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Descriptive Report:
The Presidential Initiative for Diagnosis, Registry, and Management of Spinal Muscular Atrophy Patients in Egypt

Prepared for
The Ministry of Health and Population (MOHP)

١٠٠ مليون صحة

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PREFACE

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ABSTRACT

Background and Objectives:

In Egypt the substantial political will have recently been seeking to improve the population health. This political will was translated into launching more than 15 national healthcare initiatives addressing Egypt's highest priority health issues. In response to the high burden on Spinal Muscular Atrophy (SMA) patient mainly financially due to the high cost of innovative clinical management and also lack of access to newly available innovative treatments, in July 2021, the Egyptian government launched a new health initiative aiming at an early and accurate diagnosis, registration, multidisciplinary management, and treatment of SMA patients. This descriptive report aims to illustrate the initiative methodology, steps and achievement till date of publishing 31st of July 2022.

Methodology:

A total of 24 specialized clinics were set up and funded by the national health insurance system . More than 200 laboratories and EMG testing centers covering all geographic areas in Egypt are defined to serve patients from the local SMA clinics.
The medical assessment for presenting patients is divided into three steps. The first is the physical examination and family history required to suspect SMA diagnosis, The second is the medical and laboratory investigations, and third is the genetic testing using the quick SMA-Polymerase Chain Reaction to detect SMN1 gene deletions, innovative treatments were available after managed entry agreements (MEA) between the Egyptian government and marketing authorization holders for these drugs and will begin with phase 1 of patients younger than 2 years old. This descriptive report was done from the SMA national committee reports, logs and patients records.

Results:

From the program kick-off on in July 2021 till end of July 2022 ,12,300 patients visited the 24 local clinics seeking diagnosis and treatment. Out of the 204 cases younger than 2 years old, 36 have received treatment as of May 6.

Conclusion:

The SMA initiative that was implemented in Egypt sought to improve patients' residual muscle function, slow the progression of the disease, and extend patients' quality of life. It also aimed to decrease the societal and economical burden incurred by the SMA.



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1. Introduction

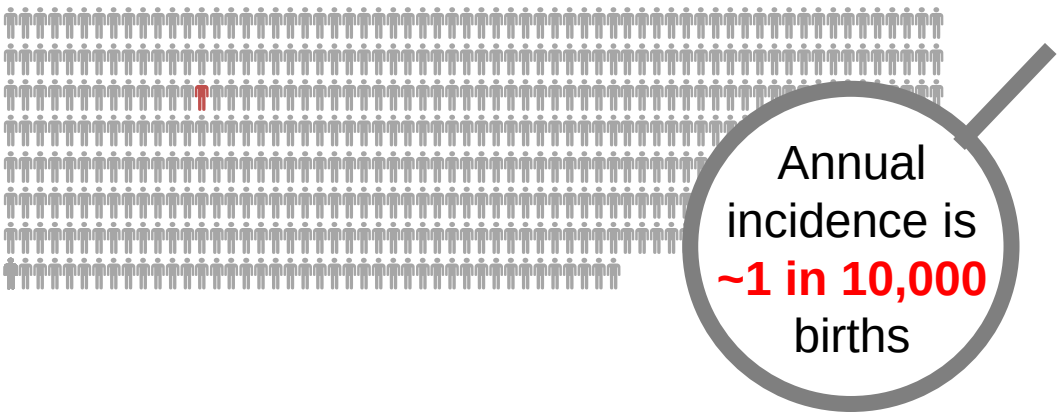
INTRODUCTION

Spinal muscular atrophy (SMA) is a rare inherited autosomal recessive neuromuscular disorder characterized by degeneration of motor neurons in the spinal cord and lower brain stem. can lead to severe and progressive muscular atrophy, loss of breathing and swallowing, and early death.

