Early Detection of 5 Neurodevelopmental Disorders of Children and Prevention of Postnatal Depression by Mobile Health App: An Observational Cross-Sectional Study

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Abstract

Background: Delay in the diagnosis of neurodevelopmental disorders (NDDs) of toddlers and postnatal depression (PND) is a major public health issue. In both cases, early intervention is crucial but too rarely implemented in practice.

Objective: Our goal was to determine if a dedicated the mobile app can improve screening of 5 NDDs (autism spectrum disorder (ASD), language delay, dyspraxia, dyslexia and attention deficit hyperactivity disorder (ADHD)), and reduce PND incidence.

Methods: We performed an observational, cross-sectional, data-based study in a population of young parents with a minimum of 1 child under 10 years of age at the time of inclusion and using Malo on a regular basis. We included between May 1, 2022, and February 8, 2024. the first 50,000 users matching the criteria and agreeing to participate. Parents received via the app, periodic questionnaires assessing skills on neurodevelopment domains. Mothers accessed a support program to prevent PND and were requested to answer regular questionnaires regarding PND. When any patient-reported outcomes matched predefined criteria, an in-app notification was sent to the user, recommending the booking of an appointment with their family physician or pediatrician.
The main outcomes were the median age of the infant at the time of notification for possible NDD and the incidence of PND detection after childbirth. One secondary outcome was the relevance of the NDD notification by a consultation as assessed by health professionals.

Results: Among 55,618 children with median age of 11-months, 439 (0,8%) had at least 1 disorder for which a consultation was critically necessary. The median age of notification for probable ASD, language delay, dyspraxia, dyslexia and ADHD was 32.5, 16, 36, 80 and 61 months, respectively. The sensitivity of the alert notifications of suspected NDDs as assessed by the physicians was 78.6%, and the specificity was 98.2%. Among 8,243 mothers who completed a PND questionnaire, highly probable PND was detected in 938 (11.4%) mothers corresponding to a reduction of -31% versus our previous study without support program).

Conclusions: The algorithm-based alert suggesting NDD was highly specific with good sensitivity as assessed by real-life practitioners. The app was efficient in the early detection 5 NDD and PND and in possible reduction of PND incidence. Clinical Trial: NCT06301087

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Abstract (448 words)

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938 (11.4%) mothers corresponding to a reduction of -31% versus our previous study without support program). The median time of detection of suspected PND was 96 days after childbirth. Among 130 users who filled in the satisfaction survey, 99.2% (129/130) found the application easy to use, 70.0% (91/130) reported that the app improved the follow-up of their child. Moreover, the application was rated 4.8-4.7/5 on iOs-Android Stores.

Conclusions: The algorithm-based early alert suggesting NDD was highly specific with good sensitivity as assessed by real-life practitioners. The app was efficient in the early detection 5 NDD and PND and in possible 31% reduction of PND incidence.

Trial Registration: ClinicalTrials.gov NCT06301087; https://clinicaltrials.gov/ct2/show/NCT06301087

Keywords: early detection; NDD; neurodevelopmental disorders; ASD; autism spectrum disorder; attention deficit hyperactivity disorder; ADHD; PND; postnatal depression; mHealth; mobile health; real-world study; smartphone; mobile phone

Introduction

After birth, the mother-child dyad can be impacted by impairments that remain undetected or are detected too late. Among these impairments, a neurodevelopmental disorder (NDD) such as autism spectrum disorder (ASD) affects 1 in 166 children [1]. The average time to diagnosis is approximately 4 to 6 years, whereas consensus statements indicate that a diagnosis could be made as early as 12 or 18 months of age [2-6]. Interestingly, parents are the main contributors to the NDD screening of their children [7]. Other disorders that deserve early screening are dyspraxia, language delay, dyslexia and attention deficit hyperactivity disorder (ADHD) [8-11]. It is crucial to provide parents with screening tools and to recommend that they consult the physician at the first symptoms to treat them as earlier as possible.

Postnatal depression (PND) of mothers is another example of an underdiagnosed disorder with severe consequences. PND—an episode of depression occurring during the first year after childbirth—has a prevalence of 17% and may have a negative impact on the synchrony or receptivity loop that is crucial to the proper neurodevelopment of the baby [12,13].

All these disorders can benefit tremendously from early detection by electronic patient-reported outcomes (ePRO) questionnaires for parents and their children, which would enable early intervention.

We thus developed Malo, an “all-in-one” multidomain digital health record ePRO app for smartphones, aiming to facilitate early screening of NDDs in children from birth to age 10 years and PND in mothers. We previously reported results of a first observational, cross-sectional, data-based study in a population of 4,242 children in 2022, showing a sensitivity of the alert notifications of suspected NDDs (possible autism spectrum disorder, vision,

audition, socialization, language, or motor disorders) as assessed by the physicians of 100%, and a specificity of 73.5%. We also reported an earlier detection of PND in 907 mothers showing an incidence rate of 16.6%. [14] Since these results, changes in algorithms were performed to improve specificity of NDD screening to avoid false positive results and we added early and continuous advice and support program after childbirth to mothers to reduce incidence of PND.

We thus report here the results of the revised algorithm aiming to be more specific for the screening of 5 NDD (ASD, language delay, dyspraxia, dyslexia and ADHD) and to assess the impact of the application and support program on the reduction of PND incidence.

Methods

Ethical considerations

We ran an ecological, observational, cross-sectional, data-based study. Our study was approved by the French National Health Data Institute (HDH approval number 16562971), which ensures ethical conduct in human subject research regarding data confidentiality and safety. The approval number for our human subject's review was F20210420115840. The study was conducted in compliance with good epidemiology practices defined by the association for French Speaking Epidemiologists. Users received written information on this study and did not object. Electronic informed consent was necessary to authorize the reporting of data for the study as well as inclusion criteria.

