RESEARCH ARTICLES

HEALTH ECONOMICS

Targeting health subsidies through a nonprice mechanism: A randomized controlled trial in Kenya

Pascaline Dupas,[1,2,3*] Vivian Hoffmann,[4*] Michael Kremer,[2,3,5*] Alix Peterson Zwane[6*]

Free provision of preventive health products can markedly increase access in low-income countries. A cost concern about free provision is that some recipients may not use the product, wasting resources (overinclusion). Yet, charging a price to screen out nonusers may screen out poor people who need and would use the product (overexclusion). We report on a randomized controlled trial of a screening mechanism that combines the free provision of chlorine solution for water treatment with a small nonmonetary cost (household vouchers that need to be redeemed monthly in order). Relative to a nonvoucher free distribution program, this mechanism reduces the quantity of chlorine procured by 60 percentage points, but reduces the share of households whose stored water tests positive for chlorine residual by only one percentage point, substantially improving the trade-off between overinclusion and overexclusion.

Policy-makers have long debated whether developing countries should charge for health products such as deworming medication, malaria medication, mosquito nets, water treatment solution, and latrines. Multiple studies have found that demand for preventive health goods is highly sensitive to price (*1*–*4*). For mosquito nets, usage appears as high among recipients who get them only when they are free or nearly free as among those able to pay a price of USD 1 or more (*2*, *5*–*8*). However, in the case of water treatment solution, Ashraf, Berry, and Shapiro (*9*) argue that households with lower willingness to pay for the product when a marketer comes to their doorstep are less likely to use it for its intended health purpose and more likely to use it for other purposes, such as washing clothes or cleaning toilets. Policy-makers may thus be concerned that free distribution of products that only part of the population values for their health purpose can generate wastage.

This study reports findings from a randomized controlled trial that compares three mechanisms for allocating dilute-chlorine water treatment solution: (i) charging a partially subsidized price; (ii) free provision during a clinic visit and a follow-up household visit (*10*); and (iii) combining free provision with a screening mechanism designed to make the water treatment solution available to those willing to expend a small effort (redemption of a month-specific voucher at a local shop) to obtain it. By testing households' stored water for chlorine residual, we assess actual use of the product and thus compare the extent to which each mechanism generates errors of inclusion (by providing the product to households that will not use it to treat water) or of exclusion (by preventing households that would use the product to treat water from obtaining the product.) We then examine how the optimal choice of mechanism for a policy-maker depends on these error rates, the cost of each mechanism, and policymakers' valuation of households' use of the water treatment solution.

We find that combining free provision with a voucher mechanism screens out 88% of those who would accept the product under free provision but not treat their water, thus markedly reducing errors of inclusion, while creating very few errors of exclusion relative to free provision. Rates of positive residual chlorine tests are almost identical when comparing free distribution and voucher provision. The proportion of households with water testing positive for residual chlorine was 32.9% in the group receiving vouchers and only 1 percentage point higher, at 33.9%, in the group with free distribution. The difference is not statistically significant. This suggests that the inconvenience of safekeeping and redeeming vouchers screened out very few of those who would have used chlorine solution if given it directly.

We also confirm previous findings that although errors of inclusion are low under cost sharing, cost sharing generates many errors of exclusion relative to free treatment. Only 12.4% of households in the cost-sharing group had chlorine in their water, many fewer than under either form of free treatment.

[1]Stanford University, Stanford, CA, USA. [2]National Bureau of Economic Research, Cambridge, MA, USA. [3]Cambridge, MA, USA. [4]International Food Policy Research Institute, Washington, DC, USA. [5]Harvard University, Cambridge, MA, USA. [6]Global Innovation Fund, Washington, DC, USA.
***Corresponding author. Email: pdupas@stanford.edu (P.D.); v.hoffmann@cgiar.org (V.H.); mkremer@fas.harvard.edu (M.K.); alix.zwane@globalinnovation.fund (A.P.Z.)**

Setting and background

Diarrhea is a major cause of child mortality (ages 1 to 59 months) globally and in Kenya (*11*). Water is a major channel for the transmission of diarrheal disease. Dilute chlorine solution kills many of the pathogens that cause diarrhea. Arnold and Colford (*12*) review 21 randomized controlled trials on the impact of point-of-use water treatment with dilute chlorine solution and find that access to point-of-use chlorination reduces reported child diarrhea by an average of 29% overall (*13*). Dilute chlorine solution is socially marketed in many countries by the nongovernmental organization (NGO) Population Services International (PSI), which receives donor support.

The study took place from November 2007 to September 2008 in western Kenya, a region with the second highest prevalence of child diarrhea in Kenya (*14*). In addition to free government provision during epidemics, the primary approach to distribution of water treatment solution in this area had been social marketing and sales to households through retail shops. PSI began marketing 150-ml bottles of dilute chlorine solution branded as "WaterGuard" in Kenya in May 2003. These bottles, expected to last a household 30 to 50 days (*15*–*17*), were sold at a price of 20 Kenyan shillings (Ksh) at the onset of this study, around US$ 0.30 at the exchange rate at that time (*18*, *19*). Although brand recognition for WaterGuard is high, as is reported understanding of the potential benefits of the technology, take-up of water chlorination in rural western Kenya is low. Kremer *et al.* (*20*) report that only 7% of rural households in this part of Kenya were using chlorine to treat their drinking water, a rate typical of many other rural African settings. Point-of-use water treatment requires repeated, proactive behavior on the part of households even when the technology is offered free of charge. Previous work in the region has found that the rate of verified water treatment is around 50% when chlorine solution is provided free, but encouragement and reminders are relatively infrequent (*20*, *21*). Limited use could be due to a number of factors, including aversion to the taste of chlorine, particularly if dosing is too high or water is consumed too soon after treatment.