Worldwide Prevalence studies are scarce, but in most cases a prevalence of around

1–2 per 100,000 persons

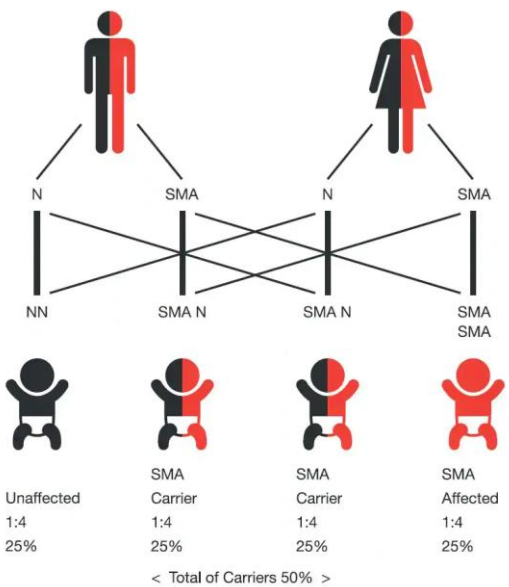


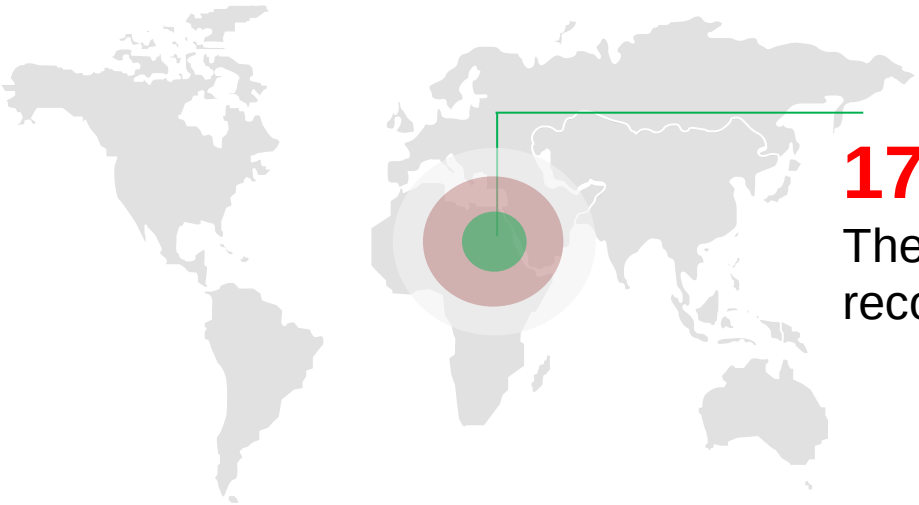


SMA prevalence in some studies was calculated of 6.56 per 100,000 persons aged less than 20 years in Italy, was estimated to occur with an incidence ranging from 1:6,000 to 1:10,000 in newborns, making it the most common fatal hereditary disease in children [1,2]

The majority of mutations responsible for SMA are either deletions or gene conversions. The complication in identifying carriers of SMN1 mutations is that humans have two nearly identical copies of SMN1 and SMN2 located on Chromosome 5 [3]

Having a child affected by SMA occurs in a pregnancy between two SMA carriers or between a SMA carrier and a person living with SMA. Two carrier parents can produce children who would be affected, carriers, or non-carriers.[4]





17.7/100,000

The frequency of SMA recorded in a local study

No Accurate epidemiological study was done in Egypt but experts estimate a higher incidence than the globe

