



# **Diabetes:**

## **Global condition, local perspective**

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# Conversation plan

- The endemic
- Diagnostic cut offs
- Patterns of health care-seeking behaviour
- Religion
- Patterns of presentation
- Quality of medication: generics vs originators



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**Pakistan** is one of the 19 countries and territories of the IDF MENA region.

415 million people have diabetes in the world and more than 35.4 million people in the MENA Region; by 2040 this will rise to 72.1 million.

There were over 7 million cases of diabetes in Pakistan in 2015.



IDF membership

## DIABETES IN PAKISTAN - 2015

Total adult population (1000s) (20-79 years)	102,252	Number of deaths in adults due to diabetes	86,364
Prevalence of diabetes in adults (20-79 years) (%)	6.9	Cost per person with diabetes (USD)	61.5
Total cases of adults (20-79 years) with diabetes (1000s)	7,028	Number of cases of diabetes in adults that are undiagnosed (1000s)	2,927.7

## Editorial

# Endemic or epidemic? Measuring the endemicity index of diabetes

**Sanjay Kalra, Arun Kumar<sup>1</sup>, Prashant Jarhyan<sup>2</sup>, Ambika Gopalakrishnan Unnikrishnan<sup>3</sup>**

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## Is diabetes endemic to Pakistan:

- IGT prevalence 7.7%
- DM prevalence 6.9%
- Diabetes endemicity index
  - $DM/IGT = 6.9/7.7 = 0.90$
  - $total\ glucose\ intolerance/IGT = 14.6/7.7 = 1.90$

# Metabolic syndrome: DHOLL vajda

Diabetes	<b>D</b>
Hypertension	<b>H</b>
Obesity	<b>O</b>
Lipids: LDL	<b>L</b>
Lipids: Triglycerides	<b>L</b>



Kalra S, Gupta Y. Metabolic Syndrome: The drums are beating. JPMA. The Journal of the Pakistan Medical Association. 2015 Nov;65(11):1148-.



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## Diagnostic Tests

Diabetes can be diagnosed by any of the following tests:

- Fasting plasma glucose (FPG)
- Oral glucose tolerance test (FPG and glucose value 2 hours after 75g glucose load).
- Glycated haemoglobin (HbA1c)
- Casual (random) plasma glucose
- Post challenge glucose is estimated by performing an oral glucose tolerance (OGTT), following directions laid down by WHO. While a single abnormal value of blood glucose is enough in symptomatic persons, two abnormal readings are mandatory in asymptomatic individuals to diagnose diabetes

**Table:** Diagnostic criteria for diabetes and 'prediabetes'.

Status	Body fluid	Normal (mg/dl)	Impaired (prediabetes) (mg/dl)	Diabetes (mg/dl)	Professional body
Fasting	plasma	<100	≥100-125	≥126	ADA, WHO
	Venous whole blood (WHO)	<100	≥100-110	≥110	WHO
	Capillary whole blood (WHO)	<100	≥100-110	≥110	WHO
Post-load	OGTT plasma 2hours glucose load	<140	≥140-199	≥200	ADA,WHO
	Venous whole blood	<120	≥120-<180	≥180	WHO
	Capillary whole blood	<140	≥140-199	≥200	WHO
HbA1c		< 5.7%	5.7% - 6.4%	≥6.5%	ADA, WHO

ADA= American Diabetes Association; WHO= World Health Organization.

## Caveats: Clinical

- In symptomatic persons, an abnormally high random plasma glucose  $>200\text{mg}\%$ , with classic symptoms of hyperglycaemia or hyperglycaemia crisis, is enough to diagnose diabetes. In an asymptomatic person, a test result should be repeated “when feasible”, to rule out a laboratory error.<sup>1</sup> Where a random plasma glucose level of  $>100\text{mg/dl}$  and  $<200\text{mg/dl}$  is detected, a FPG should be measured, or an OGTT performed, or an HbA1c measured as per International Diabetes Federation guidelines.
- Two concordant results, for example, two HbA1c readings, or one HbA1c and one plasma glucose, or two plasma glucose readings above the diagnostic threshold allow confirmation of diagnosis. Two discordant readings should prompt a repeat of the test result which is in diabetic range. For example, a person with a normal fasting and high HbA1c should undergo repeat testing by HbA1c

