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From policy to practice: Experiences from the ECHO trial following revisions of the WHO medical eligibility criteria for contraceptive use (MEC) guidance on DMPA-IM☆

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ABSTRACT

Objectives: In 2017, the World Health Organization (WHO) medical eligibility criteria (MEC) for contraception category for intramuscular depot medroxyprogesterone acetate (DMPA-IM) was changed from MEC category 1 to 2 for women at high risk of HIV acquisition. We assessed the impact of communicating this category change among women in the Evidence for Contraceptive options and HIV Outcomes (ECHO) trial.
Study design: ECHO was conducted in eSwatini, Kenya, South Africa and Zambia. Women were randomized (1:1:1) to DMPA-IM, levonorgestrel (LNG) implant or copper intrauterine device (Cu IUD). We compared the hazards of DMPA-IM discontinuation and assessed sexual behavior and DMPA-IM satisfaction before and after MEC category change.
Results: In DMPA-IM users there was a decrease in the hazards of discontinuation after the MEC change (hazard ratio 0.37; 95% CI = 0.26–0.52, $p < 0.001$). No evidence of an effect of the MEC change was observed in sexual behaviour outcomes. There was some evidence of an increase in disatisfaction with DMPA-IM immediately after the MEC change, with the odds of women reporting a higher score (more dissatisfied) increasing by 1.38 compared with before the MEC change (95% CI = 1.11–1.72).
Conclusions: While counseling on possible theoretical risks associated with contraceptive methods in the MEC is an important medical ethical standard, in this study it did not adversely impact continuation or sexual behavior, while there was some evidence on increase in dissatisfaction. There is however a need to monitor how changes in MEC categories are implemented.
Implications: Although we found no evidence in this analysis of an effect of the MEC change on any of the sexual behavioral outcomes among women after the change in category, it is still an important medical ethical standard to counsel on possible theoretical risks associated with contraceptive methods. Given the challenges of translating research findings to guidelines and further to counseling messages, evaluation of clinical guidelines implementation is necessary to understand the effects of implementation and to monitor both intended impacts and unintended consequences.

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1. Introduction

The World Health Organization (WHO) medical eligibility criteria (MEC) for contraceptive use were developed to ensure contraceptive provision was provided according to the most up-to-date and highest quality evidence [1,2].

In 2017, a review of several years of studies, suggested that the use of intramuscular depot medroxyprogesterone acetate (DMPA-IM), delivered as a three-monthly intramuscular injection of 150 mg/mL, may increase a woman's susceptibility to HIV [3–5]. However, all these studies have limitations, with some studies finding no increase in HIV incidence among DMPA-IM users [3]. In March 2017, WHO released new guidance on the use of hormonal contraceptives for women at high risk of HIV [6], stating that although these women can use all methods of contraception, it is possible the DMPA-IM injectable might increase women's risk of acquiring HIV [7]. DMPA-IM was reclassified from MEC category 1 "*A condition for which there is no restriction for the use of the contraceptive method*" to MEC category 2 "*A condition where the advantages of using the method generally outweigh the theoretical or proven risks*". This change signaled the need to ensure key messages of risks and benefits were delivered to women using this method and couples, with special attention paid to counseling vulnerable populations, such as women at high risk of acquiring HIV. However, it was stressed that access to DMPA-IM should not be restricted in any way.

At the time of the MEC change, – The Evidence for Contraceptive options and HIV Outcomes (ECHO) trial – was already in the field aiming to answer the public health question of the relative risks (HIV acquisition) and benefits (pregnancy prevention) of three commonly used, effective contraceptive methods (DMPA-IM, the levonorgestrel (LNG) implant or the copper Intrauterine device (IUD)).

Given the challenges of translating research findings to guidelines and further to counseling messages [8], this paper aims to increase understanding of what impact, if any communication of the MEC category change for DMPA-IM had on existing and new method users reported sexual behavior, rates of method discontinuation and method satisfaction before and after the WHO MEC change in 2017. In August 2019, after the results of the ECHO trial were released, the WHO MEC category for progestogen-only injectables and Cu IUDs for women at high risk of HIV moved back from a category 2 to a category 1.