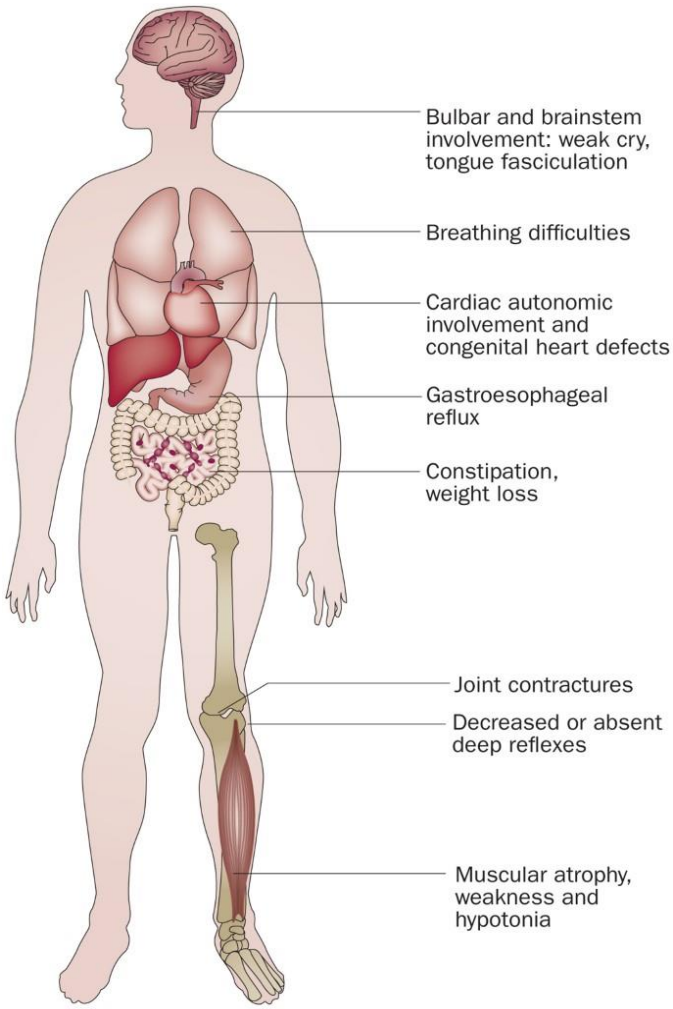
In Study at the Paediatric Hospital, Ain-Shams University during the period (year 1966–2009). The study included 117 patients with SMA out of 660,280 patients attending the Paediatric Hospital. Frequency of SMA was 17.7/100,000, which is considered high. Type I was the commonest type (60.6%), followed by type II (26.79%), and type III (8.8%). Consanguinity was reported in 45.5 and family history in 47.8% of patients. [5]

Type	Age of onset	Requires respiratory support at birth	Able to sit	Able to stand	Able to walk	Life expectancy
0	Prenatal	Yes	No	No	No	<6 months
1	<6 months	No	No	No	No	<2 years
2	6 to 18 months	No	Yes	No	No	10 to 40 years
3	>18 months	No	Yes	Yes	Assisted	Adult
4	>5 years	No	Yes	Yes	Yes	Adult

INTRODUCTION

SMA is a multi-organ disease, in a 2011 Study in Egypt, clinical presentation were recurrent chest infection, hypotonia and weakness in all type I patients (67.5%) secondary inability to walk in all type II patients (27.3%), and weakness and difficulty in walking in all type III patients (5.2%). All type I patients presented with profound weakness and hypotonia, but wasting was not marked because of early death.

Early diagnosis is the key in SMA management, which was done previously only by conservative management till the innovative therapies recently emerged.



A multidisciplinary approach is key to SMA management, monitoring various aspects involved in disease progression and providing anticipatory care.

- Pulmonologist
- Neurologist
- Physiotherapist
- Psychologist
- Orthopaedic
- Nutritionist
- Gastroenterologist
- Speech therapist

Several health interventions are now available that allow the patients with the most severe SMA phenotypes who previously would not live beyond their second year can now achieve motor milestones, such as sitting, standing, or even walking in some cases[6]

Unfortunately, Innovative health interventions come at prices beyond a typical family's affordability, especially in low- and middle-income countries.