## Caveats: Procedural

- Fasting plasma glucose should be tested after abstaining from caloric intake for at least 8 hours. The two-hour post-load plasma glucose should be tested after performing an oral glucose tolerance test (OGTT), as per 75g anhydrous glucose (82.59 glucose monohydrate, dissolved in 250-300ml water over 5 minutes).<sup>2</sup> In children, a glucose load of 1.75g glucose/kg body weight is used, up to a maximum of 75g glucose.<sup>2</sup> Two hours are counted from the beginning of the drink
- The OGTT is performed in the morning, after three days of undistracted diet (>150g carbohydrate/day) and usual physical activity. OGTT is preceded by a dinner containing 30-50g carbohydrate on the previous night, taken 8-14 hours prior to the test. Water (non-caloric) can be taken during a fast. Smoking is not allowed during an OGTT.

## Caveats: Biochemical

- One must be aware of the fluid being used in a particular laboratory, ie, venous whole blood, capillary whole blood, or plasma for determination of glucose levels. When glucose is used to establish the diagnosis of diabetes, it should be measured in venous plasma as per recommendations. There is a difference between glucose and sugar: diabetes is diagnosed and treated on the basis of glucose values, not sugar levels.
- Glucose preservatives (fluoride) cannot and do not, prevent glycolysis completely. Laboratories that use whole blood should assay the sample immediately, or centrifuge it immediately (within 30 minutes). or store it at 0-4°C. There is diurnal variation in FPG, with the mean FPG being higher in the morning than in the afternoon, indicating that many diabetes cases would be missed in patients seen in the afternoon.

## Variability

- Pre- analytic and analytic variability is least for A1C, more likely for FPG, and most likely for the 2-h PG, especially if the glucose samples remain at room temperature and are not centrifuged promptly.

### ***Glycated Haemoglobin***

- Glycated haemoglobin (HbA1c) (using a method that is certified by the National Glycohaemoglobin Standardization Programme) has been suggested by the ADA as a diagnostic criterion for diabetes. A threshold  $>6.5\%$  defines diabetes, while  $5.7\text{--}6.4\%$  implies prediabetes. In situations of abnormal red cell turnover, such as pregnancy, recent blood loss or transfusion, anaemia, haemoglobinopathy, only blood glucose criteria should be used to diagnose diabetes.<sup>1</sup>

### ***How Not To Diagnose Diabetes***

- Diabetes cannot be diagnosed on the basis of glycosuria or ketonuria, as there can be other causes of these laboratory abnormalities. Diabetes should not be diagnosed on the basis of symptoms or signs alone. But, an individual should be promptly tested by recommended tests for hyperglycaemia in such situations. History such as ants being attracted to urine should also prompt proper investigation for diabetes.



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# Health care-seeking behaviour

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

# 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 glycemia-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

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Patient-centred care in diabetology

Strategy for improving diabetes care in Nigeria

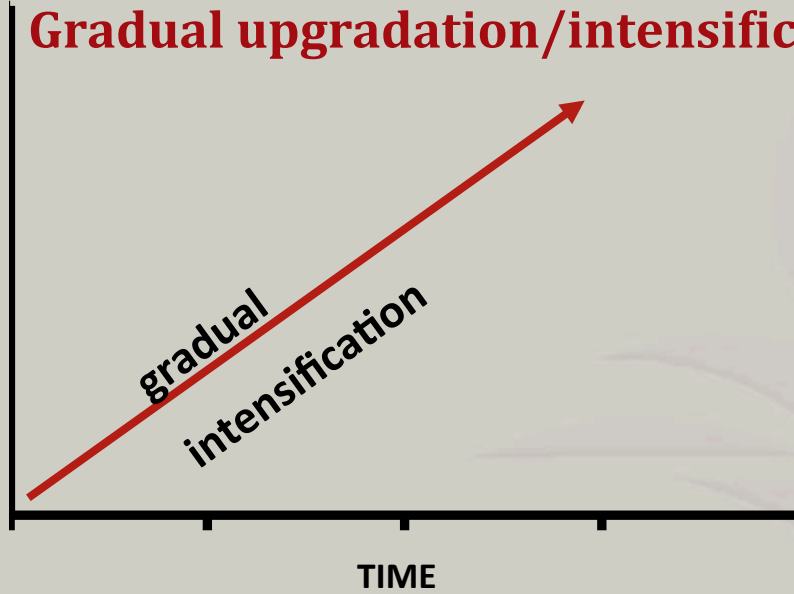
Treatment for diabetic patients with kidney disease