2. Materials and methods

2.1. Study population and sample

The ECHO randomized multicenter trial was conducted in 12 research sites in four African countries. Nine sites in South Africa, and one site each in Kenya, eSwatini and Zambia participated between December 2015 and October 2018. Enrollment commenced in December 2015 and was completed in September 2017. Women were invited to enroll into the ECHO trial if they desired effective contraception, were 16–35 years of age and were willing to be randomized to any one of the three trial contraceptive methods (DMPA-IM, LNG implant, copper IUD). Follow-up visits occurred at 1 month, 3 months and every 3 months thereafter up to 18 months, with later enrolling women completing the study at 12 or 15 months.

Women wishing to enroll into the ECHO study prior to the MEC change were given information in the informed consent form as to the current status of evidence on HIV acquisition for DMPA-IM, the implant and the IUD (Appendix A).

At baseline, we collected demographic, sexual risk behavior, and reproductive and contraceptive history. Every follow-up visit included assessment of randomized contraceptive method use and risk. The study design and primary results have been previously reported [9].

Following the change of category from WHO MEC 1 to 2 in 2017, the ECHO trial prepared counseling messages and an information sheet on the DMPA-IM MEC change (Appendix B). Between May 2017 until end of July 2017, all women newly enrolled, regardless of randomized method, and those already in follow-up, were counseled on the MEC change and given an information sheet Approximately 82.0% of participants were enrolled by the time the MEC change counseling was implemented. The counseling continued at ongoing follow-up visits until the study ended in October, 2018.

Although participants were randomized to the method in the trial, they also could exercise the choice to switch or stop their method. The aims of this analysis were to compare DMPA-IM discontinuation rates, method satisfaction and reported sexual behavior before and after the MEC category change was actively communicated to them.

2.2. Measures

We evaluated two primary outcomes- firstly, DMPA-IM discontinuation rates to compare discontinuation before the MEC change to that which occurred after the MEC change. We used a derived binary variable indicating discontinuation of the method, and the date of discontinuation.

Secondly, we assessed sexual behavior including: In the past three months:- the total number of sex partners; number of vaginal sex acts; any new partner; any condomless sex and condom use during the last sex act (or no sex act reported in previous 3 months). The estimated average count of sex acts is that predicted by the model over a 12-month period with the MEC change. The model predicts the number of sex acts in a 3-month period, so we integrate the function to get the total predicted sex acts over 12 months. For the counterfactual, the coefficients for the MEC change and time after the change are dropped from the equation – and we assume that the trend before the MEC change (the coefficient for time in the study) would continue for the entire period.

We assessed a secondary outcome of satisfaction with contraceptive method, using the question "How satisfied are you with the contraceptive method you are currently using?" which asked women to respond to a five-point scale:- "very satisfied", "somewhat satisfied", "neutral", "somewhat dissatisfied" and "totally dissatisfied".

We created a binary variable indicating whether a study visit occurred after the MEC change (to assess change in the level of the outcome) and a continuous variable for the number of months after the MEC change (to assess change in trend over time).

2.3. Analysis

Women were included in the analysis if they were randomized to and initiated DMPA-IM. All women in the analytic population were included in the analysis for discontinuation. We used Cox regression stratified on country and adjusting for age at enrollment to evaluate the hazard ratio of DMPA-IM discontinuation before and after MEC category change. We calculated person-time from the date of enrollment until the earliest of the date of DMPA-IM discontinuation or last study visit attended. In addition, as a sensitivity analysis, the hazard ratio of discontinuation before and after the MEC change was estimated restricted to women who enrolled before the MEC change date.

For sexual behavior outcomes, we included women in the analysis if they had at least one visit before and one visit after the visit at which they were counseled about the MEC change.

For the outcome of method satisfaction, we restricted the analysis to women who at least had one visit before and after the MEC counseling, and those visits when they were using DMPA-IM.

Further detail on the analysis can be found in Appendix C. Analyses were conducted with STATA Version 17.0 and SAS Version 9.4.

Written consent was obtained from all participants. Ethics approval was granted by FHI360, The World Health Organization and all participating study sites.