Pharmacological treatment are mainly:

Onasemnogene abeparvovec	Nusinersen	Risdiplam
zolgensma® (onasemnogene abeparvovec-xioi)	SPINRAZA® (nusinersen) injection 12 mg/5 mL	Evrysdi® risdiplam 60 mg powder for oral solution

The intrathecally administered Nusinersen, the oral Risdiplam, and the one-time intravenous gene replacement therapy Onasemnogene Abeparvovec.10 All the three drugs have obtained both FDA and EMA approvals. 11 Irrespective of the drug used, recent evidence suggests the treatment success depends mainly on early use before or just after the appearance of the first symptoms. [7]

Treatments come at a price way beyond the family affordability even with higher socio-economic class and needs the health sector intervention for treatment access

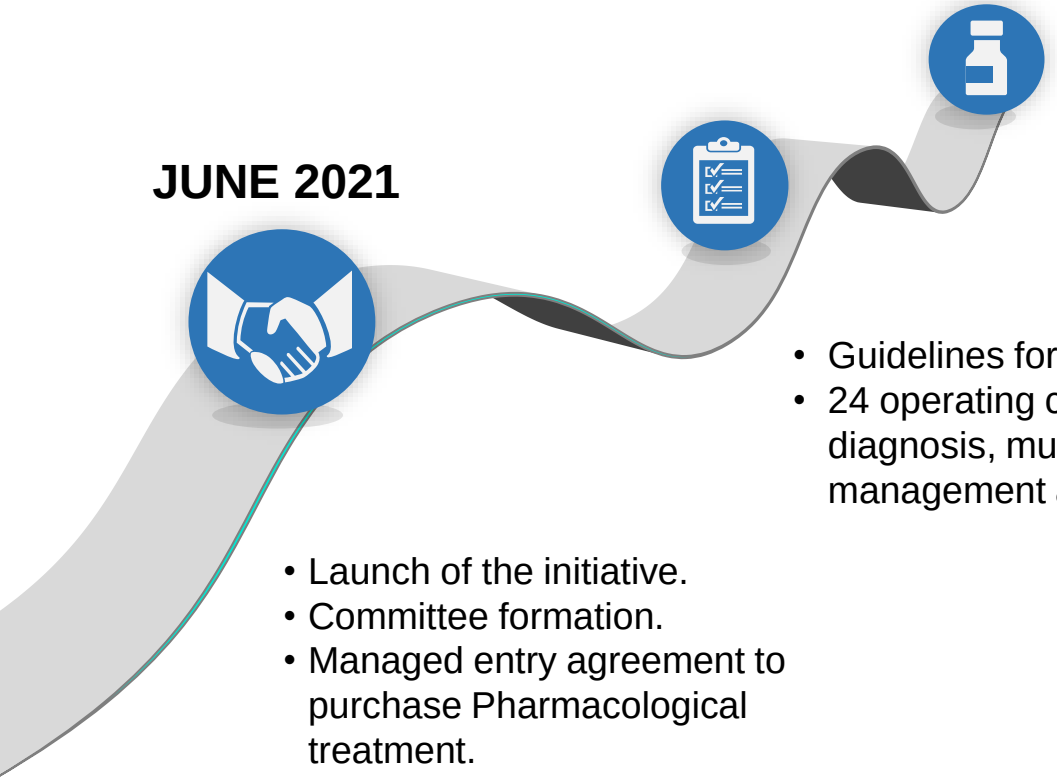


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2- SMA Initiative Specifications

OBJECTIVE AND CONTEXT

Ensure all treatment eligible SMA patients are receiving best in class management including innovative treatments reaching the global standards in treatment outcomes.



JUNE 2021

- Launch of the initiative.
- Committee formation.
- Managed entry agreement to purchase Pharmacological treatment.

- Guidelines formation
- 24 operating clinics for diagnosis, multidisciplinary management and treatment

