REVIEW





Establishing an EU-wide front-of-pack nutrition label: Review of options and model-based evaluation

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Summary

This paper reviews the effectiveness of four types of front-of-pack nutrition labels (FoPLs) in influencing calorie purchases. The four FoPL types are poised for unified implementation across European countries. Further, this study extends its analysis to evaluate the impacts of the voluntary adoption of these FoPLs within 27 EU nations. Nutri-Score displays higher potential for yielding positive health and economic outcomes, compared with other FoPLs. Across EU countries, Nutri-Score is projected to avert nearly two million cases of non-communicable diseases, in total, between 2023 and 2050. Keyhole demonstrates effects of a similar magnitude but with no statistical significance. Nutri-Repere shows smaller impacts, while Nutri-Couleurs has nonsignificant effects. Nutri-Score is projected to significantly lower annual healthcare spending by 0.05%, whereas the other labels have negligible impacts. By reducing cases of disease, FoPLs have the potential to improve employment and work productivity. Nutri-Score surpasses the other labels with an estimated annual gain of 10.6 full-time equivalent workers per 100,000 individuals of working age across EU countries. In all, mandatory implementation of any of the four labels would lead to greater effects than those obtained with a voluntary implementation, providing evidence to inform legislation proposal for an EU-wide nutrition labelling system.

KEYWORDS

cost-effectiveness analysis, front-of-pack food label, modelling

1 | INTRODUCTION

Public interest in easy-to-understand front-of-pack nutrition labels (FoPLs) is growing. Several countries across the European Union (EU) have implemented FoPLs with the specific public health objective to improve the healthiness of diets. Fourteen of the 27 EU countries have implemented FoPLs using various approaches, which span several typologies in the literature. For instance, Julia and Hercberg have categorized FoPLs into five types. The first includes logos that

summarize nutritional information per nutrient, such as non-colored nutrient-specific labels (e.g., the Italian NutrInform Battery, Reference Intakes label, Nutri-Repere), the second displays a three-color code (red, amber, green) with the nutritional information per nutrient—specifically fat, saturates, sugar, and salt—referred to as a colored nutrient-specific label (e.g., the UK Multiple Traffic Lights, Nutri-Couleurs). The third and fourth types include overall summary scoring, and take the form of a graded scale (e.g., the French Nutri-Score) or an endorsement logo (e.g., the Nordic Keyhole, Healthy Choice, Heart

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logo). Lastly, the **warning logos**—used in Chile, for instance—are affixed on foods depending on their levels of specific nutrients.

The logo most frequently used in EU countries is Nutri-Score, as it is found in six countries (Belgium, France, Germany, Luxembourg, Netherlands, and Spain), followed by Keyhole in three countries (Denmark, Sweden, and Lithuania), while other labels are implemented in single countries. A harmonized mandatory EU-wide scheme should be proposed by the European Commission, as part of its Green Deal and Europe's Beating Cancer plan. There is currently an ongoing debate at the European level regarding the implementation of this harmonized scheme. The four potential options for a harmonized mandatory EU-wide label include a graded scale (such as Nutri-Score), an endorsement logo (such as Keyhole), a color-coded nutrient-specific label (such as Nutrlnform Battery). This study focuses on these four types of FoPLs.

A large body of evidence supports that FoPLs can help people make healthier dietary choices. 4-6 For instance, simplified FoPLs increase the number of people selecting a healthier food product by 18%. 6 However, less evidence is available on the effectiveness and the cost-effectiveness that FoPLs have on actual calorie purchases, especially in supermarkets or grocery stores. Much of the previous research has focused on purchase intentions and/or utilized a virtual presentation format. 4.7.8

Therefore, this review provides a unique assessment of calorie purchases made in real grocery stores rather than virtual scenarios. It aims to review the evidence on the effectiveness of the most common types of FoPLs considered for implementation in European countries. This evidence is used to assess the health and economic consequences resulting from an EU-wide voluntary implementation. The analysis on the voluntary implementation of FoPLs is supplemented by a sensitivity analysis that assesses a mandatory implementation that also provides an evidence base to inform legislation proposal for an EU-wide nutrition labelling system.

2 | METHODS

This study is carried out in two steps. Firstly, a review of the literature is carried out to identify evidence on the impact of FoPLs. Secondly, the evidence gathered from the review is fed into a microsimulation model to evaluate the impact of scaling up the implementation of the FoPLs across all EU countries.