Methods

Parents of children aged 6 to 12 months, an age group at high risk for mortality due to diarrheal disease, were recruited from the waiting rooms of four rural maternal and child health clinics in Busia District. Once enrolled, study participants were administered a baseline survey on basic demographics, current water treatment practices, knowledge about waterborne illness and diarrhea prevention, and child health. At the end of the survey, the 1118 participants in this study sample were randomly assigned to one of three experimental arms by choosing an envelope from a

bag full of identical envelopes, each containing a letter corresponding to one of these arms. Once the respondent selected an envelope and revealed the letter, the enumerator offered the corresponding treatment. The supplementary materials provide additional information on methods and sampling. Table S1 presents baseline characteristics of our study sample, as well as tests of balance across the treatment arms. Because the baseline survey was administered in waiting rooms of clinics and not at respondents' homes, no water test could be performed at baseline, and therefore we cannot test for baseline balance on the primary end point of interest (presence of chlorine in drinking water at home).

In each of these experimental treatments, participants were offered the opportunity to obtain sufficient water treatment solution to last them much beyond the time of the follow-up survey, which was conducted during a home visit 3 to 5 months later. Comparing take-up and usage at follow-up across these groups thus allows us to identify the targeting effects of varying the price and effort cost of obtaining the product. The three experimental treatments were as follows:

Cost sharing treatment

Water treatment solution was made available for immediate purchase at a 50% discount off the retail price. Participants could purchase up to five 150-ml bottles of the solution (enough to last approximately 5 to 8 months), at 10 Ksh per bottle.

Vouchers treatment

Twelve vouchers, each redeemable for one 150-ml bottle of water treatment solution at either a local shop or the clinic itself, were provided. Each voucher was marked for a specific month, for the next 12 consecutive months, and participants were given a calendar to track the expiration of vouchers.

Free delivery treatment

Two 500-ml bottles of water treatment solution were provided, one immediately and the second given during the follow-up survey conducted at the participant's home, 3 to 5 months later (*22*). At the time they received the first bottle, participants were informed that they would receive a second bottle later. This supply of 1000 ml of water treatment solution was expected to last approximately 7 to 11 months.

A follow-up was conducted at participants' homes 3 to 5 months after enrollment. Details on the methods and attrition at follow-up survey are provided in the supplementary materials and methods.

Results

Table 1 presents dilute chlorine procurement ("take-up") by treatment arm. Whereas take-up in the free delivery arm was nearly universal (everyone took the first bottle of water treatment solution offered at the clinic, and only about 1% of participants refused to accept the second bottle offered during the follow-up home visit), only 13.4% of the five bottles offered for sale were purchased in the cost sharing group [just over half (51.9%) of those in the group purchased a bottle, and few purchased more than one] (*23*).

Take-up in the vouchers group was higher, with 39.8% of the 12 monthly vouchers redeemed per household (85.3% of households redeemed at least one voucher). Analysis presented in table S2 indicates a positive relationship between household wealth and purchase of water treatment solution in the cost sharing group, but a negative association between wealth and procurement in the vouchers group.

Table 2 shows water treatment at follow-up by arm. The first row shows the unconditional proportions of participants in each treatment group, with a positive chlorine test among those with stored drinking water at the time of the survey, while the second row shows coefficients and standard errors from a regression of positive chlorine tests on treatment arm and baseline variables from table S1, stratification variables (clinic and survey wave indicator variables), and time since enrollment. The two sets of results are very similar. We focus our discussion and analysis on the specification conditional on controls.

Table 2 confirms the earlier literature showing that user fees create substantial exclusion errors relative to free delivery: The proportion of households with a positive chlorine test was only 12.4% in the cost sharing group, 21.5 percentage points lower than in the free delivery group.

Table 2 also presents the more novel finding that is the main result of this study: The rates of positive residual chlorine tests in the free delivery and vouchers groups are almost identical. In the vouchers group, 32.9% of households had water testing positive for residual chlorine. In the free delivery group, 33.9% tested positive, so the point estimate of the difference was only 1.0 percentage point (and this was not statistically significant). The 95% confidence intervals for the vouchers and free delivery groups are [25.3, 40.5] and [26.3, 41.5], respectively. Results are very similar and also do not differ statistically when restricting attention only to those households sampled at 3 or 4 months after enrollment, which collectively account for 80% of the sample: At 3 months, the difference between free delivery and vouchers groups was 1.4%; at 4 months the difference was 2.7% (see table S3). This indicates that results are not driven by households in the free delivery group running out of chlorine. The share of households that report running out in that group at the time of follow-up was 15.1% (13.6% for those surveyed after 3 months) (*24*).