MAY 2022

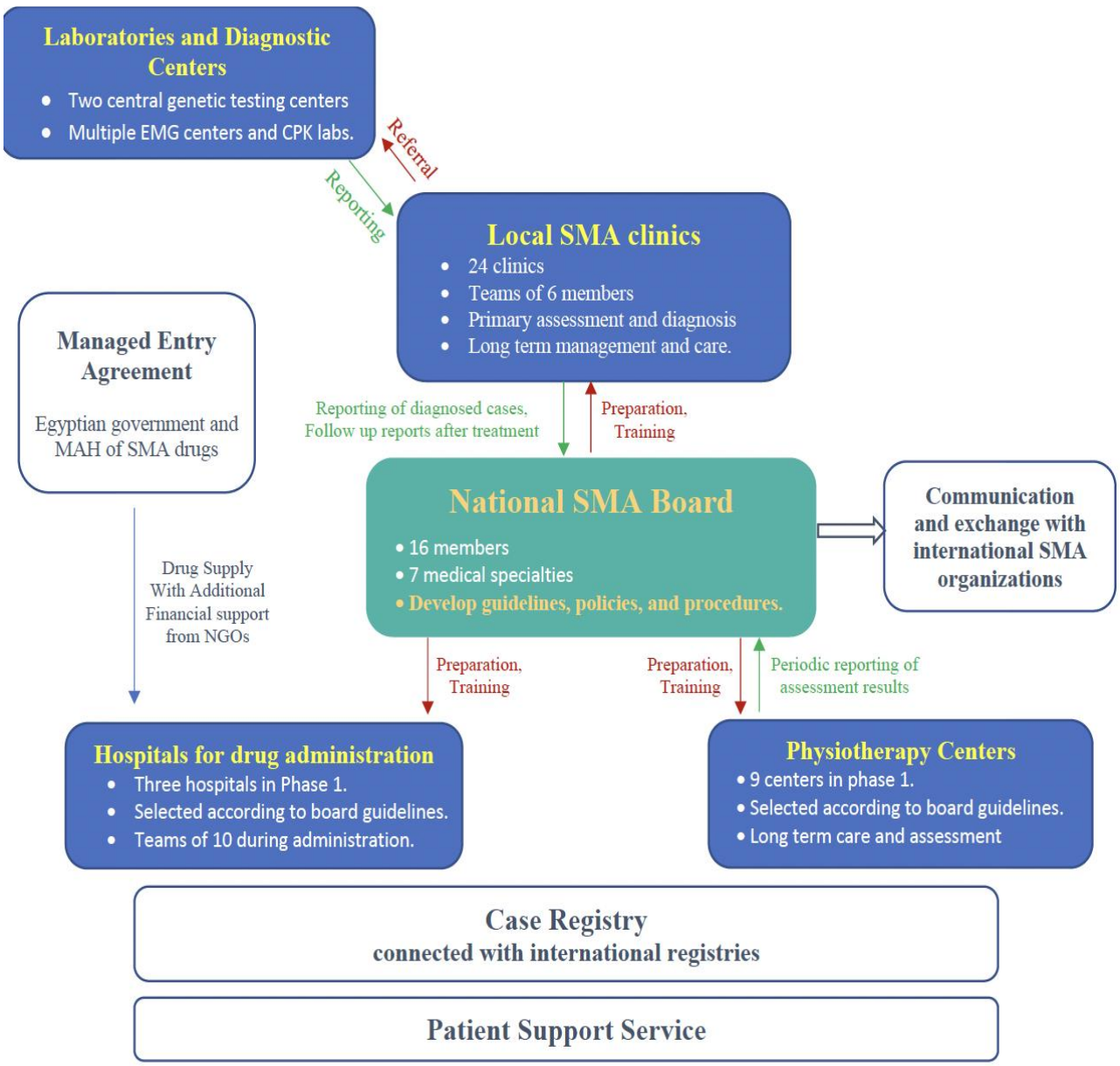
- **36 patients** less than 2 years have **received treatment**