3. Results

The ECHO study enrolled a total of 7830 women across the 12 trial sites, of whom 2606 were randomly assigned to DMPA-IM. Almost all (99%) women accepted their randomized method and more than 91% of women attended each scheduled visit to the end of follow-up in each study group. Due to the timing of the MEC change a proportion of women had already exited the study after completing their full follow-up prior to the MEC change. Additionally, some women only received the MEC change counseling at their exit visit and therefore a comparison could not be made for any change between visits. We collected sexual behavior outcomes at the month three follow-up visit and quarterly thereafter, however the method satisfaction was first collected at month one. This resulted in a slightly higher number of participants for the method satisfaction outcome, 1812/2606 (69.5%) compared to the sexual behavior outcomes (1740/2606; 66.8%). Figure 1 shows the different analytic population. Of the 2606 women in the analysis of discontinuation, 2189 enrolled before the MEC change date, and 417 enrolled on our after that date. Baseline characteristics were similar across all three randomized groups [8]. Table 1 shows the baseline demographic characteristics for the DMPA-IM group who continued (92.6%) and discontinued DMPA-IM (7.4%).

Among all women, the hazard ratio of DMPA-IM discontinuation comparing the period after MEC change to the period before the MEC change was 0.366, indicative of a reduced risk of DMPA-IM discontinuation after the MEC change (95% CI: 0.261–0.515, $p < 0.001$). In a sensitivity analysis restricted to women who were enrolled before the MEC change – the hazard ratio for discontinuation after the MEC change vs before the change was 0.332, CI = 0.22–0.49. Although the impact of the MEC change cannot be evaluated among the women who enrolled after that date, their crude rate of method discontinuation during follow-up was 3.85/1000 persons. This is similar to the rate of method discontinuation in the period after the MEC change among women who enrolled before the change (3.92/1000 person-years).

There was no evidence of a significant effect of the MEC change on any of the sexual behavioral outcomes, either in terms of an immediate change in the level of the outcome or a change in the trend over time (Table 2).

There was some evidence of an increase in disatisfaction with DMPA-IM immediately after the MEC change, with the odds of women reporting a higher score (more dissatisfied) increasing by 1.38 compared with before the MEC change (95% CI = 1.11–1.72). However, overall satisfaction with the method during the study was very high (90% of women said that they were "very satisfied"). Furthermore, the odds of women reporting a higher score in the period after the MEC change decreased by 0.92 for every month after the change (95% CI = 0.90–0.95), and the estimated proportion who were "very satisfied" with the method 3 months after the change was 90.6%.

4. Discussion

There was a significant decrease in the hazard of method discontinuation after the MEC change compared with the period before the MEC change. The importance of this finding must be viewed in the context of the very low (< 8%) overall rate of method discontinuation during the trial, half of which was in response to adverse events [9]. It is possible that women who were not happy with the method were more likely to discontinue before the MEC change, however sensitivity analysis showed no difference in discontinuation rates in those enrolled before and after the change.

The results showed no impact on reported sexual risk-taking behavior of DMPA-IM users. The regular HIV risk counseling already focused on all the study methods not being protective against HIV. Women may not have viewed the additional MEC change counseling as adding any further information. This coupled with HIV testing and condom provision may have lessened concerns of potential HIV acquisition.

There was some evidence of an increase in dissatisfaction with the method immediately after the MEC change, although the level of satisfaction with the method was reported as "very satisfied" by 91% of women 3 months after the change. The reduced risk of discontinuation in the period after the change and the slight increase in dissatisfaction immediately after the MEC change may appear contradictory but be simply a reflection of a population who were generally satisfied with DMPA-IM before the MEC change and were willing to continue use.

The ECHO trial demonstrated no statistically significant differences in HIV acquisition among women using DMPA-IM, copper IUDs, and LNG implants [9]. In August 2019, after the results of the ECHO trial were released [8], the WHO MEC were once again changed, with recommendations for progestogen-only injectables and Cu IUDs for women at high risk of HIV moving from a category 2 to a category 1 [10]. The changes in the MEC for high risk of HIV since 1996 year are summarized in Figure 2 [7].