2.1 | Reviewing effectiveness

Our research focuses on the effectiveness and cost-effectiveness of FoPLs on food purchases, especially calories that individuals consume through their food purchases. We searched for articles published in the past 5 years in both biomedical and economic databases, using PubMed and IDEAS/RePEc. The search was last updated on January 25, 2023. The search keywords were ("effect" OR "effectiveness" OR "cost-effectiveness") AND ("front-of-pack") AND ("label" OR "labels") AND ("calorie"

TABLE 1 PICO (Population, Intervention, Comparison, Outcome) inclusion and exclusion criteria.

	Inclusion	Exclusion
Population	EU countries	Non-EU countries
Intervention	FoP food labels in real-life food store or supermarket	Studies based on virtual supermarkets
Comparison	Comparison against no label	Not applicable
Outcome	Change in the total calorie amount of food products purchased	Change in purchase intention

OR "dietary quality" OR "nutritional quality") AND ("purchase data" OR "scann data" OR "scanner data" OR supermarket). Further to the collected evidence, we consulted the authors of the studies when results on calorie purchases were not directly accessible. Identified interventions were categorized according to the typology defined by Julia and Hercberg. As for the inclusion criteria, we included the studies that were published in the past five years, focused on EU countries, and analyzed real-life, actual purchase data (Table 1). Conversely, we excluded studies on purchase intention and studies based on experimental, virtual supermarket data.

2.2 | Evaluating health and economic outcomes

The cost-effectiveness analysis uses the OECD micro-simulation model for Strategic Public Health Planning for Non-Communicable Diseases (SPHeP-NCDs) to assess the impact of FoPLs at the country level from 2023 to 2050. Analyses based on the OECD SPHeP-NCDs model have been published elsewhere. Detailed information on the structure and the functioning of the model can be found in Data S1. In short, for each of the 27 EU countries, the model uses demographic, risk factor, and epidemiological characteristics by age- and sex-specific population groups from international databases. The model assesses the impact of FoPLs in terms of population health (e.g., number of disease cases avoided; life years and healthy life years gained) and economic outcomes (e.g., reduction in health expenditure; gains in workforce and related labor market cost). Confidence intervals (CIs) of the simulation outputs are estimated with a bootstrap method.

The effects of FoPL on health conditions are modelled through the effect on body mass index (BMI) of calorie intake variations—converted from calorie purchases identified in the literature review—(see Data S1 for the conversion). BMI and diseases are linked via age-and sex-specific relative risks retrieved from the Global Burden of Disease study. The modelled disease categories include diabetes, stroke, ischaemic heart disease, cancer, depression, dementia, musculoskeletal disorders (MSDs), chronic obstructive pulmonary diseases, cirrhosis, alcohol dependence, and injuries.

Healthcare costs of disease treatments are estimated based on a per-case annual cost, which is extrapolated from national healthrelated expenditure data. The additional costs of multi-morbidity are also calculated and applied. In the model, people living with an obesity-related disease continue to consume medical care for other conditions and incur medical costs. The labor market module utilizes relative risks to relate disease status to the risk of absenteeism, presenteeism (where sick individuals, even if physically present at work, are not fully productive), early retirement, and employment. These changes in employment and productivity are estimated in the number of full-time equivalent workers (FTEWs) and cost is based on a human capital approach using national average wages.¹⁷

2.3 | Sensitivity analyses

Two sensitivity analyses were conducted: to respectively assess the potential effect of a mandatory implementation of FoPLs; and to test different parameters of the effectiveness of FoPLs and population exposure. The first sensitivity analysis was carried out to assess the impact of a mandatory-instead of voluntary-implementation of the identified FoPLs across EU countries. For all the labels that are not classified as endorsement logos, it is assumed that 100% of processed food products would display the logo under a mandatory scheme. The logic is different for an endorsement logo such as Keyhole, as the logo is displayed on the packaging only if the food product is identified as a "healthy" product—and may also be applied to nonpre-packaged items such as fish, fruit, berries, vegetables, and potatoes. The sensitivity analysis thus assumes a 47% increase in the share of products displaying an endorsement logo. This figure is based on the results of a Danish study that used food purchase scanner data to compare the share of products that are eligible for Keyhole with the share of products that display Keyhole in 2008 and 2012. 18

A second sensitivity analysis aimed to test the robustness of the main analysis results, by using different model parameters for the four FoPLs, based on evidence retrieved from studies on purchase intentions. We widened the scope of the review to include studies of purchase intentions, in addition to studies focusing on actual purchases, and we replicated the main analysis.