Choosing an insulin regime in developing countries

Peripheral neuropathy in diabetic amputees

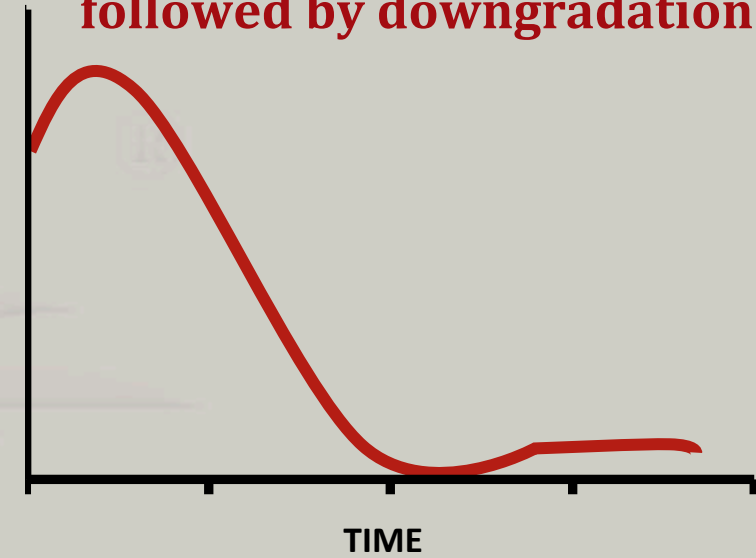
## Gradual upgradation/intensification

TREATMENT  
INTENSITY



## Initial intensive therapy, followed by downgradation

TREATMENT  
INTENSITY



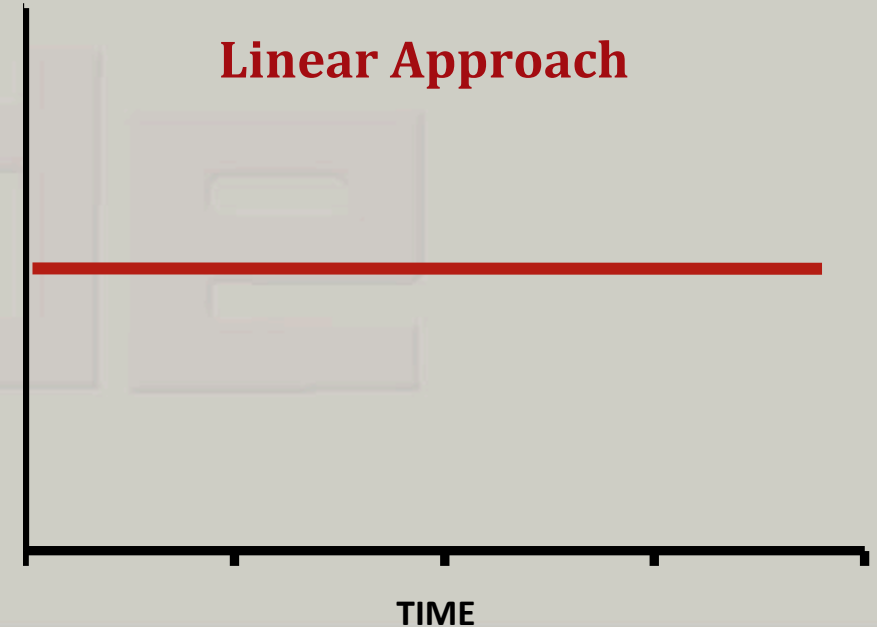
## Saw -tooth approach

TREATMENT  
INTENSITY



## Linear Approach

TREATMENT  
INTENSITY





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# Religion and diabetes

- Religiosity influences coping mechanisms
- Religiosity influences resilience
- Religiosity influences outcomes
- Religion influences lifestyle: diet, physical activity
- Religion influences health care acceptance, e.g., blood transfusions

Amadi KU, Uwakwe R, Odinka PC, Ndukuba AC, Muomah CR, Ohaeri JU. Religion, coping and outcome in out-patients with depression or diabetes mellitus. Acta Psychiatrica Scandinavica. 2015 Dec 1.

# Patient centred care in diabetology: an Islamic perspective from South Asia

Asfandiyar K Niazi  and Sanjay Kalra

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## Abstract

Patient centred care (PCC) is a healthcare model which is sensitive towards the patients' preferences, needs and values. Interest in the use of PCC in diabetology has heightened recently. There is a special need of the usage of PCC in Muslim communities. Six out of the ten countries with the highest prevalence of diabetes are Muslim majority countries. There are several religious and sociocultural issues specific to South Asian Muslim societies that merit the need of individualization of care for people with diabetes. Several such issues are presented in this article, along with recommendations for tackling them.

# Myths and diabetes

## ***Diet related:***

- Use of oily foods and bitter vegetables to restore health
- Prolonged fasting periods in Ramadan
- Excessive use of honey and dates
- Eating a lot of fruits in diabetes

## ***Physical exercise related:***

- Lack of outdoor activities for patients, especially females
- Sedentary lifestyle during Ramadan

## ***Acceptance of diagnosis and therapy:***

- Use of traditional Islamic medicine
- Lack of faith on modern medicine
- Assuming that diabetes is a form of God's test or punishment