Although we cannot directly test whether the same households that use the water treatment product under free delivery would also use it under the vouchers scheme, we can test whether confirmed users under the two schemes have similar characteristics. We do this in table S4, which shows, for the subsample of individuals in either the free delivery or vouchers groups, the coefficient estimates of a regression of confirmed water usage on baseline characteristics and interactions between baseline characteristics and the vouchers treatment. We cannot reject the null that users under the two schemes are selected along identical characteristics, which suggests that those who did not redeem vouchers would likely not have used them under free delivery.

Together, the results so far suggest that imposing the inconvenience of redeeming time-stamped vouchers does not substantially reduce water treatment relative to free distribution. Relative to free distribution, the voucher-allocation

Table 1. Take-up by treatment. Sources: Records from baseline survey (columns 1 to 3, 7); redemption data were collected from participating retailers (columns 4 to 6).

	1	2	3	4	5	6	7
	Cost sharing			Vouchers			Free delivery
	Purchased at least one bottle at clinic	Purchased at least two bottles	Proportion of five bottles purchased	Redeemed at least one voucher	Redeemed voucher month before follow-up	Proportion of 12 vouchers redeemed	Accepted water treatment solution at baseline
Mean	0.519	0.120	0.134	0.853	0.411	0.398	1.000
Observations	351	351	351	382	350	382	385

mechanism reduced errors of inclusion substantially (by 58 percentage points) and had almost no impact on errors of exclusion. Combining free provision with a voucher mechanism achieves most of the benefits of free treatment, while eliminating most of the downside of potential wastage due to errors of including people who would not use the product to treat water. As discussed more formally in the next section, our point estimates imply that unless a policy-maker is willing to accept almost 60 exclusion errors to avoid one inclusion error, the policy-maker will prefer a voucher screening mechanism to free delivery.

Although the effort required to redeem vouchers was not varied experimentally in this study, we can use variation in the location at which vouchers could be redeemed to generate a measure of the strength of the nonprice screen. Specifically, shops where the vouchers could be redeemed were in the nearest market center for 22% of respondents. Table 3, column 1, shows that participants who could redeem vouchers at the nearest market center were 15.3 percentage points more likely (adjusted *P*-value: 0.034) to have redeemed a voucher in the month before the follow-up interview than those who had to go further out of their way to do so, conditional on stratification variables (enrollment wave and clinic), time since enrollment, and baseline covariates. However, these participants were only 4.4 percentage points more likely (adjusted *P*-value: 0.532) to be using the solution to treat their water, according to chlorine test results (Table 3, column 2) (*25*). Distance to the redemption point was not randomly assigned, so it is possibly correlated with characteristics that were not measured at baseline and therefore not controlled for in the analysis. Future work could experimentally vary the location of voucher redemption to test the hypothesis that less onerous nonprice screening mechanisms generate higher take-up, but are less effective at screening out those who do not use a good for its intended purpose.

Optimal policy

To formally examine the optimal choice of mechanism for a policy-maker, let V denote the policy-maker's valuation of providing water treatment solution to a household that has children at risk of mortality from diarrheal disease and that will actually use the water treatment solution for its intended purpose. The policy-maker therefore seeks to maximize total value minus the total cost of the subsidy, or $VN_m - C_mT_m$, where the subscript m denotes the mechanism, N denotes the number of households using water treatment under mechanism m, C_m denotes the subsidy per household obtaining water treatment under mechanism m, and T_m denotes total take-up—i.e., the number of households that obtain chlorine solution under mechanism m. The policy-maker will prefer changing from delivery mechanism a to mechanism b that expands take-up relative to mechanism a, if and only if $V(N_b - N_a) > C_bT_b - C_aT_a$, which we can rewrite as

$$V(N_b - N_a) > C_b(T_b - T_a) + (C_b - C_a)T_a \quad (1)$$

The left-hand side of inequality (1) is the value to the policy-maker of additional chlorine usage, and the right-hand side is the cost to the policy-maker of achieving this change, which consists of the cost of reaching marginal consumers, $C_b(T_b - T_a)$, plus the cost of further subsidizing inframarginal consumers who would have obtained water treatment solution in any case, $(C_b - C_a)T_a$. In the special case in which the cost to the policy-maker per taker is the same under the two mechanisms ($C_b = C_a = C$), this expression simplifies and can be expressed as $(N_b - N_a)/(T_b - T_a) > C/V$, so that the ratio of new users to new recipients must be greater than the ratio of the subsidy per taker to the policy-maker's valuation of health. If the cost per user under method b (which achieves higher take-up) is greater, as will typically be the case, then this condition will be necessary (but not sufficient) for method b to be preferred.

Clearly, if policy-makers have a low enough valuation of a targeted household treating its water (any value less than the cost of the treatment and extending up to some range above this), they will want a positive price (either no subsidy or a subsidy that does not bring the price to zero). If policy-makers have a high enough valuation, they will prefer free household delivery. However, our estimates imply that it is possible to make a product available for free with little wastage, and hence that there will be a broad range of valuations over which they will prefer combining a full subsidy with a nonprice screening mechanism (*26*).

Table 4 summarizes the material cost of water treatment solution per additional user reached under the policy changes considered. The first column shows the change in chlorine usage for 100 subsidized doses, and columns 2 to 5 spell out the components of the two terms on the right-hand side of inequality (1). Column 6 indicates the total material cost per additional user, abstracting from differences in delivery costs. The first row of Table 4 illustrates the binary choice between cost sharing and free delivery, excluding the option of a voucher screening mechanism. Relative to cost sharing, delivering chlorine free of charge to users increases the proportion of households that obtain it by 86.6 percentage points, from 13.4 to 100% (columns 3

Table 2. Positive chlorine test at follow-up (3 to 5 months after intervention). Adjusted differences are computed from coefficients in a linear regression of the outcome (positive chlorine test at follow-up) on treatment indicators, controlling for clinic, recruitment wave, time since interview, and baseline controls shown in table S1. Standard errors are in parentheses.