3 | RESULTS

The literature review identified four papers, but only two papers met our inclusion criteria. The two excluded studies related either to a virtual grocery store or to purchase intentions instead of actual purchases. Therefore, our review yields evidence for four FoPLs: Nutri-Score, Keyhole, Nutri-Couleurs, and Nutri-Repere, corresponding to four types of FoPLs categorized by Julia and Hercberg.³ These include a graded scale, an endorsement logo, a color-coded nutrient-specific label, and a non-colored nutrient-specific label.

3.1 | Effectiveness of FoPLs

A randomized controlled trial (RCT) study examined real-life grocery purchases in 60 French supermarkets to assess whether FoPLs

improved food purchases. The effects of FoPLs on purchased food quality, measured with the Food Standards Agency (FSA) nutrient profiling score, were reported by Dubois et al., 19 and those on calorie purchases were published in an accompanying report in Allais et al.²⁰ The evidence was based on four types of products including bread, ready meals, fresh catering, and pastries. Nutri-Score was found to reduce the total calories of the basket of labelled products by -3.00%(CI: -4.64; -1.36), Nutri-Repere by -0.86% (CI: -2.64; 0.91) (although not significant), while Nutri-Couleurs had a small effect but was not statistically different from zero (+0.07% [CI: -1.70; 1.85]).²⁰ A Danish study using scanner data investigated the effect of Keyhole FoPLs on dietary quality, using the Healthy Eating Index, and energy share from fat, added sugar, and fiber. 5 We consulted the author to obtain the effect on calorie purchases. It was estimated that Keyhole reduces the total calories of the basket of products by -2.28% (CI: -9.71%; 5.15%) (not significant). These values are adapted to the context of label implementation (such as only for food purchased in supermarkets) (see Data S1) and serve as input in the modelling study.

3.2 | Modelled impact on cases of disease

The modelling-based analyses using the reviewed evidence suggest that voluntary implementation of the four labels would avoid several thousand disease cases over the following 28 years, although only two types of labels (Nutri-Repere and Nutri-Score) show significant reductions. Estimates obtained for Nutri-Score exceed these observations by about three times that of Nutri-Repere. Specifically, if implemented across all European countries, Nutri-Score is estimated to avoid a total of 1,125,000 cases of MSDs, 530,000 cases of cardiovascular diseases (CVDs), 161,000 cases of diabetes, 69,000 cases of dementia, and 42,000 cases of cancers related to overweight, over 2023–2050 (Figure 1). Results for Keyhole were as high in magnitude as those observed for Nutri-Score but were non-significant.

3.3 | Modelled impact on life years

Estimates of life year gains obtained with Nutri-Score are significantly greater than those obtained with Nutri-Couleurs and Nutri-Repere in all countries but Portugal where the difference with Nutri-Repere is not statistically significant. Life year gains with Nutri-Score are higher than those with Keyhole in nineteen countries, though the results for Keyhole are not statistically significant. Life years gains with Nutri-Score are significant across all EU countries and range from 9.7 per 100,000 people in Ireland to 33.9 per 100,000 people in Bulgaria. On average across EU countries, Nutri-Score would add about 18.1 life years per 100,000 people by 2050, while Keyhole would add about 16.4 life years per 100,000 people, Nutri-Repere 4.3 per 100,000 and Nutri-Couleurs a non-significant number. In terms of disability-adjusted life years (DALYs), the results are similar to life years gains although gains in DALYs are higher than those for life years. Nutri-Score is estimated to have the greatest effect with 22.2 per 100,000

FIGURE 1 Avoided cases of disease, 27 European countries, cumulative 2023–2050. *Note*: Vertical bars represent 95% confidence intervals (Cls). Keyhole upper Cl for musculoskeletal disorders (MSDs) is not displayed and stands at 2637 thousand. CVDs, cardiovascular diseases. *Source*: OECD SPHeP-NCDs, 2022.

