Impact of Medical Formula Shortage for Inborn Errors of Metabolism with Mediation Analysis

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RESEARCH OBJECTIVE

- **To examine the long-term, clinical & psychosocial impact** of medical formula shortage on patients with IEM which began in February 2022.
- **To investigate** if **strained patient-dietitian relations** due to the unexpected formula shortage **mediate** the **association** between patients' **experience of cutting back on medical formula** and having **negative perceptions of weight changes.**

BACKGROUND

Patients with Inborn Errors of Metabolism (IEM)

- Inborn errors of metabolism (IEM) : A group of inherited genetic disorders characterized by enzyme defects.
- Clinical concerns of IEM: Accumulation of toxic substances in the body.
- May lead to serious health problems, for instance, irreversible brain damage, intellectual disability, neurological problems, behavioral, emotional, developmental problems.
- Phenylketonuria (PKU) patients are largest subpopulation of IEM.
- Until gene editing is an option, most IEM are incurable. Some can be cured with a liver transplant.
- Specialized medical formulas/supplements are crucial for nutritional support for patients with IEM.
- Medical foods in the US are regulated under Food and Drug Administration (FDA).

Medical Formula Shortage in Feb. 2022

- Unexpected medical formula shortage happened in part by voluntary recalls of several formulas produced by Abbott Nutrition since the shutdown of the plant in Michigan in February 2022 due to bacterial contamination (United States Food and Drug Administration, 2023), and ongoing supply chain interruptions resulting from the COVID-19 pandemic (Calder et al., 2021).
- To date, no study has focused on the impact of medical formula shortage on pediatric and adult patients who were dependent on metabolic formulas.

Patients-Dietitian Relation

- Metabolic dietitians provided nutrition services during diagnosis, critical illness and long-term care to patients with IEM. During the medical formula shortage, they advised patients about alternative products based on patients' primary formula.

METHODS

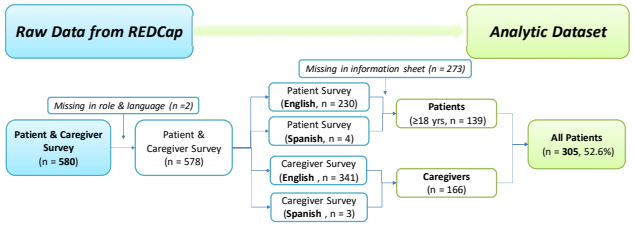
Recruit Survey Participants

- Two identical surveys (Adult patients, ≥ 18 yrs AND Caregiver/legal guardians) were disseminated through dietitians in the US between December 2023 - January 2024.
- Each survey was offered in English and Spanish.
- Patients provided demographic information and completed items on **information sheets** and **main survey questionnaire.**
- **The** (1) **psychosocial impact**, (2) **access to the medical formula and alternatives**, (3) **clinical and psychosocial changes**, and (4) **changes in relations with their dietitians**. All survey responses were stored in REDCap database.
- Responses were mostly in binary (Yes/No) or Likert-scale (0-4).

Data Management

- The raw survey data was exported from REDCap database and R software was used for data management and analysis.

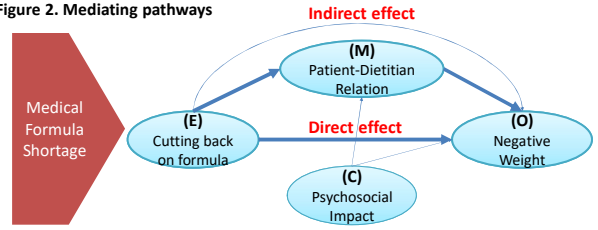
Figure 1. Data management flow chart



Statistical Analysis

- To address psychosocial impact and clinical symptoms of all patients, descriptive statistics and Chi-squared test were employed.
- To investigate the indirect effect of cutting back on formula on negative impact on weight perception via strained P-D relations, a series of logistic regression models were computed, using a 'mediate' package in R.

Figure 2. Mediating pathways



(E) Exposure : Patients' experience of cutting back on medical formula (Y/N)
(M) Mediator: Patients' experience of strained relationship with dietitians (Y/N)
(O) Outcome: Patients' negative perception on their weight changes (Y/N)
(C) Confounding: Patients' psychosocial impact sum score (0-16)

RESULTS

Demographic Information of All Patients

- The mean age of all patients was 24 years old (Min=1, Max = 82). For gender, the proportion of female (46%) and male (50.2%) patients were similar (Non-binary, 2.0%). The majority of patients were recognized as White (63.6%).
- Please find the full size table for demographic information via scanning the QR code below.