	1	2	3
	Cost sharing	**Vouchers**	**Free delivery**
Raw means	0.124	0.345	0.344
	(0.019)	(0.026)	(0.026)
Adjusting for baseline controls	0.124	0.329	0.340
	(0.019)	(0.039)	(0.039)

Table 3. Take-up and usage by distance to redemption point. Standard errors are in parentheses. Data are from participants in the vouchers treatment whose chlorine use was observed at the follow-up interview (data on location of home is not available for attriters; chlorine test results not available for those without stored water at time of survey). Adjusted differences are computed from coefficients in a linear regression of each outcome on treatment indicators, controlling for clinic, enrollment wave, time since interview, and baseline controls shown in table S1.

	1	2
	Proportion redeemed voucher month of survey	**Proportion with positive chlorine test**
Vouchers redeemable at nearest market	0.507	0.368
	(0.060)	(0.059)
Observations	71	68
Not redeemable at nearest market	0.383	0.331
	(0.031)	(0.030)
Observations	253	248
Difference of means	0.124	0.037
P-value, unadjusted difference of means	0.062	0.569
Difference of adjusted means	0.153	0.044
P-value, difference of adjusted means	0.034	0.532

and 7 in Table 1), and increases the proportion of verified chlorine users by 21.5 percentage points, from 12.4 to 33.9% (columns 1 and 3, second row of Table 2). This implies that 4.03 additional doses of water treatment solution have to be delivered for every additional dose used (86.6/21.5) (*27*). Moreover, under free delivery the policy-maker fully subsidizes water treatment for the 13.4% of households that would purchase at the cost-sharing price (*28*). This adds a cost equivalent to 0.31 doses per additional user [(13.4 × 0.5 dose)/21.5 = 0.31], which brings the total cost to 4.34 doses for every new user (*29*). If a policy-maker has a high value of health, this could be a cost worth bearing to achieve high coverage, but a policy-maker with a lower value of health may choose a cost-sharing approach.

Once the possibility of a voucher screening mechanism is introduced, policy-makers with a broad range of valuations of health will prefer this approach to either cost sharing or full subsidy via free delivery (*30*).This result is shown in rows 2 and 3 of Table 4. Moving from cost sharing to a voucher-based screen implies that the policy-maker must provide 1.7 additional units of treatment solution for every additional chlorine-using household. To see this, it is apparent that in the vouchers treatment, 41.1% of recipients redeemed a voucher in the month before the follow-up visit, and 39.8% of total vouchers were redeemed over the 12-month span of their validity (columns 5 and 6, Table 1). Based on the prior-month redemption figure and the adjusted confirmed usage rate of 32.9% (Table 2, column 2) in this group, the proportion of households obtaining chlorine increases by 27.7 percentage points, relative to cost sharing, while the proportion of users increases by 20.5 percentage points, relative to cost sharing. Thus, moving from cost sharing to a voucher-based screen implies that the policy-maker must provide 27.7/20.5 = 1.35 additional units of treatment solution for every additional household with confirmed chlorine residual. Adding the cost of fully subsidizing those who would use under cost sharing, as calculated above, brings the full cost of the policy change to 1.68 units per new user.

If the additional value (beyond that of the household itself) that policy-makers place on a household treating its water is less than the cost of one dose, then they would not want to fully subsidize treatment. If they value it at between 1 and 1.68 times the cost of a dose, then the wastage associated with a voucher-based approach would lead them to reject such a program. If water treatment is valued above 1.68 times the cost of a dose, voucher programs are potentially attractive.

Moving from vouchers to universal free delivery, under which 33.9% of households were confirmed to be chlorinating at the follow-up visit, entails providing 58.9 additional units of treatment solution to reach one additional using household (100% take-up under free delivery minus 41.1% coupon redemption to achieve an increase of 1% in usage). If the value of reaching that one additional household is extremely high, a policy-maker might choose the free delivery mechanism. However, it is easy to see that for a wide range of values placed on the health of this 34th household, the voucher mechanism would be preferred to full subsidy via free delivery, as it is substantially cheaper.

We can be more specific about how policy-makers' decisions will depend on their valuation of averting a disability-adjusted life year (DALY) and their expectations about the number of DALYs saved per household chlorinating their water (*31*). For the purposes of illustration, we use the estimated impact of point-of-use chlorination on diarrheal disease reported by Arnold and Colford (*12*) and assume that the reduction in child deaths achieved through treatment of drinking water is roughly proportional to diarrhea cases averted. (If policy-makers believed that water treatment is half as effective as implied by these assumptions, they would simply require valuations twice as high as those reported here to make each decision.) Using estimates of the total under-5 mortality rate and under-5 diarrheal mortality rate in Kenya provided by the UN Inter-agency Group for Child Mortality Estimation (*32*) and Health Epidemiology Reference Group (*33*), respectively, a policy-maker would arrive at estimates of the material costs per DALY and life saved via water treatment shown in columns 7 and 8 of Table 4. Underlying data and assumptions are described in the supplementary materials and methods.