Data collection was embedded in the app. Data were anonymously collected in a French labelled health data cloud. Respondents anonymously self-entered the age and gender of their infants. The app also allowed for the entry of the children's height, weight, vaccination status, medical background, and ongoing or previous treatments.

No compensation was provided to subjects in this study.

Population

Malo is a mobile health app' application available on iOS and Android app only available in France.

The kick-off of the first version of application was historically initiated by a French national media campaign that was disseminated through social media between November 11 and 18, 2021. Details of kick-off modalities are provided in Denis et al article. [14] The places of recruitment were multiple: maternity units, day-care centers, social media and insurers.

For the current study, we included between May 1, 2022 and February 8, 2024, 55,618

users matching the criteria and agreeing to participate. Enrollment in the study was strictly optional. Recruitment was open with no exclusion criteria. The inclusion criteria were to download the app, to have at least one child at least 10 and to provide informed consent (in-app). We extended the inclusion age of children up to 10 years to allow assessment of the incidence of DYS disorders which can occur during this period.

Data Collection

Questionnaires and scales, each containing 25-50 questions assessing neurodevelopment skills, were automatically submitted every month from birth to 9 months, then at 11, 12, 16, 18, 21, 24, 30, and 36 months and every 6 months until 10 years of age. Questionnaires were focused on sociability, attention/activity, motricity, language of their infants, and possible autism spectrum disorder to screen for ASD, language delay, dyspraxia, dyslexia, and ADHD.

Questionnaires and notifications were based on French health authorities' reports, international recommendations, and experts' agreements [15-17].

The questionnaire for the screening of postnatal depression was submitted to mothers every 2 to 4 weeks for 7 months after childbirth, using a modified questionnaire of the Edinburgh Postnatal Depression Scale adapted to self-assessment.

Threshold-Based In-App Notification and Outcome of NDDs module of the app.

Notifications were sent automatically to the user if some symptoms matched predefined criteria and a physician consultation was recommended.

Regarding NDDs, once a threshold of concern was reached, a notification was sent recommending that the mothers discuss their symptoms with their general practitioner or pediatrician.

The main outcome of the study was the median age of possible NDD notification of infants. The secondary outcomes were : (1) user satisfaction regarding app experience and the level of support in child follow-up; (2) relevance of the NDD notifications assessed by physicians, using a specific optional survey asking parents the following questions:

- In the past month, did your doctor detect a developmental disorder in your child during a follow-up consultation? YES/NO
- If you had a notification by Malo, did you follow the recommendation of the app to visit a physician? YES/NO
- Which of the following reflects the physicians' reply? (A) The notification is not relevant, (B) the notification is relevant and a medical surveillance of the evolution of the symptom is needed, (C) The advice of an expert is needed, or (D) a treatment is indicated.

Threshold-Based In-App Notification and Outcome of PND module of the app.

Regarding maternal postnatal depression (PND), there were 4 grades of notifications sent to the mother: grade 0 (score lower than 25) was associated with a message indicating that

everything is ok; grade 1 (score between 26 and 50) was associated with a recommendation to talk about symptoms with a close relative; grade 2 (score between 51 and 65) recommended that they quickly discuss their symptoms with a family doctor; and grade 3 (score higher than 65) recommended that they meet a family doctor as soon as possible. Grades 2 and 3 were considered at high probability for PND. This algorithm and questionnaire were the same as those used in our previous study. [14]

To reduce PND incidence, we added, since 2022, a support program in the current version of the application with early and continuous advice after childbirth to lead parents to take care of their mental burden and to be aware of burnout and postnatal depression. We also provided them with the option of joining speaking groups and accessing testimonials from other mothers.

The last secondary outcome was the rate and the median time of the mothers' PND notifications after childbirth subsequently to the support and prevention program.

Analysis

The analysis was performed on the 55,618 users matching criteria were assessable for analysis and at least 1 neurodevelopment disorder strongly requiring a consultation was observed in 439 children.

Sensitivity, specificity, predictive positive and negative values, and the Youden index of algorithms triggering notifications of suspected NDDs were calculated according to the physician's feedback. A notification was considered relevant if a physician suggested a specific medical surveillance of the disorder or the consultation of an expert or a therapist or initiated therapy.

