 2 diabetes, 2014–15. Melbourne: The Royal Australian College of General Practitioners and Diabetes Australia. 2014. <https://www.diabetesaustralia.com.au/best-practice-guidelines>; 4. Harper *et al. Can J Diabetes* 2013;37(Suppl. 1):S61–8 (Appendix 3); 5. NICE. Type 2 diabetes in adults: management. NICE Clinical Guideline 28 (2 December 2015) <https://www.nice.org.uk/guidance/ng28> [accessed December 2015]; 6. Garber *et al. Endocr Pract* 2015;21:438–47



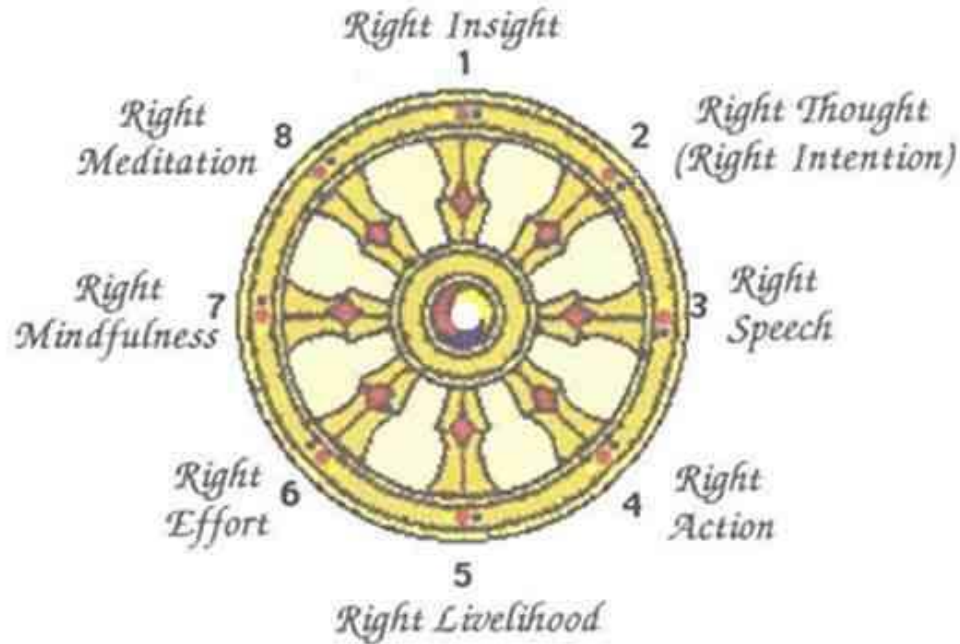


**Table 6: Modification of insulin**

Modification	Indication
Dose titration	<ul style="list-style-type: none"><li>• Mild deviation from glycemic target</li><li>• Newly begun regime</li></ul>
Change of preparation, e.g., <ul style="list-style-type: none"><li>• Human to analogue</li><li>• Long-acting to ultra-long acting</li><li>• Premixed to dual action co-formulation</li><li>• Low dose premix to high mix</li></ul>	<ul style="list-style-type: none"><li>• Mild deviation from glycemic target</li><li>• Patient unwilling to increase dose frequency</li><li>• Glycemic variability</li></ul>
Change of injection frequency, e.g., <ul style="list-style-type: none"><li>• Basal plus 1 to basal plus 2</li></ul>	<ul style="list-style-type: none"><li>• Gross deviation from glycemic target</li><li>• Isolated postprandial hyperglycemia</li></ul>
Change of regime, e.g., <ul style="list-style-type: none"><li>• Basal to basal plus</li><li>• Basal to premixed</li><li>• Premixed to basal plus</li></ul>	<ul style="list-style-type: none"><li>• Gross deviation from glycemic target</li><li>• Postprandial hyperglycemia</li></ul>