In this example, setting aside issues of differences in distribution costs between the options, policy-makers who value a DALY saved at between $70 and $2475 (or a statistical life at between $2134 and $74,921) will prefer the voucher screening approach to the other options. The range of valuations for which the voucher approach is preferred is very wide, encompassing values far below the very stringent standard of $246 per DALY corresponding to the current dollar value of the $150/DALY threshold implicitly suggested by the World Bank in the 1993 World Development Report (*34*, *35*) and extending above the more generous approach taken by the World Health Organization (WHO) (*36*, *37*) of considering interventions costing less than the gross domestic product per capita of the country (currently $1245 for Kenya) as highly cost effective. Policy-makers with valuations below $70/DALY would likely prefer cost sharing, whereas policy-makers with valuations above $2475/DALY would prefer free distribution.

This analysis considers only the cost of the water treatment itself. Administering a voucher

Table 4. Policy comparisons. Calculations reflect material cost of water treatment solution only; differences in delivery costs are not included. "Dose" refers to a yearly dose (12 bottles of 150 ml). At the time of writing, the exchange rate was Ksh 103 to USD 1; thus, a yearly dose costs (12 × 20)/103 = USD 2.33.

	1	2	3	4	5	6	7	8
	Additional verified users for 100 doses subsidized ($N_b - N_a$)	**Additional takers for 100 doses subsidized ($T_b - T_a$)**	**Doses fully subsidized per marginal user (col 1/col 2)**	**Full-dose equivalent for inframarginal users (Table 1 col 3 × 1/2)**	**Full-dose equivalent subsidy for inframarginal users, per marginal user (col 4/col 2)**	**Total additional doses provided per new user (col 3 + col 5)**	**Cost per additional DALY saved, USD***	**Cost per additional life saved, USD***
Policy change considered:								
1. Cost sharing to free delivery	21.5	86.6	4.03	6.70	0.31	4.34	182	5,520
2. Cost sharing to vouchers	20.5	27.7	1.35	6.70	0.33	1.68	70	2,134
3. Vouchers to free delivery	1.00	58.9	58.9	0	0	58.9	2,475	74,921

*See supplementary materials for assumptions used in calculations of costs per DALY and cost per life saved.

system could generate some additional costs relative to a partial subsidy system without vouchers; the magnitude of these costs is an important question when considering operationalizing such a program. Similarly, free household delivery would be substantially more expensive than a voucher system. Although delivering a 500-ml bottle at the clinic is relatively cheap, because children are vulnerable to diarrhea until age 5 and because dilute chlorine solution has a limited shelf life (18 months from the date of manufacture, so 6 to 12 months given distribution lags), additional bottles would have to be provided later on. Arranging for these to be delivered to households would be very expensive relative to vouchers (*38*). This suggests that only policymakers with a very high valuation of health would prefer free delivery to a voucher system.

Discussion

Ashraf *et al.* (*9*) report that use of a price mechanism to target a preventive health product—dilute chlorine solution for water treatment—disproportionately targets those who will use it, but also excludes many potential users. The results presented here suggest that combining free provision with a nonprice screening mechanism—requiring people to redeem vouchers—can also greatly reduce wastage but without a corresponding increase in the exclusion of those who would use treatment. This study makes several contributions. First, it extends a literature in economics on "ordeal mechanisms" as targeting mechanisms. Second, the findings demonstrate proof of concept for a novel approach to the distribution of water treatment solution.

An existing literature in economics discusses the effectiveness of "ordeal mechanisms," such as requiring work for welfare, in targeting redistributive transfers to the poor (*39*, *40*). For example, some food subsidy programs focus on coarser grains that richer households are less likely to consume to reduce errors of inclusion of richer households. This study takes the idea in a new direction, by examining the extent to which what might be termed "micro-ordeals" can target merit goods (goods for which the policy-maker values consumption beyond the value at which the household values consumption) to those who will use them as intended by the policy-maker. We provide evidence that time and money costs have different selection properties, and in particular that compared to free delivery, charging selects a richer group of households to obtain water treatment, whereas a voucher system selects a poorer group of households, consistent with a model in which richer households have a higher value of time. This differential pattern of selection suggests that price-based selection mechanisms are unlikely to be able to duplicate the pattern of selection created by the voucher redemption mechanism. To the extent that poorer households are more likely to experience mortality from diarrheal disease, the voucher system induces a pattern of selection that is likely to yield greater health benefits per person treating their water.

There are several possible reasons why, in our context, willingness to redeem vouchers predicted usage well, whereas willingness to pay a monetary cost led to many errors of exclusion of those who would use the water treatment solution. Perhaps households with a low valuation of time were more likely both to redeem vouchers and to use water treatment solution. Perhaps households that are motivated and organized enough to safekeep and redeem vouchers were also motivated and organized enough to treat their water, but labor market imperfections made it difficult for these households to convert their time to money that could be used to purchase the product.