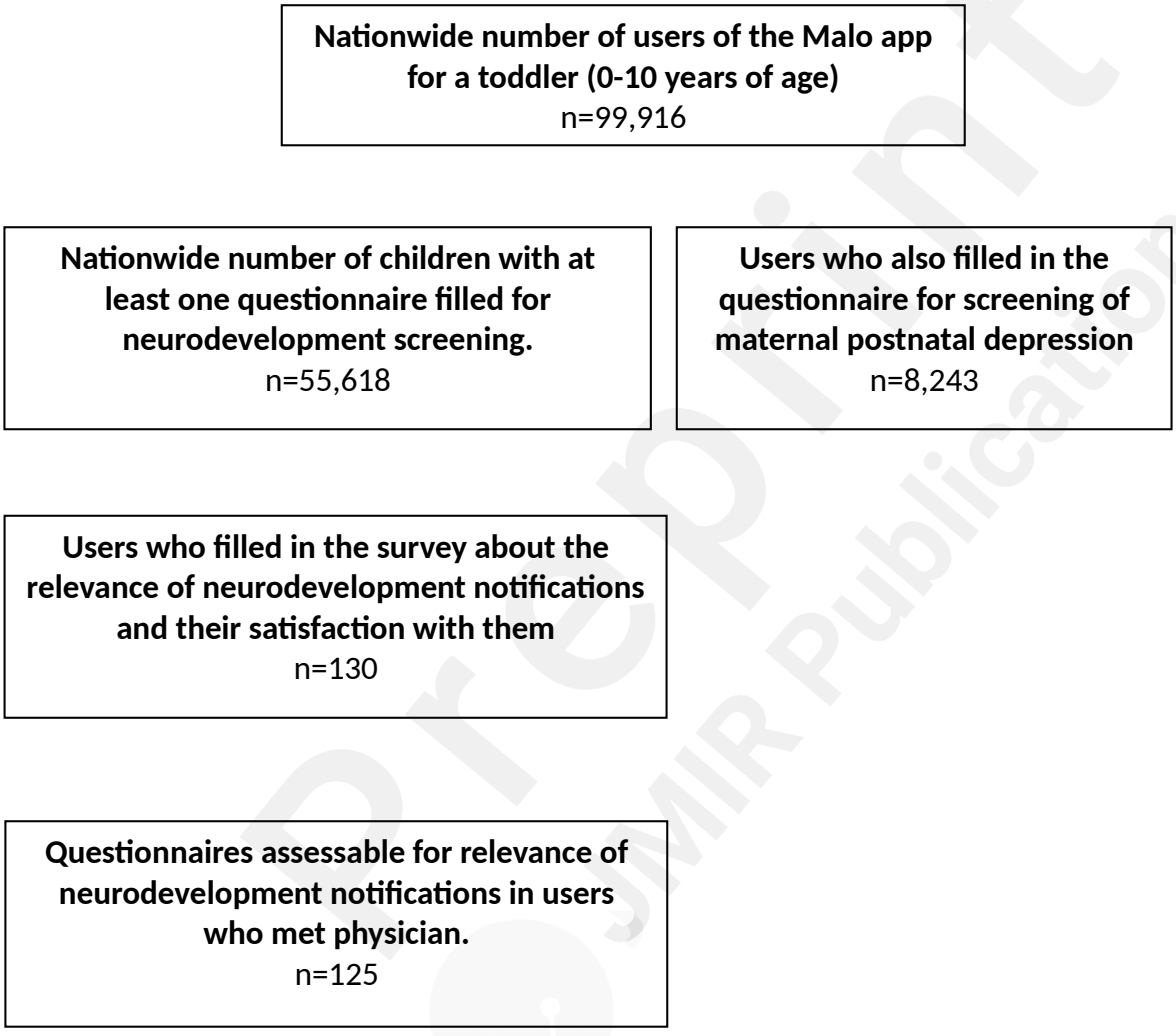
Chi-square test was used in 2×2 tables to assess the statistical association between the medical relevance of the notification (relevant or not) and the notification results (notification or no notification of a possible NDD). We also assessed the rate of probable PND of mothers having a score >50 in the survey and the changes of the rate of PND along time after childbirth.

The level of statistical significance was 5% for all statistical tests.

Results

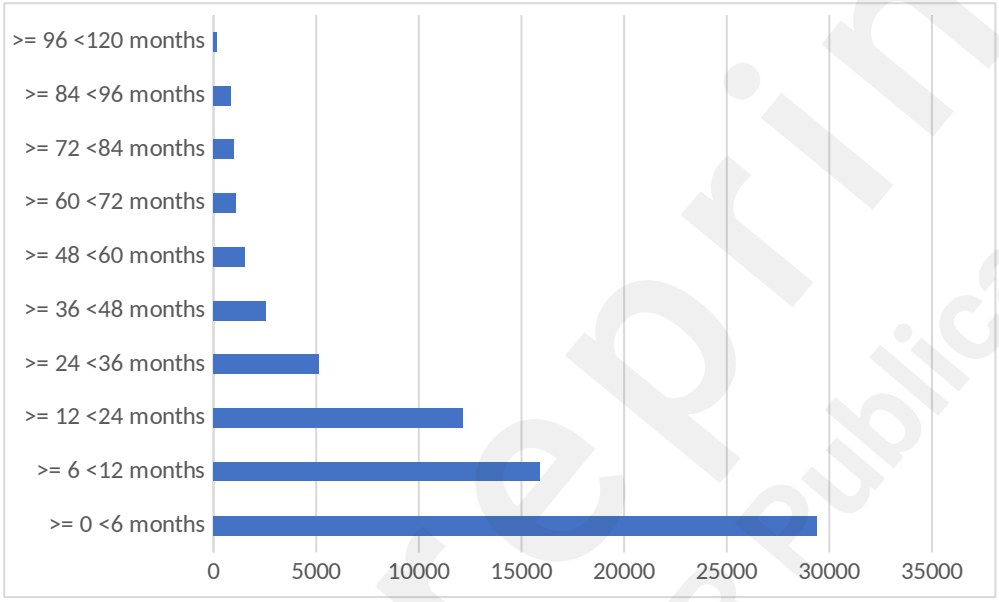
Among 99,916 nationwide users of the application between May 1, 2022, and February 8, 2024, 55,618 children met inclusion criteria. (Figure 1)

Figure 1: Flowchart of users of the Malo app. To determine if a dedicated mobile app can improve screening of 5 NDDs (autism spectrum disorder (ASD), language delay, dyspraxia, dyslexia and attention deficit hyperactivity disorder (ADHD)), and reduce PND incidence, we performed an observational, cross-sectional, data-based study in a population of young parents in France with a minimum of 1 child under 10 years of age at the time of inclusion and using Malo. An Analysis of the assessment of the relevance of the alerts by the physician was done concerning the physician consultation feedback to parents following notification of possible NDD and to assess the satisfaction of users in 125 parents and satisfaction was assessable in 130 parents who agreed to answer the survey.