DALYS gained on average across EU countries. Estimates obtained with Nutri-Score are significant for all EU countries (see Data S1).

3.4 | Modelled impact on health expenditure

FoPLs are estimated to reduce healthcare expenditure. On average, across EU countries, Nutri-Score would reduce annual health expenditure by 0.050%, Keyhole by 0.052% but the result is non-significant, Nutri-Repere by 0.017%, and Nutri-Couleurs by 0.003% (Table 2). Reductions in annual health expenditure obtained with Nutri-Score are significant in all countries, ranging from 0.035% in the Czech Republic to 0.084% in the Netherlands. In absolute terms, Nutri-Score would save EUR 0.93 per capita per year in health expenditure, ranging from EUR 0.19 in Estonia to EUR 2.22 in the Netherlands (see Data S1).

3.5 | Modelled impact on employment and productivity

On average, across EU countries, Nutri-Score is estimated to increase the annual workforce by adding the equivalent of 10.6 FTEWs per 100,000 individuals of working age. This rate is estimated at 10.0 FTEWs per 100,000 individuals for Keyhole, but the result is non-significant, 2.9 FTEWs per 100,000 individuals for Nutri-Repere, and practically 0 FTEWs per 100,000 individuals for Nutri-Couleurs. When expressed in monetary terms using average wages, the labor-related

economic cost saved is estimated at EUR 2.89 per capita for Nutri-Score, EUR 2.66 for Keyhole, and below EUR 1 for Nutri-Repere and Nutri-Couleurs, on average across countries (see Data S1). In most of the studied countries, the results for Nutri-Score exceed the results for other labels.

3.6 | Sensitivity analysis results

The evaluation of the potential effect of mandatory implementation of FoPLs shows consistent results with those of voluntary implementation but with larger effects. Results for each outcome indicate that a mandatory Nutri-Score system performs better than the three other FOPLs in their mandatory form. On average across EU countries, Nutri-Score would result in an annual average of 28.8 life years gained per 100,000 individuals, in comparison with effectively 0 life years per 100,000 individuals for Nutri-Couleurs, 8.4 life years per 100,000 individuals for Nutri-Repere, and 23.9 life years per 100,000 individuals for Keyhole. In terms of life years in good health, Nutri-Score would result in a gain of 35.9 DALYs per 100,000 individuals, in comparison with 0 DALYs per 100,000 individuals for Nutri-Couleurs, 10.6 DALYs per 100,000 individuals for Nutri-Repere, and 29.8 DALYs per 100,000 individuals for Keyhole. For MSD cases, Nutri-Score would result in a reduction of 1.9 million cases in comparison with -0.02 million for Nutri-Couleurs, 0.5 million for Nutri-Repere, and 1.6 million for Keyhole. In terms of CVDs, Nutri-Score would result in a reduction of 0.93 million cases in comparison with -0.02million for Nutri-Couleurs, 0.26 million for Nutri-Repere, and 0.78