Such micro-ordeal screens could potentially be used more broadly. For example, it might be the case that having to fill out application forms to apply for a college scholarship targets students who will later study diligently and thus use the college education most productively. As this example indicates, such judgments will have to be made on a case-by-case basis using the empirical evidence for that case. In some cases, a micro-ordeal might be insufficient to screen out people who would use a product in a way other than the policy-maker intended. For example, in the same area of Kenya, Cohen *et al.* (*41*) find that, conditional on having an episode of fever, willingness to pay the effort cost of visiting a local drug shop to redeem a voucher for highly subsidized antimalarial medication is poorly correlated with actual malaria status—specifically, 44% of those redeeming an antimalarial voucher do not have malaria (but think they do). This is due to poor access to accurate malaria diagnosis combined with the very high benefit of appropriately treating malaria when it truly is the underlying cause of the fever. Ma *et al.* (*42*) find that 90% of households in China redeem vouchers for free prescription eyeglasses for myopic children, even though less than half of the children end up wearing the eyeglasses regularly. This could be because for such a product, as in water chlorination, users need to try the product out to know the usage cost, and the option value of learning outweighs the redemption cost for most households. Unlike water chlorination, eyeglasses cannot be distributed in monthly doses, so the voucher mechanism cannot be used to screen out, over time, those who have learned that the usage costs are too high for them. In other cases, almost everyone who takes a product distributed for free may use it as intended, so there is no need for a micro-ordeal. [See, for example, (*6*) on antimalarial bed nets.]

Because many real-world free distribution programs do not involve in-person free delivery, but instead require those seeking a product to make some effort to obtain the product, our results suggest caution in extrapolating adoption rates from studies in which surveyors visit households and offer highly subsidized or free products, to predict the impact of scaled programs in which households must expend some effort to obtain a subsidized product. The very high uptake rate of dilute chlorine solution in the free delivery arm is consistent with the hypothesis that respondents who knew they were unlikely to use chlorine solution might have been reluctant to turn down the free gift because this might be perceived as rude or as signaling a lack of commitment to child health. To reduce the possibility of experimenter demand effects, it may be better to assess demand for products by examining whether households redeem coupons for products because this does not involve an enumerator directly observing the action of the survey respondent.

A voucher-based subsidy for water treatment solution seems potentially scalable. The NGO PATH and the U.S. Centers for Disease Control and Prevention have explored a similar approach of distributing dilute chlorine through antenatal clinics in Malawi (*43*), and the Tanzania National Voucher Scheme (*44*) provides a discount voucher for insecticide-treated mosquito nets to pregnant women and parents of young children through health centers. Vouchers could easily be bundled in safe birthing kits, which are an increasingly common intervention, and could also be implemented electronically using mobile phones.

There are several reasons that a voucher program could be appealing, in addition to avoiding wastage. One advantage of this approach is that it facilitates targeting subsidies to particular populations—in this case, households with young children at risk of diarrheal mortality and morbidity. Also, a voucher-based subsidy complements the existing system of social marketing by generating more business for shops that sell dilute chlorine solution, which may encourage shops to carry the product and avoid stockouts. To the extent that this approach leads households to continue using chlorine solution after their children have passed the age at which subsidies are provided, it may have broader benefits (*45*). As discussed further in the supplementary materials, vouchers also seem to target the poor, whereas richer households are more likely to adopt vouchers under cost sharing. Insofar as children from poor households may be at highest risk of diarrheal mortality and other outcomes such as stunting, this represents another advantage of free distribution through vouchers. Such a program, if implemented through the health care system (i.e., vouchers distributed during well-baby checkups), would also provide at least some increased incentive for households to bring children into clinics.

We note three limitations of this study. First, we do not report on health outcomes. Self-reported diarrhea in the context of a trial through which recipients were provided free water treatment solution may be subject to bias, and collection of observational data on this outcome was beyond the available budget. Second, the volume of water treatment solution offered to participants differed across treatments for logistical reasons. Although analysis of subgroups by time of follow-up data collection indicates that results were not driven by households differentially running out of water treatment solution across arms, it is possible that

larger quantities were interpreted as a signal of lower quality. However, this seems unlikely because all groups were given the same information on the importance of treating water with chlorine and on the potency of the product. Finally, although we show that screening with a voucher mechanism eliminates most of the wastage of water treatment solution associated with free delivery, with very little cost in terms of reduced water treatment, owing to budget constraints, we could not examine the full space of potential policies. Given our results, it would be of considerable intellectual interest for future work to examine a range of nonprice mechanisms, a range of prices, and the space combining price and nonprice mechanisms in various combinations (for example, by requiring households to both travel to a redemption center to redeem vouchers, and to make a payment), as well as the health consequences of the differential patterns of selection of different mechanisms. Because this space is extensive, fully exploring it would likely require multiple studies.

Future work could also formally examine a range of potential underlying mechanisms. For example, the finding that price and nonprice mechanisms have different patterns of heterogeneous effects with assets is consistent with the idea that liquidity constraints play a major role, as shown in previous work on mosquito nets (*46*). By examining a finer range of subsidy levels between 50 and 100% and by more fully examining heterogeneity among households with different levels of assets, it might be possible to test the hypothesis that a substantial fraction of households are severely credit constrained, with zero or extremely limited liquid assets but with access to labor that cannot easily be transformed into liquid assets, and thus that even if the price were as low as a single Kenyan shilling, rates of water treatment would be substantially lower than under free delivery, and thus that it would not be possible to replicate the pattern of selection induced by the nonprice mechanism. Future work could also examine hypotheses from psychology that households may seek to avoid the decision-making costs associated with making any choice to spend money or that there may be a discontinuity in behavior around a price of zero. Finally, future work could examine the hypothesis that differential social costs of refusing to accept water treatment solution during household visits, visits to clinics, and visits to shops induce different patterns of selection of those who will use water treatment solution.