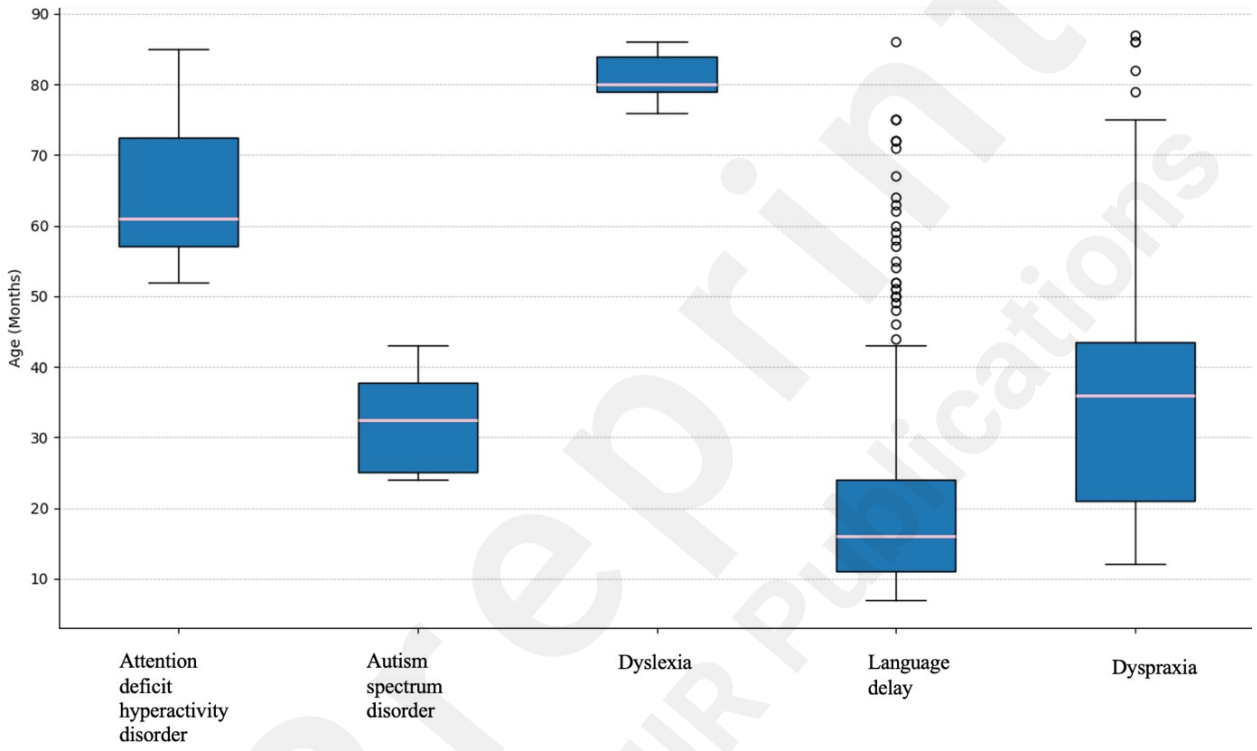
Median age of assessable children was 11-months, and 344,640 questionnaires were analyzed. Data analysis was performed at the end of February 2024. The distribution by age of children is in figure 2.

Figure 2: Distribution of assessed children with at least one questionnaire filled for neurodevelopment screening for NDD screening according to their age.



Among children, 0.8% (439/55,618) had at least one possible NDD strongly requiring a consultation. The median age of notification for probable ASD, language delay, dyspraxia, dyslexia, and ADHD was 32, 16, 36, 80 and 61 months, respectively. Figure_3

Figure 3. Distribution of the notifications of possible neurodevelopmental disorders and their type according to children age. The median age of notification for probable attention deficit hyperactivity disorder (ADHD), autism spectrum disorder (ASD), dyslexia, language delay and dyspraxia were 61, 32, 80, 16 and 36 months, respectively. The top and bottom sides of the box are the lower and upper quartiles. The box covers the interquartile range, where 50% of the data falls. The horizontal line that divides the box in two represents the median. The whiskers are the two vertical lines on the outside of the box ; they extend from the minimum to the lower quartile (the start of the box) and from the upper quartile (the end of the box) to the maximum.



The rate of probable attention deficit hyperactivity disorder (ADHD), autism spectrum disorder (ASD), dyslexia, language delay and dyspraxia in the population of children of the age included between the detection limits of each alert was 1.48%, 0.21%, 1.52%, 0.91%, 0.37% respectively.

Analysis of the Assessment of the Relevance of the Alerts by the Physician

A one-week survey was done at the end of January 2024 concerning the physician consultation feedback to parents following a notification of possible NDD and to assess satisfaction of users.

Among the 130 parents who agreed to answer the survey, 113 had no alert, and 17 (13.1%) had received an alert of a possible NDD, which suggested a visit to their physician.

Among users who received a notification suggesting a visit to their physician for a neurodevelopmental issue, 70,6% (12/17) answered “YES” to the question “If you had a notification, did you follow the recommendation of the app to visit a physician?”

As 5 users with notification did not meet their physician, they were not included in the analysis of the clinical relevance of the alerts assessed by the physician. Data of the 125 assessable users who met physician after notification showed a sensitivity of notification of 78.6%, a specificity of 98.2%, a positive predictive value of 84.6%, a negative predictive value of 97.3%, and a Youden index of 0.77 (*P*<.001).

Among the 11 children with true positive notifications of a possible NDD suggested by the app, medical surveillance of the evolution of the symptoms was proposed in 6 cases (54.5% of relevant notifications), the advice of an expert was needed in 2 cases (18.2%) and treatment was immediately initiated in 3 cases (27.3%).