Initiative milestones to identify and treat SMA patients

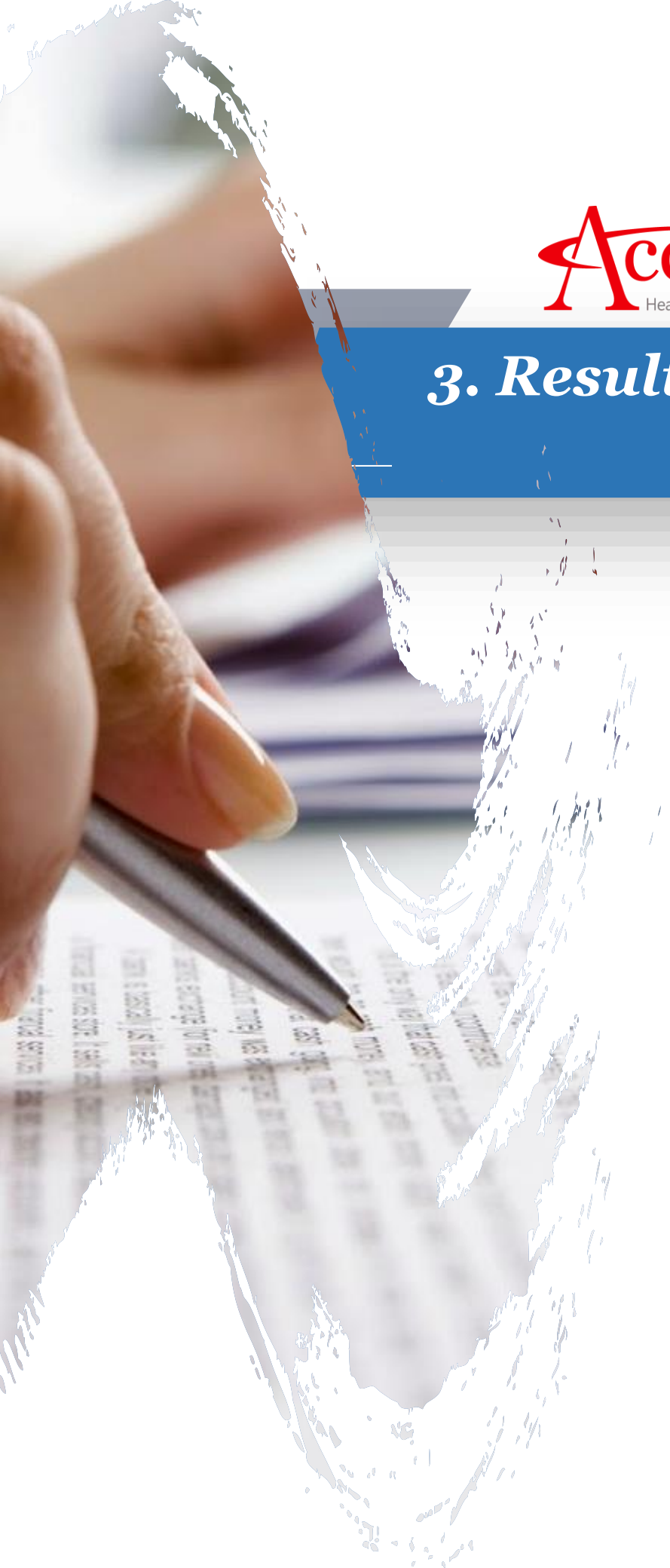
PROGRAM FLOWCHART

The initiative began with national SMA board responsible for:

- Legislation, board formation, and guidelines development
- Preparation of medical facilities and the working staff
- Access and use of SMA treatments
- Patient registry and support services