MEC category changes are commonly based on clinical evidence which may be more conclusive to a provider and client. The change in this study required women to assess their own risk after considering complex evidence which was based on data that had limitations. Introduction of evidence based clinical guidelines have the potential to improve quality of care and patient outcomes [11]. Guideline implementation is a complex process that can face individual, organizational, and system-level barriers and they are commonly introduced without implementation strategies [12,13]. After reviewing over 70 guidelines and their implementation over a 10-year period in the Netherlands, Grol (2001) [14] concluded that a program to implement a guideline should be well designed, well prepared, and preferably pilot tested before use. More research into the details of implementation is needed to better understand the critical determinants of change in practice. This would improve understanding of how changes in MEC impact policy makers, health providers and women in real-world settings.

4.1. Limitations

This analysis has some limitations. Women were not interviewed to ask if MEC changed counseling or some external influence like media coverage, community advocacy initiatives influenced their satisfaction with the method, sexual behavior or decision to discontinue. Although method discontinuation was well documented, satisfaction with the method was self-reported and may have been positively influenced by long term participation in the study where participants received regular care and counseling on contraception.

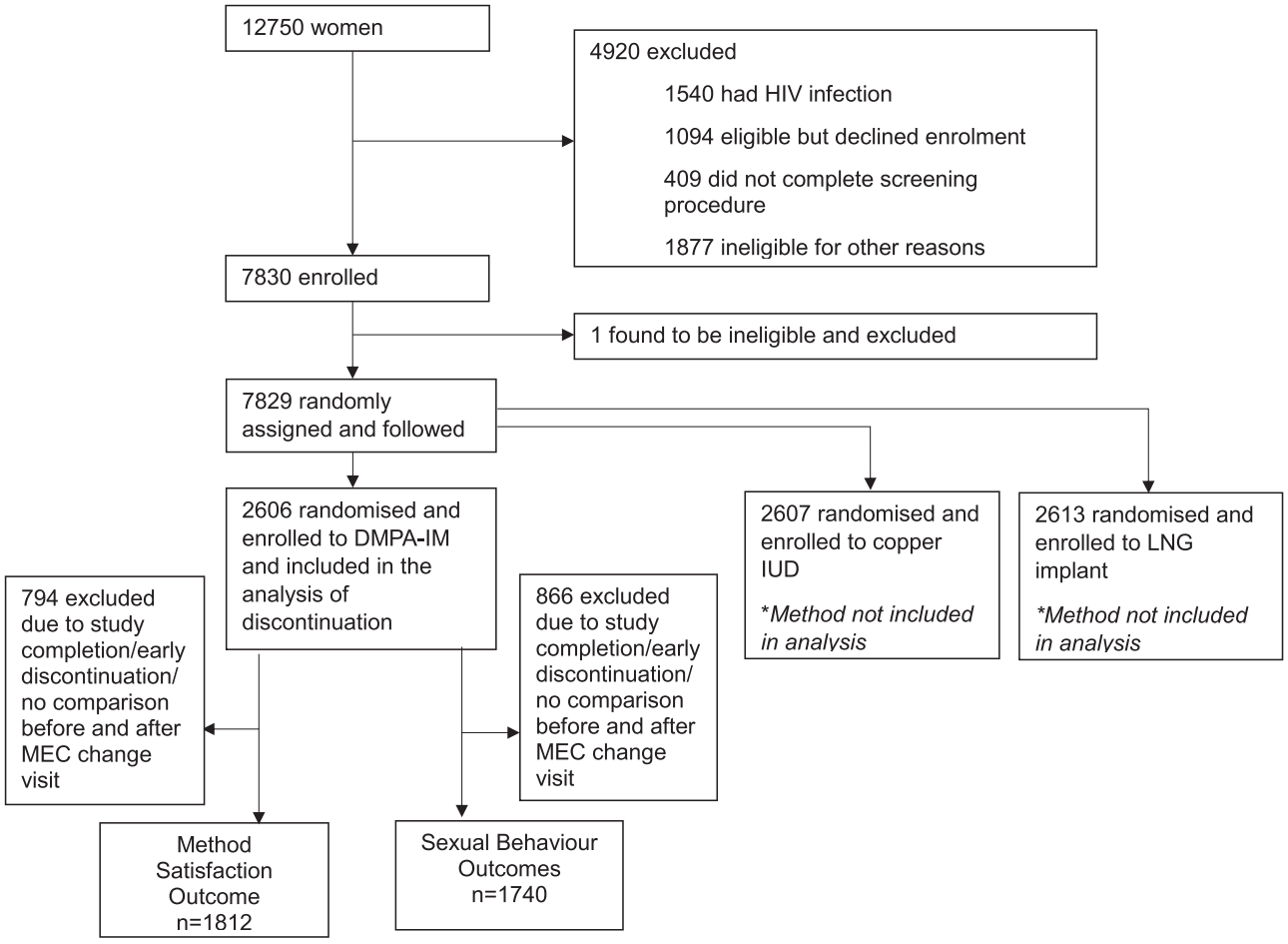

Fig. 1. Analytic population flow chart ECHO trial 2015–2018. More women were excluded for Sexual Outcomes as data was first collected at Month 3 compared to Month 1 for Method Satisfaction. ECHO = Evidence for Contraceptive options and HIV Outcomes.

Table 1
Baseline characteristics of women randomized to DMPA-IM in the ECHO trial 2015–2018

Characteristic	*N* (%) or median [IQR]		
	Overall (*N* = 2606)	DMPA-IM continued (*N* = 2413)	DMPA -IM discontinued (*N* = 193)
Age	23 [20–26]	23 [20–26]	23 [20–26]
Marital status			
Never married	2085 (80%)	1916 (79%)	169 (88%)
Married	501 (19%)	480 (20%)	21 (11%)
Previously married	20 (1%)	17 (1%)	3 (2%)
Education			
No schooling	16 (1%)	16 (1%)	0