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23. It is plausible that a substantial proportion of the population face liquidity constraints and that they might have bought more water treatment solution in steady state under a policy in which everyone knew in advance that the solution would be available to parents of young children at half price in clinics. However, a separate study conducted in fall 2006 in the study region provides suggestive evidence that take-up levels under the cost-sharing treatment would have been similar even if households could have purchased the water treatment solution over time. In that study, 210 households received 12 monthly coupons for a 50% subsidy on WaterGuard bottles redeemable at local shops (*20*). The authors report that ~10% of the 2520 coupons distributed were redeemed, a rate comparable to, if slightly lower than, the 13.4% purchase rate found in our study. Although the two samples were different [our study sampled parents of young children at clinics whereas Kremer *et al*. (*20*) had a representative sample], this nevertheless suggests that take-up is low even when households are given a month to find the money. This suggests that the cost sharing treatment yields estimates of take-up that are likely not very far from what would have been observed had this discount been offered over an extended period.
24. The follow-up survey recorded whether the initial Aquaguard bottle could be seen on the compound. It could be seen with Aquaguard in it in 72.6% of the compounds. Of recipients, 11.5% declared having given the bottle away to neighbors. See table S5.
25. The one clinic that served as a redemption point was not located in a market center, so all of the participants recruited at this clinic are included in the group unable to redeem at the nearest market. Omitting this subsample from the analysis does not affect the pattern or statistical significance of the results.
26. Policy-makers will not want to choose a negative price if households can freely and unobservably dispose of chlorine solution, because then people with no valuation of the water treatment solution will nonetheless obtain it to get the subsidy, but will simply throw it away.
27. We cannot rule out the possibility that some of these additional doses delivered were not "wasted" but were, for example, given to other households, or used after the period of water testing. However, because we assume that the policy-maker values water treatment in households with children in the age range at greatest risk of diarrheal mortality, and because dilute chlorine solution expires over time, we will treat the policy-maker as valuing verified water treatment.
28. We thus consider the problem of a health planner, who seeks to maximize health gains with a given fiscal expenditure and who does not value the implicit transfer involved in subsidies to inframarginal households. A social planner who valued household income would place at least some value on the implicit transfer to inframarginal households and would thus focus more on the figures that include only the cost of wastage. This slightly reduces the cost of moving from cost sharing to either of these policies, but does not alter the basic conclusions of this analysis.
29. This analysis considers only the cost of the water treatment solution, valued at 20 Kenyan shillings per 150 ml, the price at which WaterGuard is sold in Kenya. See below for a discussion of how the analysis might be affected by considering full delivery costs from implementing different policies at scale.
30. The time cost to recipients of redeeming vouchers is ignored in this analysis. Taking this cost into consideration reduces the cost-effectiveness of the voucher-based screening mechanism slightly; however, under reasonable assumptions on the value of time in this setting, the voucher policy remains preferred over a wide range of valuations on health.
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SUPPLEMENTARY MATERIALS

www.sciencemag.org/content/353/6302/889/suppl/DC1
Materials and Methods
Supplementary Text
Tables S1 to S5
References (*47*–*57*)

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STRUCTURAL BIOLOGY

Structure of a yeast catalytic step I spliceosome at 3.4 Å resolution

Ruixue Wan,* Chuangye Yan,* Rui Bai,* Gaoxingyu Huang,* Yigong Shi†

Each cycle of pre–messenger RNA splicing, carried out by the spliceosome, comprises two sequential transesterification reactions, which result in the removal of an intron and the joining of two exons. Here we report an atomic structure of a catalytic step I spliceosome (known as the C complex) from *Saccharomyces cerevisiae*, as determined by cryo–electron microscopy at an average resolution of 3.4 angstroms. In the structure, the 2′-OH of the invariant adenine nucleotide in the branch point sequence (BPS) is covalently joined to the phosphate at the 5′ end of the 5′ splice site (5′SS), forming an intron lariat. The freed 5′ exon remains anchored to loop I of U5 small nuclear RNA (snRNA), and the 5′SS and BPS of the intron form duplexes with conserved U6 and U2 snRNA sequences, respectively. Specific placement of these RNA elements at the catalytic cavity of Prp8 is stabilized by 15 protein components, including Snu114 and the splicing factors Cwc21, Cwc22, Cwc25, and Yju2. These features, representing the conformation of the spliceosome after the first-step reaction, predict structural changes that are needed for the execution of the second-step transesterification reaction.

Each cycle of pre-mRNA splicing results in the removal of an intron and the joining of two exons, through two sequential, S_N2-type transesterification reactions (*1*–*3*). In the first-step reaction, the 2′-OH of an invariant adenine nucleotide in the branch point sequence (BPS) of an intron serves as a nucleophile to attack the phosphorous atom of the guanine nucleotide at the 5′ end of the 5′ splice site (5′SS), forming an intron lariat–3′-exon intermediate and freeing the 5′ exon. In the second-step reaction, the 3′-OH of the RNA nucleotide at the 3′ end of the 5′ exon serves as a nucleophile to attack the phosphorous atom of the nucleotide at the 5′ end of the 3′ exon, joining the two exons and releasing the intron lariat (*2*). These two reactions are executed by a highly dynamic spliceosome that assumes at least six distinct states known as the B, B^{act}, B*, C, P, and ILS complexes (*4*).