Initiative program flowchart



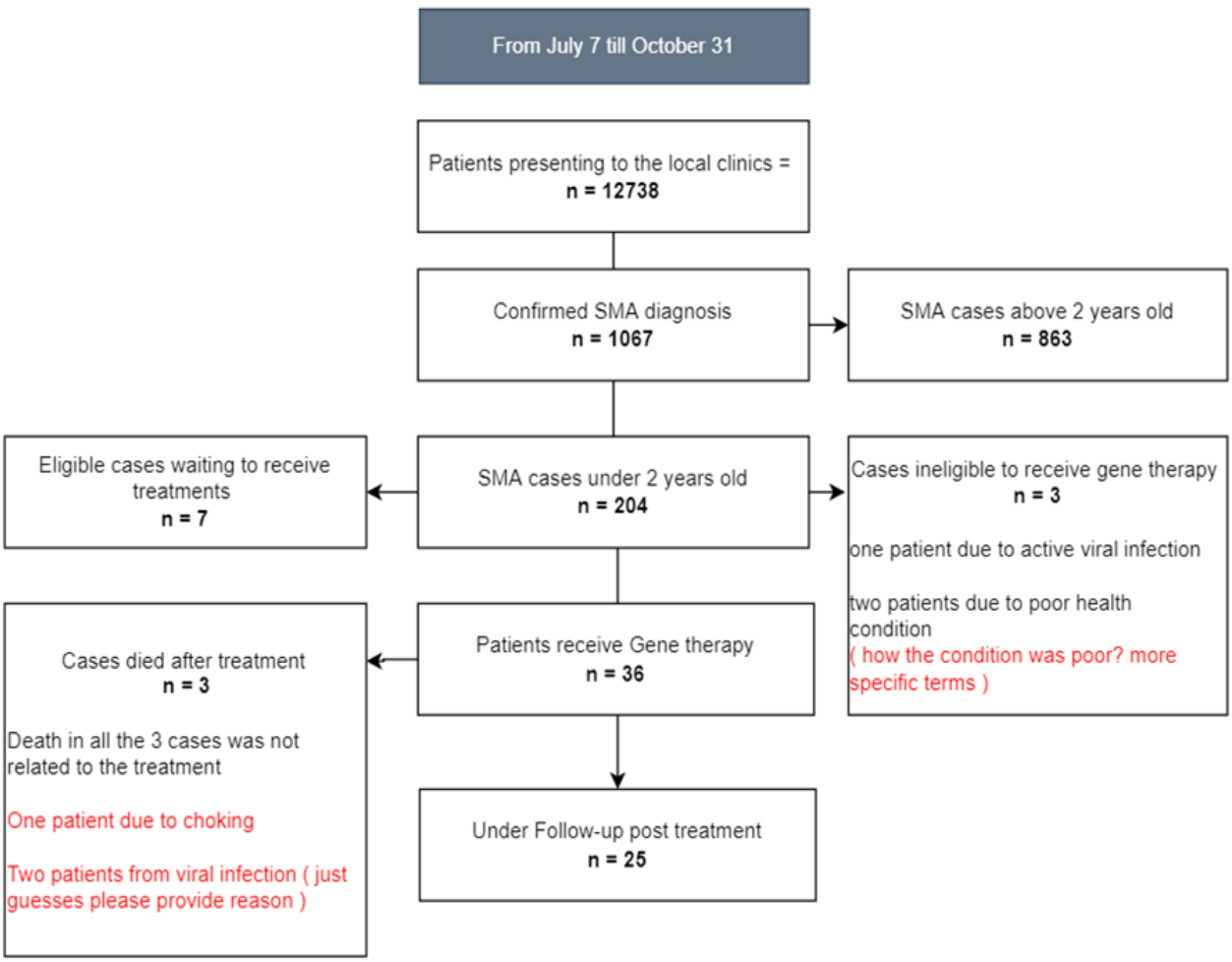
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3. Results

INITIATIVE RESULTS

From the program kick-off in July 2021, **12300 patients visited the 24 local clinics seeking diagnosis** and treatment. Based on the physical and genetic assessment, **1067 received a genetically confirmed diagnosis of SMA**. The mean age of SMA confirmed cases was 7.3 (± 7.63), ranging from 5 weeks to 57 years old. There are 204 patients below the age of 2, representing 19% of the cases and 81% above two years. Of all cases, 5.3% were older than 18 years. There were 652 male patients (61%) and 415 females (39%).