- Considering insulin a forbidden substance
- Not using insulin injections because they may cause diseases



# Pro-active quotes on health

## Evidence from Quran

- “Eat and drink healthy and be not prodigal (7:31).
- Do not kill (or harm) yourselves: for verily Allah hath been to you Most Merciful! (4:29)
- And make not your own hands contribute to (your) own destruction (harm) (2:195)

## Evidence from Hadiths


- “The strong believer is better and more loved by Allah than the weaker one” (Muslim)
- “The most beloved by Allah of things He is asked to grant is (Al-aafiyah) good health” (Tirmidi)
- Narrated by Usamah Bin Shareek (may Allah be pleased with him): ‘I was with the Prophet (PBUH) and some Arabs came to him asking “O Messenger of Allah, should we take medicines for any disease?” He said, “Yes. O You servants of Allah take medicine as Allah has not created a disease without creating a cure except for One”. They asked which one, he replied “old age”’.
- The Prophet (PBUH) said: “There are two blessings which many people do not appreciate: health and leisure”.
- He (PBUH) also said: “No blessing other than faith is better than well-being”.



## Journal of Diabetes & Metabolic Disorders

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# Patient centered care in Islam: distinguishing between religious and sociocultural factors

Asfandiyar Khan Niazi  and Sanjay Kalra

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# JPMA

Journal Of Pakistan Medical Association

*Ramadan and Diabetes*

S-1

EDITORIAL

## **Diabetes care in Ramadan: An exemplar of person centered care**

Fatema Jawad,<sup>1</sup> Sanjay Kalra<sup>2</sup>

## Culture-specific challenges: Ramadan

- Calorie-dense diet
- Erratic meal timings/Inability to follow 3+3 meal pattern
- Limited physical activity: availability, accessibility, affordability
- Concordance between religious beliefs and science
- Concordance between gluco-gram and drugs



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# Unique types of diabetes

- Type 1
- Type 2
- GDM
- Pancreatic diabetes
- Type 1.5
- Type 3

## Type 1.5 diabetes

- LADA = Latent Autoimmune Diabetes of Adults
  - Adult type 1 diabetes
  - Lean type 2 diabetes
- Flatbush diabetes = Ketosis –prone type 2 diabetes.