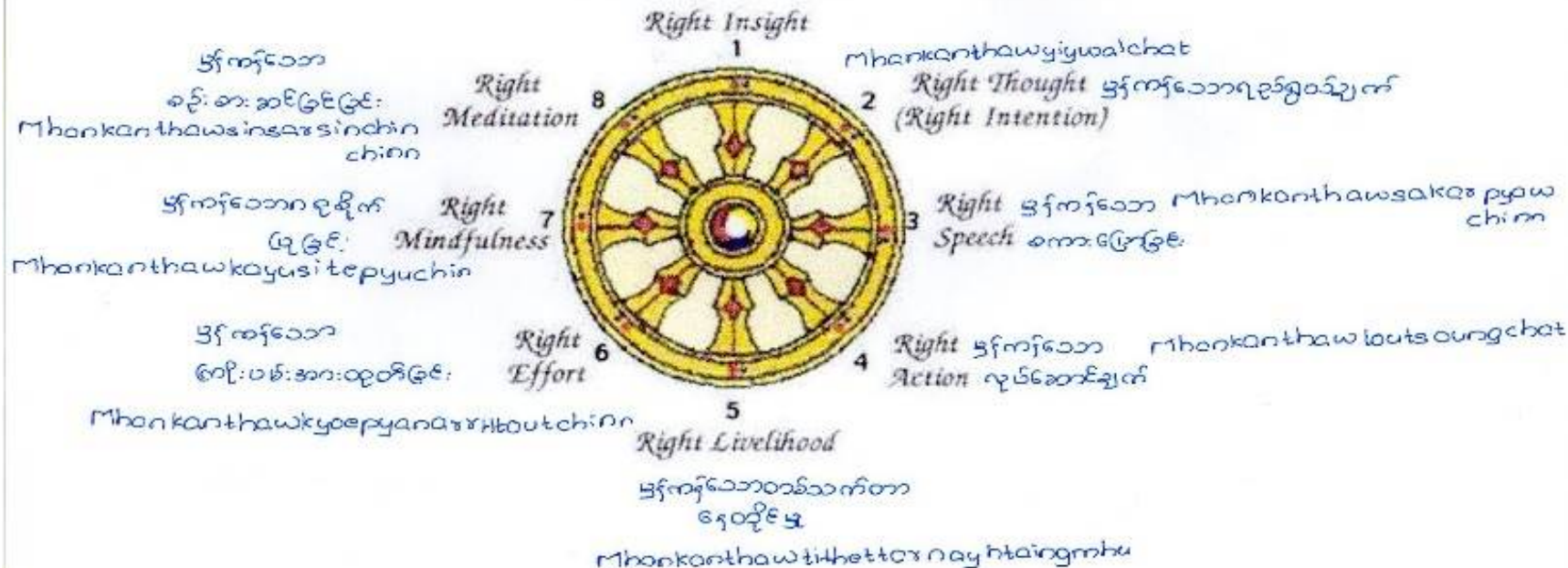
## 8 Rights that Matter

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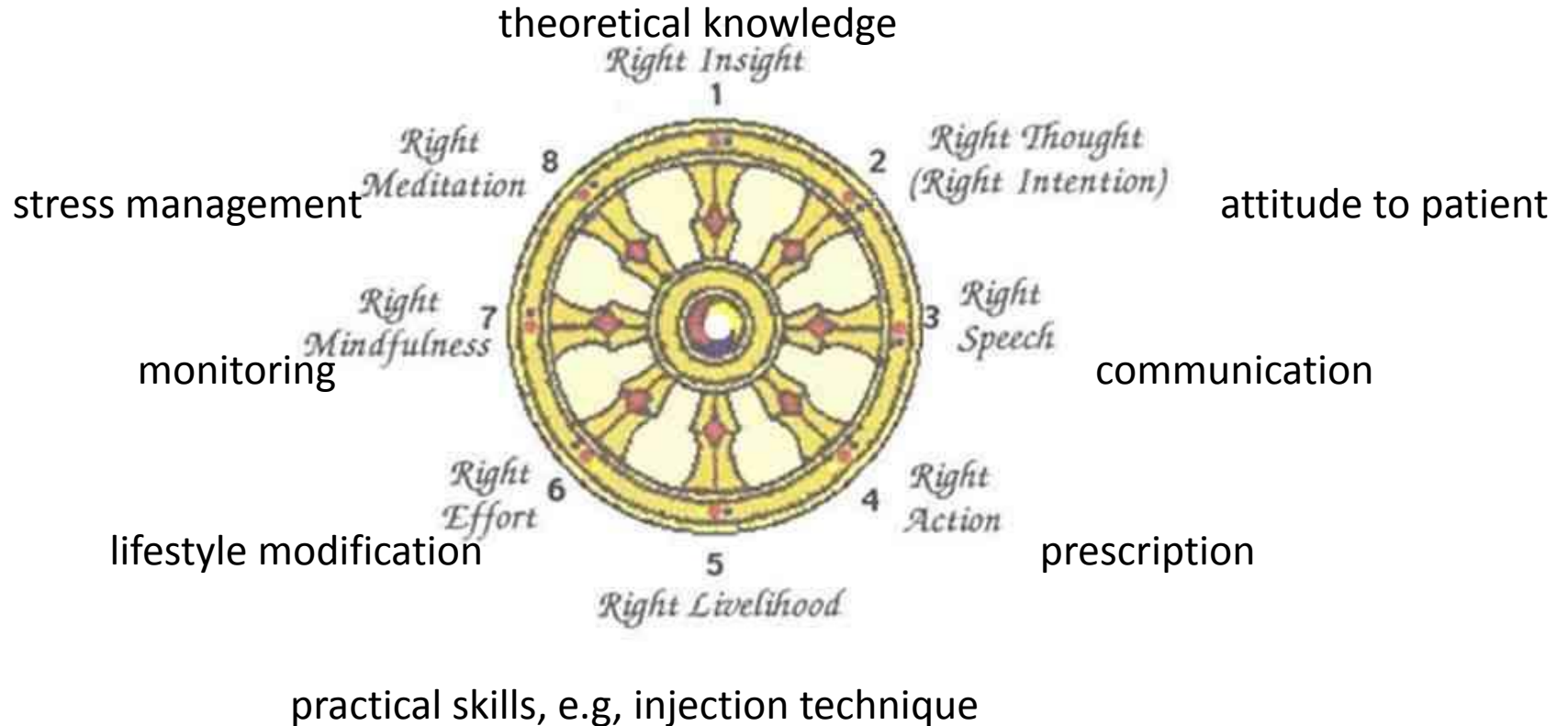
# 8 Rights that Matter

၎င်းတို့သည် နိဗ္ဗာန်သို့  
 မရောက်နိုင်အောင် ဖြစ်စေရန်  
 ရှိသည်။



## 8 Rights that Matter

---



# 8 Rights that Matter

Ayuasamsaingyo pyinyo bahuthuta

အယူအဆသိရှိမှု ပညာစာပေပညာ

theoretical knowledge

Right Insight

1

Right Thought  
(Right Intention)

Satesheythawtabawthakhan

စိတ်စွန့်သောသဘာဝသက်  
attitude to patient (ချေပဲသိမ်း)

Phisichan kinaq pyumukyintkyanpon  