Satisfaction Analysis

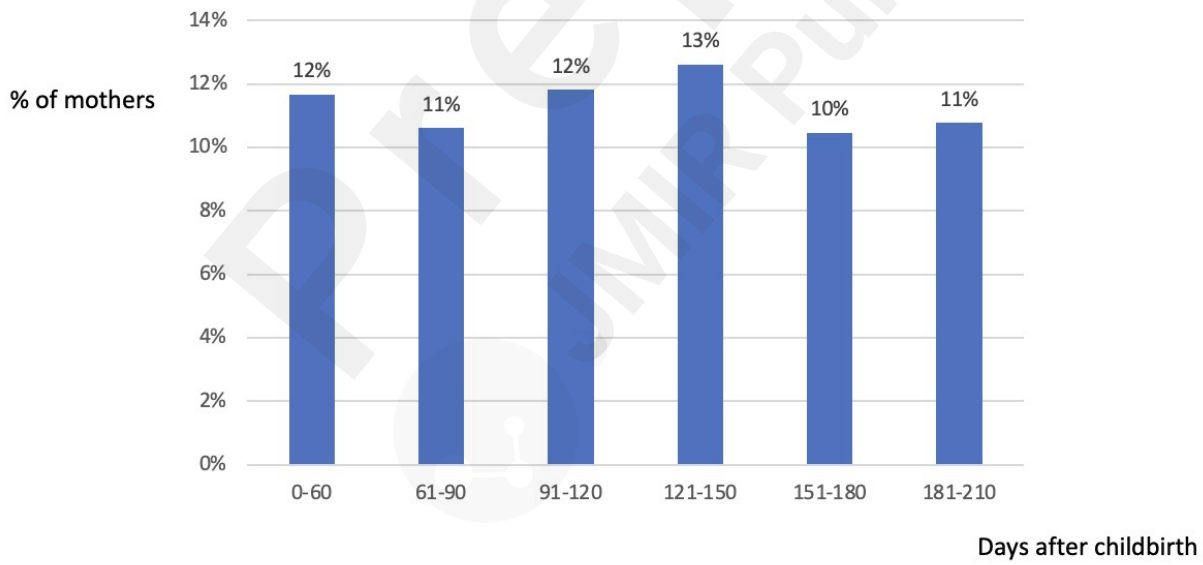
Among 130 users who filled in the satisfaction survey, 99.2% (129/130) found the application easy to use, 70.0% (91/130) reported that the app improved the follow-up of

their child. Moreover, the application was rated 4.8/5 on iOs Stores with 990 votes and 4.7/5 on Android Stores with 1,100 votes.

Screening of Post Natal Depression

Among 8,243 mothers who completed a PND questionnaire, highly probable PND (grades 2 or 3) was suspected in 938 (11.4%). Grades 1 or 2 or 3 were reported in 54.2% mothers. The median time of detection of suspected PND was 96 days after childbirth and the incidence of supposed PND was equivalent during the 7-months follow-up ($p<0.001$). Figure 4

Figure 4. Distribution of the incidence of the maternal postnatal depression screening which triggered a notification to visit a physician according to the number of weeks after childbirth.



Discussion

Our study prospectively assessed, in a “real-world” manner, in over 55,000 users, the benefit of mother-child dyad follow-up via a dedicated multidomain familial mobile health (mHealth) smartphone app providing early detection of 5 NDDs and leading to reduced incidence of maternal PND.

The main result is that the median age of alert of 5 NDD (ASD, language delay, dyspraxia, dyslexia and ADHD) by this smartphone screening application containing a dedicated questionnaire for parents seems to allow earlier assessment than in historical data. It also appears that relevance of notifications was confirmed by physicians consulted following a notification with high sensitivity (78.6%) and high specificity (98.2%).

Optimization of the neurodevelopment follow-up of children is very important as the identification of the first symptoms of NDDs is usually done by parents (without a dedicated digital device) in 61% of cases and by a health professional in only 14% as reported in a recent French study. [7] In our study, the median age of notification for probable ASD, ADHD, dyspraxia, dyslexia language delay was 32.5, 61, 36, 80 and 16 months, respectively while time to diagnosis in France is usually 78 and 120 months for ASD and ADHD respectively, that is 4-5 years later, and between 6 to 10 years of age for dyspraxia and dyslexia and 2-3 years for language delay. [7, 15, 16, 18, 19]

The incidence of each disorder suspected in the study was similar to those historically reported, therefore strongly suggesting that our cohort was representative of the general population: 0,21% for ASD (0,6% in literature [1]), 1.48% for ADHD (0.4 to 5% in literature [20]), 0.91% for language delay (2% in France [21]), a little lower for dyslexia 1.52% in our study versus 3 to 6% in literature [10, 21]) and for dyspraxia (0.37% in our study versus 3% in literature. [21] The lower rates of dyslexia and dyspraxia screening in our study is

probably caused by a reduced sensibility of the algorithm.

We also performed an analysis of physician feedback after an alert about a possible NDD. Most users (13/18, 72.2%) followed the recommendation of the app to visit their family doctor or pediatrician after an alert. In our previous study published in 2022 with the older version of NDD trigger algorithm, the rate of parents following the recommendation of the was 84.4%. Both results suggest a high level of confidence of parents to the notification. [14]

The main modification of the algorithm and forms between previous and current version of the application consisted of a reduction in sensitivity to optimize specificity of NDD suspicion notification by displaying several sub-questionnaires for confirmation and investigation of suspicious symptoms on the main form. In the current study, the sensibility of notification was reduced to 78.6% while it was 100% in the 2022 study, but the specificity was higher with new algorithms (98.2% versus 73.5%). This was a deliberate choice to improve specificity by reducing false positive alerts, as observed in the 2022 version of the application to reduce inopportune and anxiogenic alerts to parents. This is also associated with a high negative predictive value of 97.3% which is interesting to reassure parents in the absence of alerts. The high positive predictive value is also an important factor for the confidence of doctors confronted with an alert, delivered by the application. It suggested that 84.6% of notifications were considered relevant by physician. Among these alerts, the physician triggered a specific medical surveillance in 54.5% of notifications or initiated a treatment or recommended parents to an expert in 45.5%.

Although these data were declarative by users and were not directly confirmed by physicians, we assume that the specificity of the ASD notifications is close to the result of Pierce et al, showing an overall stability or specificity of an autism spectrum diagnosis of 84% at earlier than 18 months of age through a universal screening program in primary

care. [6] In a recent diagnostic accuracy study including 13,511 children aged 11-42 months, Barbaro et al showed an 83% positive predictive value and 99% estimated negative predictive value of the Social Attention and Communication Surveillance-Revised tool for autism identification when it was used by nurses for 12-month-old children. [22] Our results seem to be similar when parents perform a screening using our app.

The inclusion of efficient digital tools is important in the logic of care pathways because it promotes acceptability and relevance by families and professionals. Early screening allows for early diagnosis and interventions as reported by works on the efficacy of early treatments of cases among young children and recent promising studies on early interventions [9-11, 23, 25, 26].