- Autoimmune diabetes
- Adult onset
- Slow progression
- No dramatic features
- Slow s/o catabolism
- LADA-1: TWO ANTIBODIES, HIGH TITRE; LESS HYPERTENSION
- LADA-2

## LADA phenotype

- Lean built
- No hirsutism
- Fair skin, eyes, hair
- Soft goitre
- Autoimmune stigmata
- Autoimmune hepatitis





# Flatbush Diabetes

- Initial ketosis/ketonuria/ DKA
- Initial control with insulin
- Lipotoxicity + Glucotoxicity
- Long term control with OHAs/LSM

## Phenotype

- obese, hirsute, dark
- stigmata of metabolic syndrome
- NASH
- balanoposthitis /pruritis vulvae
- no autoimmune comorbidity

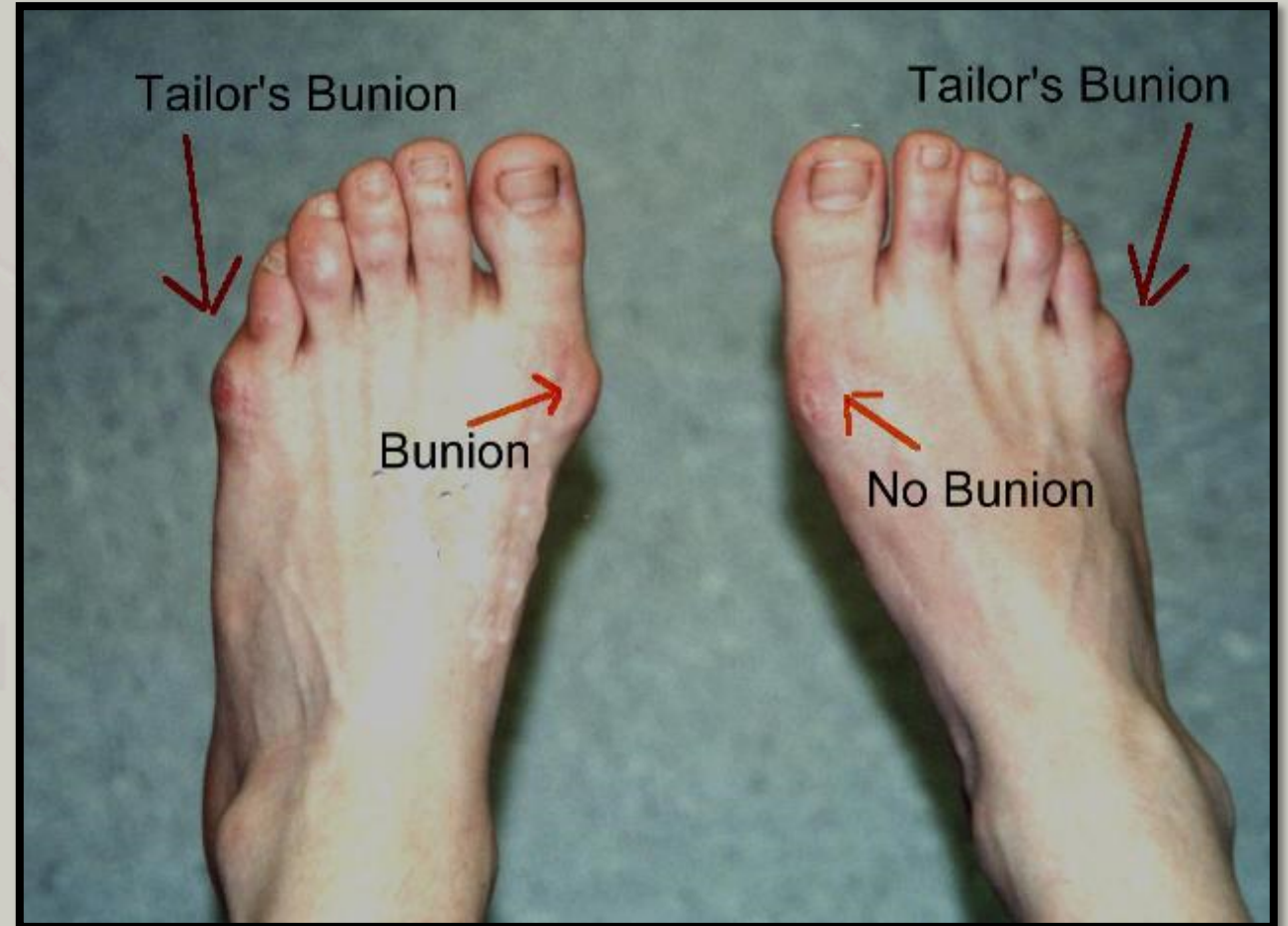
# Investigations

- Antibody positivity  $\pm$
- SGOT/SGPT high
- uric acid high
- homocysteine high
- dyslipidemia



# Diabetic foot

- Tailor foot
- Silencer foot



# Hierarchy of Management

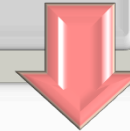
**History**



**Physical Examination**



**Investigation**



**Treatment**

## DIETS: causes of poor control

D:

- diet, drugs

I:

- infection, indigenous

E:

- exercise, emotions, endocrine

T:

- technique, treatment choice

S:

- sleep, stress



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## Editorial

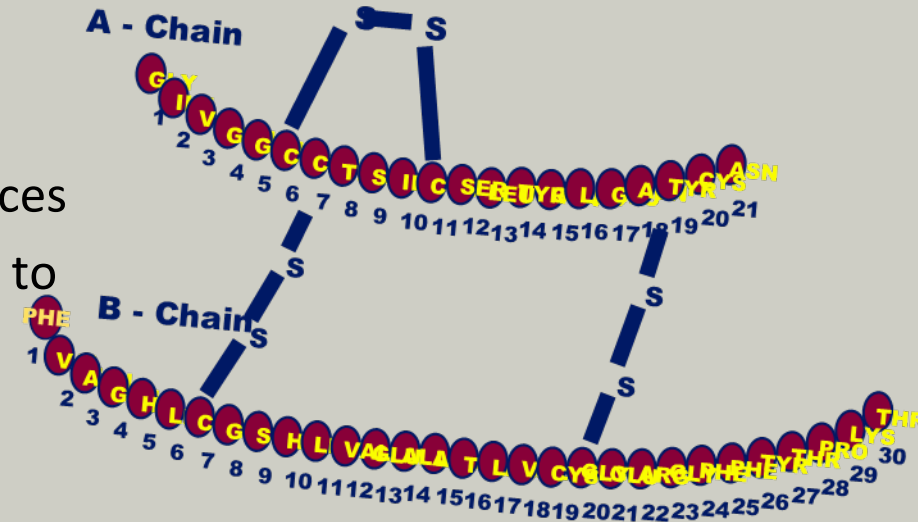
# Biosimilar insulins: Informed choice for South Asia

**Sanjay Kalra, A. K. Azad Khan<sup>1</sup>, Syed Abbas Raza<sup>2</sup>, Noel Somasundaram<sup>3</sup>, Dina Shrestha<sup>4</sup>, Zafar Ahmed Latif<sup>5</sup>, Sarita Bajaj<sup>6</sup>, Md. Faruque Pathan<sup>7</sup>, Rakesh Sahay<sup>8</sup>, Hajera Mahtab<sup>9</sup>**

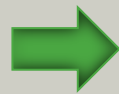
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# Biologics are produced by living organisms

- Medicinal products with active substances produced by, or extracted from, biological sources and for which characteristics are directly linked to a specific manufacturing process