stress management

ဖိစီးခြင်း ကင်းသောနေ့ရက် ယူဆခြင်း

monitoring

Right  
Mindfulness

Right  
Effort

lifestyle modification

ဘဝနေထိုင်မှုအရာများ ပြောင်းလဲခြင်း

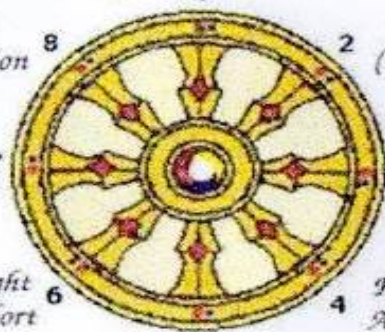
Bawandayhtinmuandengepyupayin

pyaung laehtachinn

practical skills, e.g. injection technique

ပျော်လှယ်နိုင်ခြင်း၊ ပြုပြင်ဆင်ဆင်တတ်သည့်အားရှိခြင်း၊ ၁ ညှပ်၊ ဆေးသွင်းခြင်း၊ အသုံးပြုခြင်း

Pyuloutndingchinnyintsoing the w tatti loimachinn, namunax sayhtoochin ninnor nitaya



wasimychachinn  
communication ချောမွေ့ခြင်း

prescription နည့်ပြခြင်း

nyounpyachinn