Primary school	216 (8%)	207 (9%)	9 (5%)
Secondary school	1964 (75%)	1823 (76%)	141 (73%)
Post-secondary school	410 (16%)	367 (15%)	43 (22%)
Previous pregnancy	2097 (80%)	1967 (82%)	130 (67%)
Sexual behaviors in past 3 mo			
More than one sex partner	173 (7%)	157 (7%)	16 (8%)
Number of vaginal sex acts	9 [4–20]	9 [4–20]	7 [4–15]
Any new sex partner	122 (5%)	112 (5%)	10 (5%)
Any sex without a condom	1887 (72%)	1743 (72%)	144 (75%)
No condom last vaginal sex	1229 (47%)	1132 (47%)	97 (50%)
Methods used before study			
DMPA	1292 (50%)	1211 (50%)	81 (42%)
NET-EN	592 (23%)	542 (22%)	50 (26%)
Implant	164 (6%)	155 (6%)	9 (5%)
OCs	303 (12%)	267 (11%)	36 (19%)
No previous method use	205 (8%)	193 (8%)	12 (6%)

DMPA-IM, intramuscular depot medroxyprogesterone acetate; ECHO, evidence for contraceptive options and HIV outcomes; MEC, medical eligibility criteria; NET-EN, norethisterone enanthate; OCs, oral contraceptives.
Eighty-two percent of women were randomized and initiated method by the time of the MEC change.

Table 2
Effect estimates of changes in sexual behavior and method satisfaction after MEC change counseling: ECHO study 2015–2018

Outcome	Immediate change after MEC counseling (change in level) (95% CI)	Change in pre vs post trend: (95% CI)	Estimated average count 12 mo after MEC counseling	
			With MEC change	Without MEC change (counterfactual)
Past 3 mo				
Number of sex partners	OR = 1.138 (0.869–1.491)	OR = 1.013 (0.966–1.061)	NA	NA
Number of vaginal sex acts	IRR = 1.019 (0.960–1.082)	IRR = 0.992 (0.981–1.003)	62.602	64.338
Any new partner	RR = 1.010 (0.674–1.512)	RR = 0.982 (0.918–1.051)	NA	NA
Any sex without a condom	RR = 1.000 (0.960–1.043)	RR = 1.001 (0.993–1.008)	NA	NA
Condom use at last sex act	RR = 1.000 (0.943–1.062)	RR = 1.004 (0.994–1.015)	NA	NA
Dissatisfaction with method	OR = 1.380 (1.109–1.719)	OR = 0.973 (0.940–1.007)	NA	NA

ECHO, evidence for contraceptive options and HIV Outcomes; MEC, medical eligibility criteria.
OR, odds ratio (estimated from ordinal logistic model with GEE); IRR incident rate ratio (estimated from negative binomial model); RR, risk ratio (estimated from log Poisson model with GEE); HR, hazard ratio (estimated from Cox regression). The following variables are included in the model: months since enrollment in the study, a binary MEC change indicator, months after MEC counseling date, age at enrollment and country.