We also reported a lower incidence of maternal postnatal depression (11.4%) assessed in 8,243 mothers than in our previous study performed in 2022 (16.6% in 907 assessed mothers). The form and algorithms were not modified for the part relating to maternal postpartum depression between previous and current veriosn of the application.To prevent PND rate, we added to the early PND screening a prevention program to be initiated by mothers after childbirth. PND is well known to disrupt the crucial mother-infant relationship on which optimal child development depends. It is the most common complication associated with childbirth, and it may exert harmful effects on children such as increased risk of ASD [27]. It is usually under detected or detected after many months. The early treatment of PND is effective, avoid negative impact on child development and does not necessarily require drugs to improve symptoms in the earliest stages [28]. Its prevalence in France is 18%.

In our previous study performed in 2022 with the old version of the application, we reported that 16.6% of mother users had probable PND and a median time of detection between 8 and 12 weeks after childbirth. We thus added a support program since 2022 in the new

version of the app, consisting of advice, information, sensitization to PND, as well as access to speaking groups and testimonials of mothers. The current study reported a lower rate of suspected PND of 11.4%, that is a 31% reduction of PND incidence compared to the results of the 2022 study. There were no change in questionnaire, the same algorithm for PND detection was active in both versions of the application, but only the prevention program was added. Interestingly, the incidence of all grades of assessment (1, 2 or 3) was similar between both studies (56.7%, 515/907 mothers in 2022 study versus 54.2%, 4,465/8,243), suggesting that a switch to lower grade symptoms was associated with the new support program which in turn was associated with a diminished incidence of PND. This is, as far as we know, the first time that reduction of PND incidence can be observed through the use of a smartphone application.

The level of satisfaction was also high (between 70% and 99.2% according to the assessed domains) and contributed to the high rate of adoption.

Study Limitations

Limitations of our study are the following. First, it was an observational study without a control group. Therefore, even though our sample was very significant, we could only proceed to indirect (historical) comparison when intending to assess the efficacy of the tool regarding detection of mental problems. Sample selection bias is always possible in the absence of randomization, due to social media recruitment modalities and because using the mobile app requires possession of a smartphone. We could have asked users questions about their educational level, practice classification (rural or urban), technical experience, and marital status, but we designed the app to collect as little personal data as possible. However, the very high rate of smartphone penetration in France (92% in a 2018

survey) in people aged 25-39 years led us to believe that the risk of a selection bias associated with smartphone use was low. Nonetheless, we do note that parents without smartphones cannot benefit from the app [29].

The second limitation is that the data were declarative by users without a comparative arm, but we found similar results than in our previous study in terms of NDD incidence and time to the detection of benefit.

The third limitation is that NDD suspicion were not directly transmitted by physicians. As diagnostic confirmation takes time, prospective follow-up of patients can be interesting to assess if suspicion is confirmed and makes it possible to study the confirmation rate of suspicions.

Fourth, the attrition rate (ie, the discontinuation of eHealth app use) was not assessed, but it could be interesting to study whether the benefit of early detection of NDD is maintained over time thanks to prolonged use [30]. We need further studies to improve lack of follow-up rate which is usually high in real-life study of e-health instruments.

Conclusion

To our knowledge, this multidomain mHealth app dedicated to both the early detection of 5 NDDs in children and the early detection and prevention of maternal PND is the first app with real-life data of clinical relevance. Results based in a large population of more than 55,000 users confirmed previous results and suggest that a multidomain familial mHealth app is suitable and effective for regular use in the mother-child dyad follow-up.

Acknowledgments

No one received compensation for their contributions.

Data availability

The datasets generated and/or analysed during the current study are not publicly available due to the sensitive nature of the patient data which includes protected health information (PHI) under privacy regulations but are available from the corresponding author on reasonable request.

Authors' Contributions

All authors had full access to all data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. FD conceptualized and designed the study. All authors contributed to the acquisition, analysis, and interpretation of the data and drafting the manuscript. Critical revision of the manuscript for important intellectual content was done by FD, FLG, MD and AG. FD, FG, GF and MD oversaw statistical analysis as well as administrative, technical, and material support.

Conflicts of Interest

FD reports receiving personal fees from AstraZeneca, Ipsen, Kelindi, Pfizer, Chugai, and Roche and has stocks in Kelindi and Institute for Smarthealth. FLG, AG, and MD have stocks in Kelindi. The other authors declare no conflicts of interest.

Abbreviations

ePRO: electronic patient reported outcome
GP: general practitioner
mHealth: mobile health
NDD: neurodevelopmental disorder
PND: postnatal depression
ASD: autism spectrum disorder

