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LETTER TO THE EDITOR

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From bench to bedside: future prospects in stem cell therapy for diabetes

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To the editor:

Diabetes is characterized by hyperglycemia resulting from insulin secretion or action disorders. As a chronic metabolic disease, diabetes has been identified by the World Health Organization as a major global health threat, affecting individual quality of life, public health, and the global economy [1, 2]. It is projected that by 2050, the number of diabetes patients will increase from 529 million in 2021 to 1.31 billion. Since the advent of induced pluripotent stem cell (iPSC) technology a decade ago, significant progress has been made in stem cell biology and regenerative medicine research. iPSCs have been widely applied in disease modeling, drug discovery, and cell therapy, demonstrating immense therapeutic potential [3]. Recently, an article in the journal Cell reported that pancreatic islet cells derived from chemically induced pluripotent stem cells (CiPSCs) were successfully transplanted into the subrectus sheath of the abdomen of a patient with type 1 diabetes mellitus (T1DM), achieving all safety and efficacy benchmarks during a 1-year follow-up period [4]. Another Chinese research group reported in Cell Discovery that they successfully transplanted insulin-producing programmed pancreatic stem cells into the liver of a patient with type 2 diabetes mellitus for 25 years of disease duration, who subsequently stopped using insulin. These studies are pioneering trials of stem cell therapy for diabetes, marking significant progress in the clinical translation of stem cell therapies [5].

We searched the Informa database (https://pharma.id.informa.com/), China Clinical Trial Registration Platform (http://www.chinadrugtrials.org.cn/index.html), and U.S. Clinical Trial Registry (https://clinicaltrials.gov/) for clinical trials on stem cell therapies for diabetes, limited to September 31, 2024. We screened and ultimately identified 143 clinical trials of stem cell therapies for treating diabetes. This study analyzes the trends in the number, types, clinical stages, indications, and other parameters of these clinical trials to explore the efficacy and applicability of stem cell therapies and identify effective treatment strategies for diabetes.

From 2000 to 2024, the number of clinical trials for stem cell therapies for diabetes experienced fluctuations, peaking in 2009–2010, 2017, 2019, and 2022. These 143 clinical trials are distributed across 31 countries, with China dominating (47 trials, 33.3%). Most trials are in phases I–II (119 trials, 83.2%), with only a few reaching phases III/IV (16 trials, 11.2%), indicating that the field is still in its early exploratory stage. A total of 19 trials (13.3%) are ongoing, 21 trials (14.7%) have been terminated, and 87 trials (60.8%) have been completed (Fig. 1).

T1DM is an autoimmune disease characterized by the immune system attacking insulin-producing β-cells, leading to insulin deficiency and altered gut microbiota. In contrast, T2DM is caused by insulin resistance and gradual insulin secretion reduction due to metabolic factors. In clinical trials of stem cell therapies for diabetes, T1DM accounts for the majority (99 trials, 69.2%). With innovations incellular therapies and drug delivery technologies, drug products combined with stem

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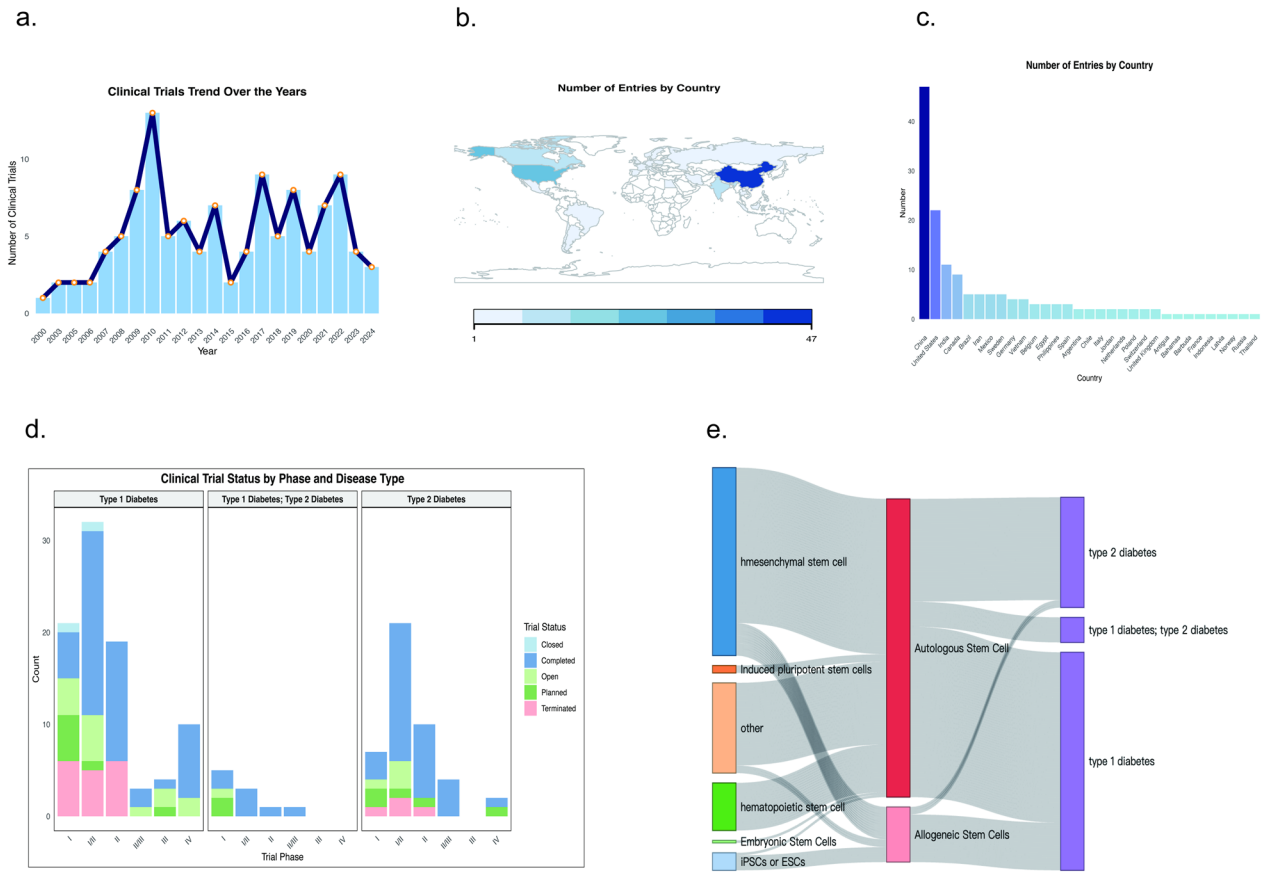