Psychosocial Impact on Patients

Among all patients (n = 305), 155 (51%) patients felt the formula shortage was too difficult to handle, 100 (33%) patients felt frustrated or angry, 118 (39%) patients felt nervous or stressed about not having enough medical formula, and 104 (34%) patients had worried about health status at least often or always.

Figure 3. Psychosocial Impact of Formula shortage

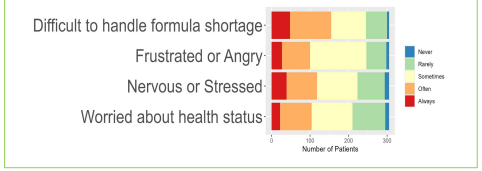


Table 1. Negative Changes in Weight vs. Strained Relations

Characteristic	Strained P-D Relations: No, N = 183[1]	Yes, N = 116[1]	p-value[2]
Negative impact on weight			<0.001
No	163 (89%)	81 (70%)	
Yes	20 (11%)	35 (30%)	

[1] n (%)
[2] Pearson's Chi-squared test

Association between a Clinical Symptom (perception of negative weight change) and Strained Relation with Dietitian

Patients' perceived negative weight change was significantly associated with having strained relations with dietitians.
(Chi-squared test, p-value < 0.001)

Direct Effect of Cutting back medical formula on Negative weight changes

Patients' cutting back on medical formula (E) was significantly associated with having negative weight (O) changes (OR = 2.67, 95% CI = 1.40, 5.41).

Indirect Effect of Cutting back medical formula on Negative weight change perceptions (via Mediator, Strained patient-dietitian relations)

- As a predictor of negative weight changes (O), patient's experience of formula cutbacks (E) was changed to be non significant when considering with a mediator (M), having strained relations with dietitian, adjusting for psychosocial impact (OR = 1.84, 95% CI = 0.92, 3.84).
- There was a significant indirect effect (OR = 1.04, 95% CI = 1.01, 1.07) was detected.

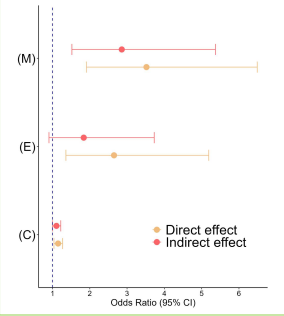
Table 2. Logistic Regression Results

	Model 1			Model 2			Model 3		
Y = (O) Negative Weight change	OR[1]	95% CI[1]	p-value	OR[1]	95% CI[1]	p-value	OR[1]	95% CI[1]	p-value
(E) Cutback on medical formula									
No	—	—		—	—		—	—	
Yes	2.67	1.40, 5.41	0.004	2.28	1.17, 4.68	0.019	1.84	0.92, 3.84	0.092
(C) Psychosocial impact score				1.12	1.01, 1.24	0.027	1.11	1.00, 1.23	0.048
(M) Strained Relations between patient-dietitian									
No							—	—	
Yes							2.86	1.53, 5.44	0.001

[1] OR = Odds Ratio, CI = Confidence Interval

Model 1 (Univariate Model): $logit(p_i) = \beta_0 + \beta_1 * E$
Model 2 (Multivariate Model w/o Mediator): $logit(p_i) = \beta_0 + \beta_1 * E + \beta_2 * C$
Model 3 (Multivariate Model w Mediator): $logit(p_i) = \beta_0 + \beta_1 * E + \beta_2 * C + \beta_3 * M$
where $p_i = Pr(Yi = 1|Xi)$

Figure 4. Forest Plot



CONCLUSION

- Patients with IEM have endured an unexpectedly long-term medical formula shortage that may have negative clinical and psychosocial impacts.
- Medical formula cutbacks due to the formula shortage were significantly associated with having direct negative impacts on patients' weight perception.
- This association was significantly mediated through strained patient-dietitian relations.
- Study results have implications for dietitians, highlighting the importance of maintaining positive relationships with their patients which may improve clinical outcomes for patients with IEM.

REFERENCE