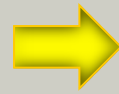


Registered  
according to  
specific  
regulatory  
requirements



## Originator biologics

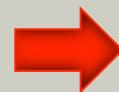
Biologic that has been granted market access on the basis of a full data



## Biosimilars

- Attempted “copy” of a originator biologic
- Biologic that has been granted access on the basis of an abbreviated dataset
- Also called: similar biological medicinal product (EU) or follow-on biologic (US)

In absence of  
regulatory  
framework



Non-innovator copy biologics

# Biosimilar insulins and insulin analogs marketed in South Asia

**Table 4: Biosimilar insulins and insulin analogs marketed in South Asia**

Country	Biosimilar insulins	Biosimilar insulin analogs		
		Glargine	Aspart	Lispro
Sri Lanka	None	None		
Pakistan	Insuget R, 70/30, N Innogen R, 70/30, N Zansulin R, 70/30, N	Basagine		
Nepal	Wosulin R, 30/70, N	Glaritus		
India	Insugen R, 30/70,50/50, N Humstard 30/70 Humarap Lupisulin-R, M30, M50, N Recosulin-R, 30/70, 50/50, N Human Fastact, Mixact 30/70 Wosulin R, 30/70,50/50, N	Basalog Basugine Glaritus		
Bangladesh	Insul R, 30/70, 50/50, N Maxulin R, 30/70, 50/50, N Ansulin R, 30/70,50/50, N Diasulin R, 30/70,50/50, N Insulet R, 30/70,50/50, N	Glargin Glargin C Vibreanta Insulet glargine Glarine	Glyset R, Glyset Mix Acilog, Acilog R Insulet Asp, Insulet Asp 30/70	Insul Lispro, Insul Lispro C





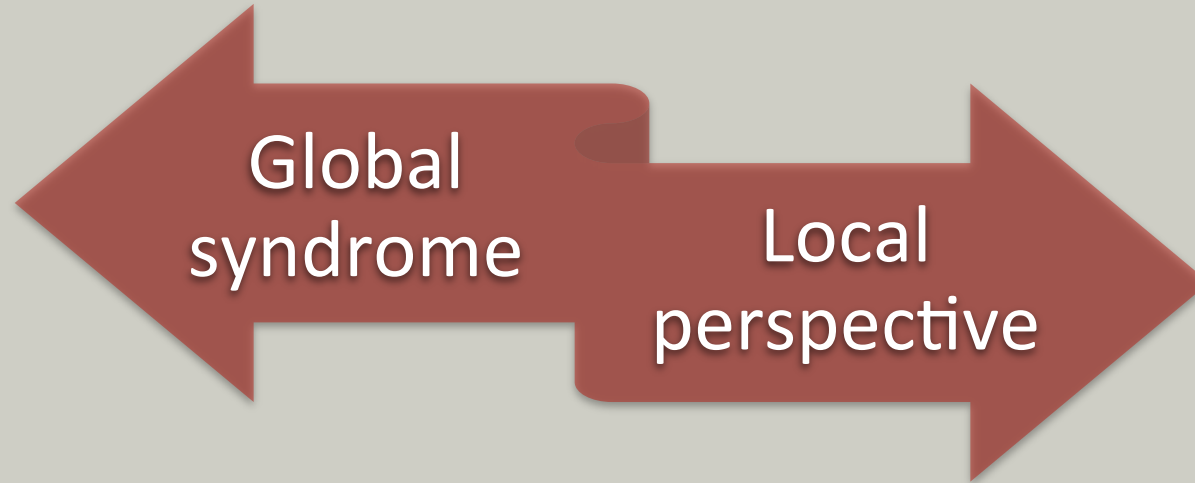
## Expert opinion

- Prescription sanctity
- Non-interchangeability
- Informed choice
- Shared decision making
- Health economics – long term costs, hidden/indirect costs
- Labelling
- Pharmacovigilance
- **Caution: look before we leap**
- **Safety first**

## Spot the err- - - error:



## Summary



### Therapeutic implication:

What is good for the goose  
may not be good for the gander