ADHD: attention deficit hyperactivity disorder

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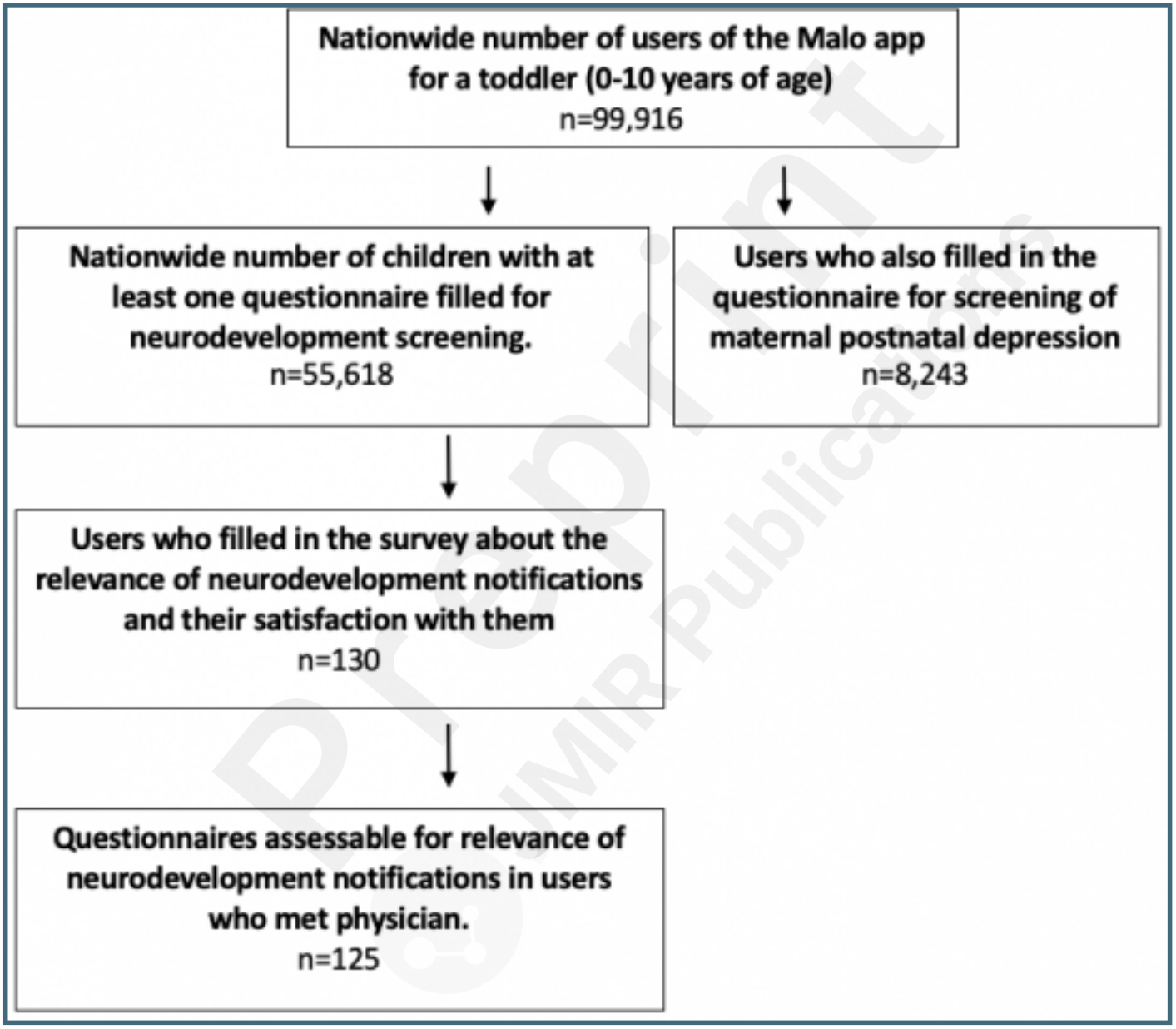
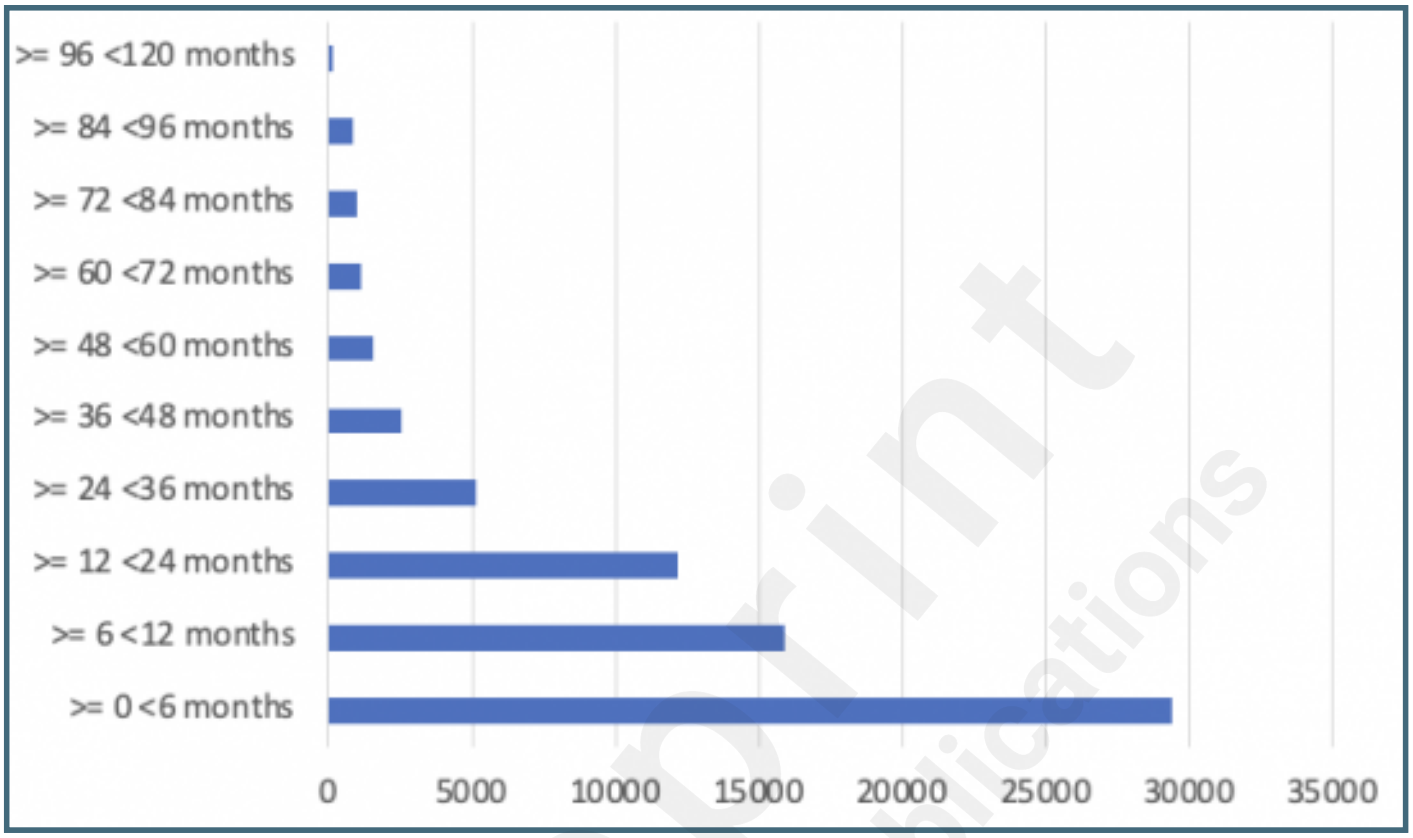
Supplementary Files