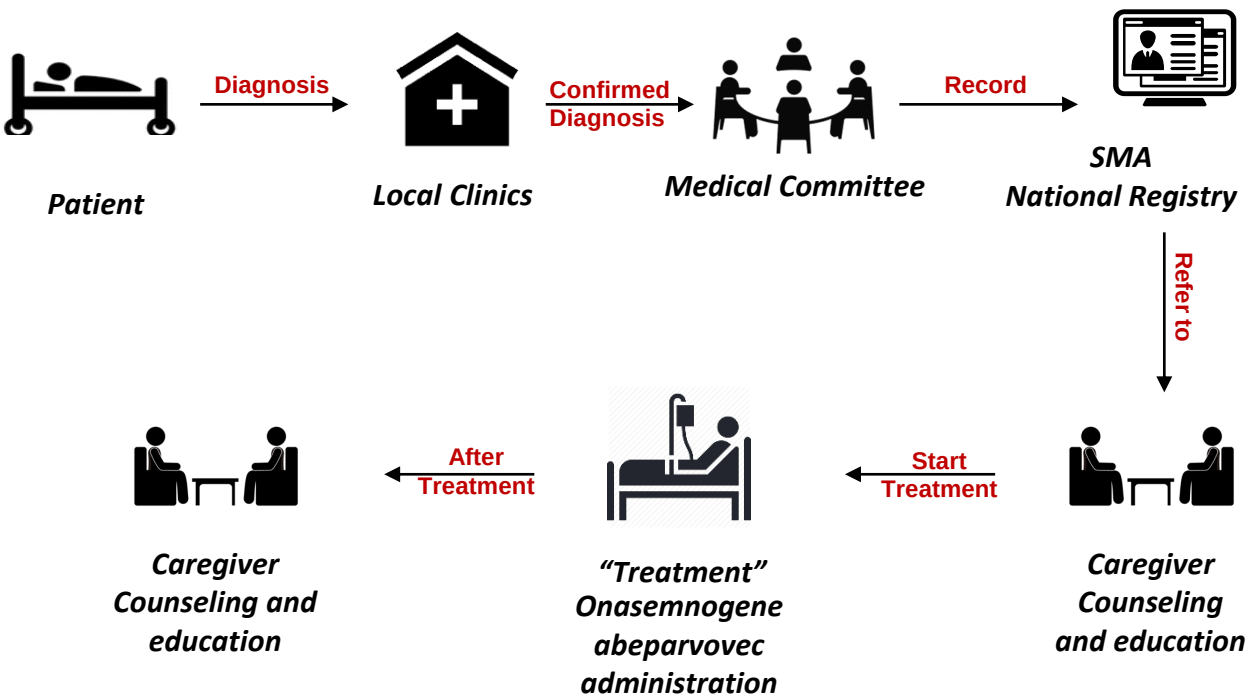
Out of **the 204 cases younger than 2 years old, 36 have received treatment**. Three patients were prepared for treatment but excluded due to active viral infection or poor general health condition . Of the treated cases, three have died after injection. Clinical assessment revealed no relation between death events and the medication.



Initiative Patient Flow

The treatment already used in the program is the gene therapy intravenous onasemnogene abeparvovec. This is considered the first phase, then Nusinersen, is planned to be supplied for 100 to 150 children every year in phase 2 as well as ongoing negotiations to include Risdiplam as well.

All patients with confirmed SMA diagnosis who visited the local clinics are recorded in a newly established national registry connected with the global SMA registry.
All eligible cases referred from the local clinics were discussed in the national SMA board for confirmatory assessment, prioritization, and final decision-making to start drug treatment. The board also defined three main recommendations before and after receiving gene therapy.



Patient Journey

RECOMMENDATIONS

Despite the high price, obstacles of access, the program managed to reach significant patients in the first year, ensuring correct and proper diagnosis, administrating the gene therapy on time, and follow the guidelines. A continuity of the program is recommended with extension to the other treatment with economically suitable managed entry agreement (MEA), as long as it meets the allocated budget.



Preventive campaign by premarital screening



Include treatments for more than 2 years old with economically efficient MEA



1ST

Continue leadership in diagnosis, multidisciplinary management and treatment with more center of excellence clinics



Safety & Tolerability profile evaluated in large scale safety study, Ongoing patient reported outcome studies and registry for QoL tracking

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