Country	Nutri-Couleurs	Nutri-Repere	Keyhole	Nutri-Score
Austria	0.0127* (0.0067)	0.0252* (0.0067)	0.0575 (0.0374)	0.0643* (0.0065)
Belgium	0.0093 (0.0073)	0.0188* (0.0072)	0.0654 (0.0418)	0.0663* (0.0071)
Bulgaria	-0.0042 (0.0069)	0.0138 (0.0107)	0.0492 (0.0371)	0.0395* (0.0062)
Cyprus	-0.0005 (0.0074)	0.0193* (0.0072)	0.0652 (0.0421)	0.0635* (0.0073)
Czech Republic	0.0068 (0.0054)	0.0212* (0.0068)	0.0477 (0.0306)	0.0349* (0.0049)
Germany	-0.0018 (0.0076)	0.0108 (0.0079)	0.0593 (0.0423)	0.0543* (0.0074)
Denmark	0.0009 (0.0072)	0.0112 (0.0072)	0.0499 (0.0406)	0.0594* (0.0067)
Spain	0.0009 (0.0068)	0.0101 (0.0071)	0.0538 (0.0402)	0.056* (0.007)
Estonia	-0.0068 (0.0044)	0.0161* (0.0059)	0.0366 (0.0244)	0.0364* (0.0039)
EU	0.0029 (0.0065)	0.0169* (0.0075)	0.0517 (0.0361)	0.0503* (0.0062)
Finland	0.0091 (0.0064)	0.0147* (0.0074)	0.0571 (0.0366)	0.0514* (0.0064)
France	0.0024 (0.0046)	0.0145* (0.0046)	0.034 (0.0251)	0.0349* (0.0043)
Greece	0.0091 (0.0071)	0.0265* (0.0078)	0.0557 (0.0384)	0.0566* (0.0066)
Croatia	0.007 (0.006)	0.0123 (0.0081)	0.0519 (0.0321)	0.0401* (0.0059)
Hungary	0.0056 (0.0054)	0.012 (0.0084)	0.0405 (0.0299)	0.0424* (0.0052)
Ireland	0.0061 (0.0068)	0.0304* (0.0063)	0.0514 (0.0371)	0.048* (0.0063)
Italy	0.0029 (0.0074)	0.0242* (0.0075)	0.0604 (0.0407)	0.0572* (0.0072)
Lithuania	0.0218* (0.0051)	0.0257* (0.0081)	0.0516 (0.0276)	0.0419* (0.0048)
Luxembourg	-0.0013 (0.0069)	0.0157* (0.0064)	0.0592 (0.0389)	0.0533* (0.0062)
Latvia	-0.0076 (0.0058)	0.0065 (0.0099)	0.0339 (0.028)	0.045* (0.0049)
Malta	0.0025 (0.0073)	0.0247* (0.0074)	0.0516 (0.0407)	0.0518* (0.007)
Netherlands	0.0055 (0.0093)	0.0151 (0.0089)	0.0595 (0.0514)	0.0836* (0.0089)
Poland	-0.0088* (0.0051)	0.0091 (0.007)	0.0423 (0.029)	0.0378* (0.005)
Portugal	-0.0077 (0.0079)	0.0109 (0.0082)	0.0654 (0.0443)	0.0616* (0.0076)
Romania	-0.0008 (0.0061)	0.0149 (0.0086)	0.0431 (0.0339)	0.0442* (0.0059)
Slovak Republic	0.0094 (0.0059)	0.0264* (0.0073)	0.0567 (0.0332)	0.0412* (0.0057)
Slovenia	0.0018 (0.0053)	0.0108 (0.0059)	0.0435 (0.0296)	0.0387* (0.0051)
Sweden	0.005 (0.0073)	0.0158* (0.0074)	0.0549 (0.0399)	0.0526* (0.0069)

^{*}Means significant at 5%.

Source: OECD SPHeP-NCDs, 2022.

million for Keyhole. Nutri-Couleurs and Keyhole display results that are statistically non-significant. It is further estimated that in the case of a mandatory Nutri-Score system for all EU countries, the annual healthcare expenditure would be lowered by 0.088% on average in the EU, compared with 0.001% with Nutri-Couleurs, 0.028% with Nutri-Repere, and 0.073% with Keyhole. Further, the EU would gain 17.1 FTEWs per 100,000 individuals of working age per year, higher than those with Nutri-Couleurs (-0.3 non-significant), Nutri-Repere (5.2), and Keyhole (14.5 non-significant). Country-specific results of the potential effect of mandatory implementation of FoPLs are available in Data \$1.

The second sensitivity analysis used evidence from purchase intention studies to test alternative model parameters. Compared with studies on real-life actual purchases, those on purchase intentions indicate a greater effect of FoPLs on calorie purchases. According to the results of the sensitivity analysis, all four FoPLs have a higher potential impact, with no changes in relative positioning between labels (see Data S1). For instance, Nutri-Score is projected to

significantly lower annual healthcare spending by 0.15% in the sensitivity analysis, compared with 0.05% in the main analysis. Regarding labor market impacts, Nutri-Score would increase employment and productivity by the equivalent of 29.1 FTEWs per 100,000 individuals of working age in the sensitivity analysis, compared with 10.6 FTEWs in the main analysis.