The precatalytic spliceosome (B complex) contains all five small nuclear ribonucleoprotein particles (snRNPs): U1, U2, U4, U5, and U6. Dissociation of U1 and U4 snRNPs and recruitment of the nineteen complex (NTC) and NTC-related complex (NTR) trigger formation of the activated spliceosome (B^{act} complex). The B^{act} complex is converted to the catalytically activated spliceosome (B* complex), which executes the first-step reaction. The catalytic step I spliceosome, also known as the C complex, catalyzes the second-step transesterification with the help of a few splicing factors (*5*). The resulting P complex contains an intron lariat and a ligated exon, which is released in the ILS complex.

The spliceosome is a metalloribozyme (*6*–*8*), and conserved nucleotides in the intramolecular stem loop (ISL) of U6 snRNA coordinate the catalytic magnesium (Mg^{2+}) ions (*1*, *9*–*12*). During the first-step reaction, nucleotides at the 3′ end of the 5′ exon are anchored by loop I of U5 snRNA, whereas the 5′SS and BPS are recognized by U6 and U2 snRNA, respectively. The splicing active site, located in a catalytic cavity on the central spliceosomal component Prp8 (*13*), comprises the ISL of U6 snRNA, helix I of the U2/U6 duplex, loop I of U5 snRNA, and at least two Mg^{2+} ions (*11*, *12*).

Structures of individual spliceosomal components have been elucidated, primarily through x-ray crystallography (*14*–*21*). Investigations of the intact spliceosome, which is known for its conformational and compositional variability (*3*, *22*), have relied on electron microscopy (EM). Structures of various spliceosomal complexes over a wide range of resolution limits have been obtained (*11*, *12*, *23*–*42*). The 3.6 Å structure of the ILS complex from *Schizosaccharomyces pombe* unveils a detailed arrangement of U2, U5, and U6 snRNAs and specific interactions at the active site (*11*, *12*). More recently, the 3.5 Å structure of the B^{act} complex from *Saccharomyces cerevisiae* reveals how catalytic latency is maintained by the protein components surrounding the active site (*43*). Here we report the 3.4 Å structure of a spliceosomal C complex, which reveals the inner workings of the RNA elements together with their protein cofactors after the first-step transesterification reaction.

Beijing Advanced Innovation Center for Structural Biology, Tsinghua-Peking Joint Center for Life Sciences, School of Life Sciences, Tsinghua University, Beijing 100084, China.
*These authors contributed equally to this work. **†Corresponding author. Email: shi-lab@tsinghua.edu.cn**

Cryo-EM analysis

Using the NTC component Cef1 as an affinity-tagged protein, we purified a mixture of different spliceosomal complexes and used two-dimensional (2D) and 3D classifications to separate these distinct structural entities (*43*). Among the original set of 761,767 particles, 84,486 were used for reconstruction of the activated B^{act} complex at 3.52 Å resolution (*43*). The strategy of applying multiple simultaneous 3D classifications and merging all relevant classes proved to be important for the maximal inclusion of particles that represent the B^{act} complex. Starting from the same set of 761,767 particles, we applied the same strategy to identify those that represent the C complex (figs. S1 and S2A). After two rounds of 3D classification, 161,066 particles yielded a reconstruction at an average resolution of 3.95 Å, which, through particle polishing and autorefinement, was improved to 3.41 Å on the basis of the gold-standard Fourier shell correlation criteria (fig. S2B and tables S1 to S4).

The local resolutions vary greatly in the C complex (fig. S2C). The actual resolution in the central regions of the spliceosome reaches 2.9 to 3.5 Å, allowing atomic modeling. At the periphery, however, the EM density becomes contiguous only after being low-pass filtered to 10 Å (fig. S2D). To facilitate model building in the peripheral regions, we performed two more rounds of 3D classification, focusing on only the class that displays structural features in these regions (fig. S3). This effort generated two distinct reconstructions at 3.65 and 4.6 Å (fig. S4 and tables S1 to S4). In the central regions of the 3.41 Å density maps, most secondary structural elements are well defined, and a large proportion of amino acid side chains are identifiable (figs. S5 to S7). The RNA elements at the catalytic center and the surrounding protein components are marked by distinguishable features in the density maps (figs. S8 to S11), allowing atomic modeling of RNA nucleotides.

Overall structure

The refined model of the C complex from *S. cerevisiae* contains 8587 amino acids from 35 proteins, 377 nucleotides from three snRNAs,

Science

Targeting health subsidies through a nonprice mechanism: A randomized controlled trial in Kenya

Pascaline Dupas, Vivian Hoffmann, Michael Kremer and Alix Peterson Zwane

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Delivering chlorine to those who use it

In developed countries, a consumer's valuation of a health product can be measured by his or her willingness to pay for it. But poorer individuals, especially those in developing countries, might want and need a product yet be unable to pay for it with money. Dupas *et al.* demonstrate that a nonprice voucher mechanism can be used to deliver chlorine for water treatment to people in Kenya who are too poor to pay for it, but who use it when they get it (see the Perspective by Olken). Having to redeem the vouchers screens out people who would accept the free chlorine solution but not use it.

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