Figures

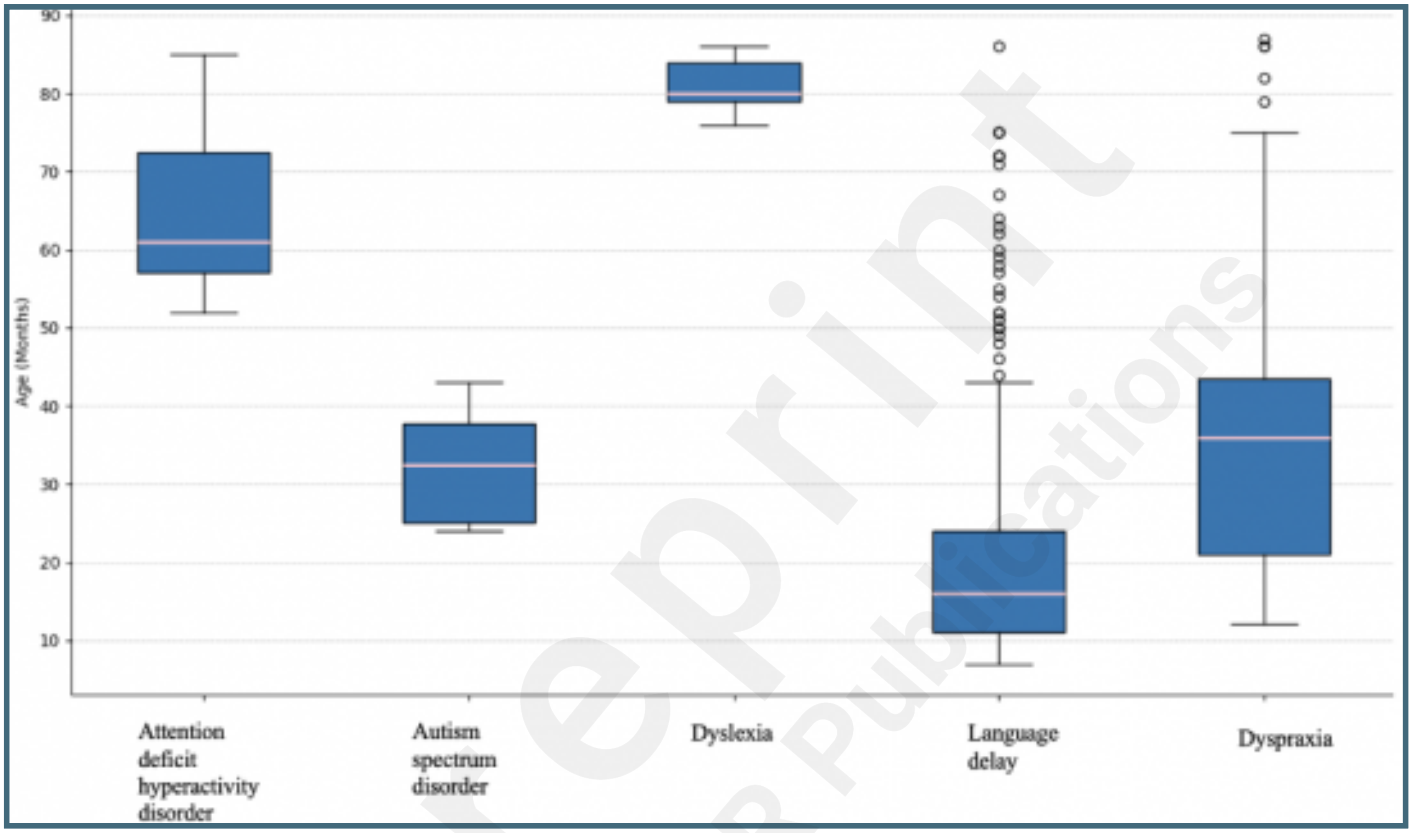
Flowchart of users of the Malo app. To determine if a dedicated mobile app can improve screening of 5 NDDs (autism spectrum disorder (ASD), language delay, dyspraxia, dyslexia and attention deficit hyperactivity disorder (ADHD)), and reduce PND incidence, we performed an observational, cross-sectional, data-based study in a population of young parents in France with a minimum of 1 child under 10 years of age at the time of inclusion and using Malo regularly. An Analysis of the assessment of the relevance of the alerts by the physician was done concerning the physician consultation feedback to parents following notification of possible NDD and to assess the satisfaction of users in 125 parents, and satisfaction was assessable in 130 parents who agreed to answer the survey.



Distribution of assessed children with at least one questionnaire filled for neurodevelopment screening for NDD screening according to their age.



Distribution of the notifications of possible neurodevelopmental disorders and their type according to children age. The median age of notification for probable attention deficit hyperactivity disorder (ADHD), autism spectrum disorder (ASD), dyslexia, language delay and dyspraxia were 61, 32, 80, 16 and 36 months, respectively. The top and bottom sides of the box are the lower and upper quartiles. The box covers the interquartile range, where 50% of the data falls. The horizontal line that divides the box in two represents the median. The whiskers are the two vertical lines on the outside of the box ; they extend from the minimum to the lower quartile (the start of the box) and from the upper quartile (the end of the box) to the maximum.



Distribution of the results of the maternal postnatal depression screening which triggered a notification to visit a physician according to the number of weeks after childbirth.