

## Physio-Friendly Remission-Facilitating Pharmacotherapy (PRP) in Type 2 Diabetes

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### Abstract

This brief communication describes the concept of physio-friendly pharmacotherapy for type 2 diabetes mellitus. Physio-friendly therapy is defined as that which restores metabolic, including glycaemic and weight homeostasis, to near normal levels. Drugs such as glucagon like peptide 1 receptor agonists (GLP1RA), sodium glucose co-transporter-2 inhibitors (SGLT2i), and alfa glucosidase inhibitors, along with metformin, work in a physio-friendly manner and may facilitate remission. Thus, they can also be termed as remission-facilitating drugs.

**Keywords:** Diabetes, relapse, remission, person centred care, type 2 diabetes

**DOI:** <https://doi.org/10.47391/JPMA.24-89>

### Introduction

As modern diabetes care continues to innovate and improve, our aims and aspirations tend to increase. One recent phenomenon is the concept of diabetes remission. Defined as an HbA1c < 6.5% (48 mmol/mol) measured at least 3 months after cessation of glucose-lowering pharmacotherapy,<sup>1</sup> remission is a controversial topic. While some commentators feel it is impractical, others view it as a motivational tool, and a beacon of hope. Experts suggest that remission should be the primary clinical goal of diabetes management.<sup>2</sup>

### Remission is Possible

Diabetes remission is a realistic target as well, provided proper patient selection is done.<sup>3</sup> The ABCDEFG mnemonic, based upon Lee et al's ABCD rubric,<sup>4</sup> provides a simple tool to identify persons with high probability of remission (Table 1). If remission is achieved even in a few persons, for a short period of time, this will result in massive long-term benefits. The reduction in chronic complications, with their associated morbidity, expenditure and mortality, is

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**Table-1:** The Diabetes Remission Probability Septad.

|   |
|---|
| <b>A</b> age - young adults                           |
| <b>B</b> body mass index - high                       |
| <b>C</b> C-peptide/pancreatic reserve - adequate      |
| <b>D</b> duration of diabetes - short                 |
| <b>E</b> energy and enthusiasm of patient - high      |
| <b>E</b> engagement and education – high              |
| <b>F</b> facilitatory family support - optimal        |
| <b>G</b> guided physio-friendly drug choice - optimal |

These are predictors of high probability of diabetes remission

advantageous for both individuals and public health.

### Facilitation of Remission

Physicians can facilitate remission in appropriately chosen type 2 diabetes patients by many ways (Table 2). One of these is to choose physio-friendly glucose-lowering therapy.<sup>3,5</sup> Physio-friendly drugs act by restoring metabolic homeostasis in a safe and sustainable manner. This includes not only glycaemic control, but homeostasis of weight, with associated behavioural and metabolic risk factors as well.

### Choice of Drugs

Modern glucose-lowering drugs, such as glucagon like peptide 1 receptor agonists (GLP1RA), sodium glucose cotransporter-2 inhibitors (SGLT2i), and alpha glucosidase inhibitors work in a physio-friendly manner.<sup>5</sup> All work, in differing ways, as calorie restriction mimetics, reduces the carbohydrate/caloric burden on the body. The risk of hypoglycaemia is minimal with these drugs. GLP1RA also enhance insulin secretion through a physiological incretin-mediated pathway. All three classes offer pleiotropic benefits as well, and have been proven to reduce cardiovascular outcomes at varying levels of dysglycaemia. GLP1RA are approved in different formulations and doses, for the management of not only diabetes, but obesity as well. In this manner, they are able to break the KgA1c paradox that is noted with conventional diabetes treatment.<sup>6</sup>

### Physio-Friendly Approach

Using these physio-friendly medications allows achievement of glycaemic control, along with multiple other benefits. The improvement in glucotoxicity (and weight) helps de-stress the beta cells, and brings the islets of Langerhans to near-physiological state.<sup>7</sup> This, in turn,

**Table-2:** Facilitation of Remission In Type 2 Diabetes: Physio-Friendly Psycho-Friendly Person-Friendly (PPP) Model.**Physio-Friendly Pharmacotherapy**

- Advise drugs with mechanism of action that is/are
  - Insulin-independent
  - Beta cell sparing
  - Low risk of hypoglycaemia
  - Weight reducing effect
  - Pleiotropic benefits/cardiovascular safety and protection
- Ensure regular exercise and dietary modification
- Initiate metformin with any of GLP1RA, SGLT2i, AGI as per requirement
- Obesity-reducing medications can be used as indicated
- Understand person-centric needs, wishes and preferences while prescribing pharmacotherapy

**Psycho-Friendly Partnership**

- Share information about remission in an
  - Accurate
  - Empathic
  - Interactive
  - Optimistic
  - Understanding and realistic manner
- Stress upon the
  - Advantages of good glucose control
  - Existence of physio-friendly medications
  - Importance of lifestyle modification and monitoring
  - Opportunities for health
  - Unique characteristics of each individual

**Person-Friendly Praxis**

- Agree upon desirable outcomes in terms of good health and happiness, rather than cessation of pharmacotherapy
- Explore potential facilitators and barriers to diabetes care
- Initiate appropriate lifestyle and medical management, with vascular risk reduction
- Observe/monitor regularly, and titrate/ therapy as required
- Undertake to continue monitoring and lifestyle modification even after pharmacological remission has been achieved.

reduces the dose requirement of glucose-lowering drugs, and may facilitate remission. The duration of remission usually depends upon adherence to prescribed lifestyle changes.

**Psycho-Friendly Approach**

The other way of facilitating remission is to offer therapeutic patient education (TPE) in a psycho-friendly manner. Accurate and appropriate, information about diabetes should be shared. One should always use salutogenic language, focussing on the advantages of good glucose and weight control, rather than the risk of complications. Discussion on remission should be conducted with an optimistic, but realistic attitude.

**The First Thousand Days**

One way of counselling persons with newly detected diabetes is to view this as the beginning of a new life, rather than the end of life. Just as a new born child needs tender, loving care, so does a person with newly detected diabetes. The first 1000 days of this life determine not only short term, but long-term outcomes as well. Using physio-friendly medication to achieve safe and positive glycaemic legacy, which improves cardiovascular and renal health, and extends longevity. Such a conversation sets the stage for acceptance of and adherence to, suggested therapy. Psycho-friendly language also promotes patient physician bonding and improves satisfaction with health care.

**Summary**

Diabetes remission in type 2 diabetes has been shown to be a practical target in newly diagnosed young overweight/obese adults with type 2 diabetes, who have adequate C-peptide reserve. Remission can be facilitated by using physio-friendly medication, coupled with psycho-friendly communication and counselling.

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