Fig. 1 Analysis of Clinical Trials for Stem Cell Therapies in Diabetes from 2000 to 2024: **a** Start of clinical trials of stem cell therapy for diabetes between 2000 and 2024. **b** Global distribution of clinical trials, with darker blue indicating higher registration numbers. **c** Number of registered clinical trials by country, ranked from highest to lowest. **d** The figure shows the distribution of the number of clinical trials for different types of diabetes (type 1 diabetes, combination of type 1 and type 2 diabetes, type 2 diabetes) in different phases (phase I, I/II, II, II/III, III, IV) and the status of the trials in each phase in the form of bar charts. **e** TheSankeydiagram demonstrates the therapeutic flow and distribution ratios between stem cell types (e.g., MSCs, induced pluripotent stem cells), source (autologous or allogeneic stem cells), and type of diabetes (type 1 diabetes, type 2 diabetes, and combinations thereof)

cell therapies are becoming increasingly popular. Such as VC-01, VC-02, VX-880, VCTX211, VCTX210Afor T1DM have emerged (Table 1). In comparison, stem cell therapies for T2DM started later, with 54 clinical trials since 2006.

Mesenchymal stem cell therapies constitute the majority of stem cell therapies (75 trials, 52.4%), sourced from bone marrow, adipose tissue, umbilical cord, dental pulp, and muscle, followed by hematopoietic stem cell therapies (19 trials, 13.3%) and induced pluripotent stem cell therapies (12 trials, 8.4%), and embryonic stem cell therapies(10, 6.9%). For the treatment of diabetes, only 24 trials (16.8%) documented allogeneic stem cell therapy.

The use of stem cell therapy in diabetes treatment has been preliminarily validated through several preclinical studies and a limited number of clinical cases, showing potential, especially in immunomodulation and β-cell function restoration. Breakthroughs in induced pluripotent stem cell (iPSC) technology have provided a new direction for diabetes treatment; however, available clinical data focus on short-term efficacy (1–2 years), and there is a lack of sufficient evidence for long-term efficacy, especially the sustainability of β-cell function recovery. Although stem cell therapy shows remarkable promise, it still faces several challenges such as immune rejection, the durability of efficacy, and tumor risk. Too advance the clinical application of stem cell therapy in diabetes, future research should focus on the long-term efficacy and safety of stem cell therapy, the prevention and management of immune rejection, as well as its economic feasibility, to promote the maturity of this innovative therapy and revolutionize the treatment options for diabetes patients.

Table 1 Summary of registered clinical trials involving stem cell therapy for diabetes

Product	Introduction	Protocol/Trial ID	Trial phase	Trial status	Disease	Countries
VC-01		NCT04678557	I/II	Terminated	Type 1	United States
VC-01	Pancreatic Endodermal Cells (PEC-01) with Recyclable Semi-Permeable Encapsulated Device Drug Delivery System	NCT02939118	II	Completed	Type 1	Canada; United States
VC-01		NCT02239354	I/II	Terminated	Type 1	Canada; United States
VC-02		NCT03162926	I	Completed	Type 1	Canada
VC-02	Improved vascularization and immunoprotection based on VC-01	TrialTroveID-364656	I	Terminated	Type 1	Belgium
VC-02		NCT03163511	I/II	Completed	Type 1	Belgium; Canada; United States
VCTX210A	Pancreatic endodermal cells (PEC210A) derived from human embryonic stem cells (hESC) were used and genetically modified by CRISPR/Cas9 technology	NCT05210530	I	Completed	Type 1	Canada
VCTX211	VCTX211 is a human embryonic stem cell (hESC)-based pancreatic endodermal cell (PEC) product cell therapy and genetic engineering technology	NCT05565248	I/II	Open	Type 1	Canada
VX880	VX880 is a fully differentiated hESC-derived islet cell product	NCT04786262	I/II	Open	Type 1	Canada; France; Germany; Italy; Netherlands; Norway; Switzerland; United Kingdom; United States

Supplementary Information

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Supplementary Material 1.

Supplementary Material 2.

Supplementary Material 3.

Supplementary Material 4.

Supplementary Material 5.

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Availability of data and materials
All data generated or analyzed during this study are included in this published article.

Declarations

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Not applicable.

Consent for publication
Not applicable.

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The authors declare that they have no competing interests.

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