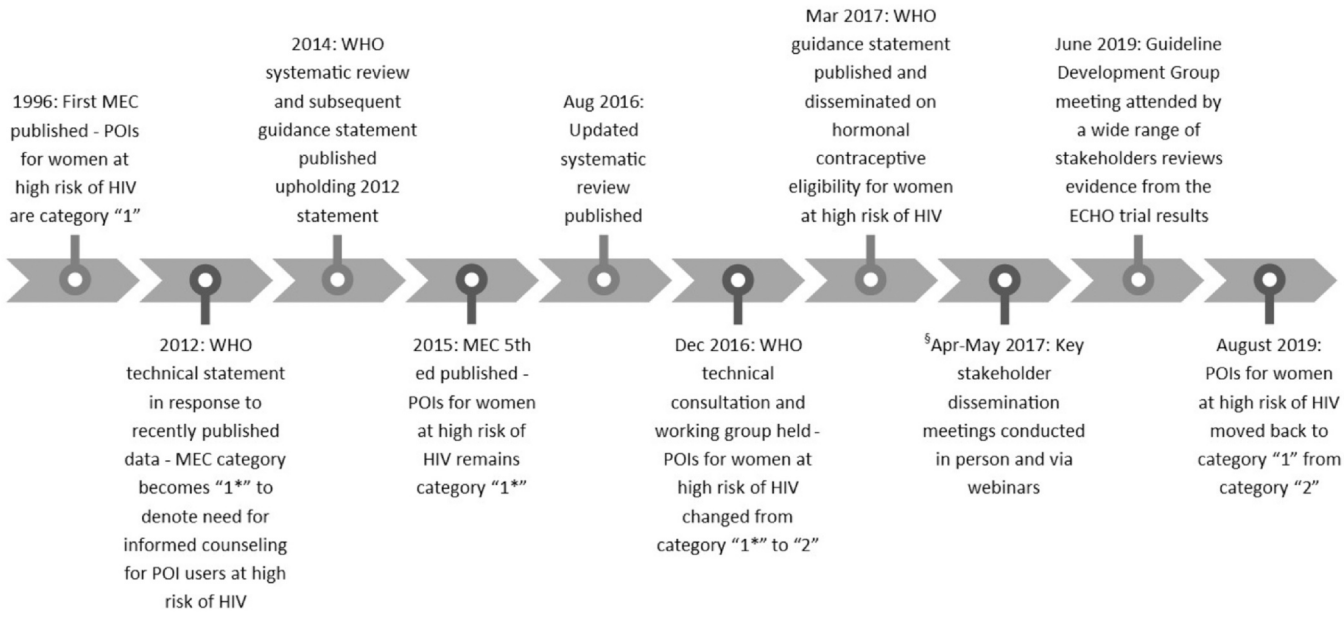

Fig. 2. WHO Timeline of events from publication of research on possible increased risk of HIV acquisition in progestogen only injectable users to guideline dissemination to policy implementation. WHO = World Health Organization.

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M.E.B.: Writing – review & editing, Writing – original draft, Project administration, Methodology, Data curation. J.N.K.: Writing – review & editing, Writing – original draft, Supervision, Methodology, Conceptualization. P.S.: Writing – review & editing, Writing – original draft, Supervision, Project administration, Methodology, Funding acquisition, Data curation, Conceptualization. G.J.H.: Writing – review & editing, Writing – original draft, Methodology, Investigation, Conceptualization. T.P.-P.: Writing – review & editing, Project administration. D.T.: Writing – review & editing, Writing – original draft, Formal analysis. M.S.-M.: Writing – review & editing, Project administration. J.A.S.: Writing – review & editing, Writing – original draft, Conceptualization. K.B.: Writing – review & editing, Writing – original draft, Supervision, Formal analysis. M.P.: Writing – review & editing, Writing – original draft, Supervision, Project administration. H.-Z.T.: Writing – original draft, Methodology, Formal analysis, Data curation.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supporting material

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.conx.2024.100111.

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