DISCUSSION

This paper reviews the effectiveness of four types of FoPLs on calorie purchases and presents a unique and novel assessment of their costeffectiveness. The four FoPL types studied were a graded scale, an endorsement logo, a color-coded nutrient-specific label, and a non-colored nutrient-specific label, which correspond to the four options proposed for a harmonized mandatory EU-wide scheme. Overall, the results indicate that scaling up a voluntary implementation of a graded scale such as Nutri-Score yields higher gains-both

financially and health-wise—compared with the three other FoPL schemes. One possible explanation for this finding is that the ease of understanding of the Nutri-Score helps consumers to make healthier food choices more effectively. Nutri-Score is an overall summary score, while Nutri-Couleurs and Nutri-Repere are nutrient-specific labels. Keyhole is also a logo that is easy to understand. Its effects are equivalent in magnitude to those of Nutri-Score, but they are statistically insignificant. The results of the mandatory implementation of the four labels are in line with the voluntary scheme but with greater effects. These findings provide an evidence base to inform legislation proposal for an EU-wide nutrition labelling system.

Similar to another study (Allais et al.²⁰), our findings show that a non-colored nutrient-specific label such as Nutri-Repere is more effective than a colored nutrient-specific label such as Nutri-Couleurs when assessing the effect on calorie purchases. This result needs to be viewed with caution and qualified by the findings from other studies. For instance, the effect of Nutri-Repere on calorie purchase was found to be not statistically different from the control group with no label.^{21,22} Besides, Nutri-Couleurs is more effective than Nutri-Repere when assessing the effect on the FSA nutrient profiling score.^{19,20} This difference can be explained because the FSA score captures various nutrition dimensions and caloric content is only one of these. However, studies converge to show that Nutri-Score is more effective than both Nutri-Couleurs and Nutri-Repere, increasing the consistency and the validity of our findings.

An important strength of our study is that the review focuses on studies based on real-life shopping data, which provides robust evidence that is closer to reality. Other important strengths include the innovative assessment of FoPLs and the ability to capture the returns of modified nutrition choices, accounting for long-term changes in BMI, incidence of non-communicable diseases, healthcare expenditure, and labor market impacts.

This study is not without limitations. First, the results of the modelling-based assessment are prospective, meaning that they are reliant on assumptions rather than actual observations. However, these assumptions are robust and built on observational studies retrieved from the literature, and all results reported 95% CIs, which increases the quality of the modelling-based findings. Second, the impact of FoPLs on food purchases is expected to be comparable across all countries, although some cultural, dietary, and environmental factors may vary across countries, which might lead to different purchasing behaviors. Third, this study only focuses on the positive effect on caloric intake that FoPLs may have. However, the implementation of FoPLs also has a favorable impact on the composition of an individual's diet. For example, one may decrease the consumption of saturated fat, sugar, and sodium, and increase the intake of whole grains.^{7,8} Therefore, the results of this study should be considered conservative and FoPLs are likely to provide greater health benefits. Fourth, our assessment of FoPLs is based on only two studies, one of which is an experimental study involving a narrow range of food items. In the study by Allais and colleagues, the effect of Nutri-Score, Nutri-Repere, and Nutri-Couleurs was observed on four food categories (bread, ready meals, fresh catering, and pastries) and, in the

absence of specific data, it was assumed that this effect could be generalized to all pre-packaged processed food products. We also assumed that a fixed proportion (55%) of products are labelled but this proportion has been increasing over time. Further, we estimated that 65% of food products are pre-packaged processed food, but this percentage could increase to 75% if minimally processed food, such as pasta and rice, is considered.²³ Given the limited number of food categories, short duration of the experiment and conservative assumptions about the proportion of labelled products and the share of pre-packaged processed food, it is likely that the impacts of these labels may be greater than estimated. This uncertainty is investigated in a sensitivity analysis. Fifth and last, the lack of data disaggregated by socio-economic groups prevented an evaluation of the equity impacts of the different types of labels. However, evidence suggests that easy-to-understand FoPLs tend to be more effective in lower socio-economic groups. 20,24

5 | CONCLUSION

FoPLs have the potential to change consumer's shopping habits towards healthier food choices and reduce energy intake. In the long term, this will translate into greater population health outcomes, lower healthcare expenditure, and increased labor market outcomes. Scaling up a voluntary implementation of a graded scale such as Nutri-Score would result in higher health and economic gains compared with the three other FoPL schemes examined. A mandatory implementation would yield even greater effects. This study provides useful evidence and an economic evaluation of FoPLs to help inform policymaking. Further research would be needed to assess the equity impacts of FoPLs.

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CONFLICT OF INTEREST STATEMENT

None.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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