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Money matters (II): costs of maize inbred line conversion schemes at CIMMYT using conventional and marker-assisted selection

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Abstract

This article presents selected results of a study carried out in Mexico at the International Maize and Wheat Improvement Center (CIMMYT) to compare the cost-effectiveness of conventional and biotechnology-assisted maize breeding. Costs associated with the use of conventional and marker-assisted selection (MAS) methods at CIMMYT were estimated using a spreadsheet-based budgeting approach. This information was used to compare the costs of conventional and MAS methods for a particular breeding application: introgressing an elite allele at a single dominant gene into an elite maize line (line conversion). At CIMMYT, neither method shows clear superiority in terms of both cost and speed: conventional breeding schemes are less expensive, but MAS-based breeding schemes can be completed in less time. For applications involving tradeoffs between time and money, relative profitability can be evaluated using conventional investment theory. Using a simple model of a plant breeding program, we show that the optimal choice of a breeding technology depends on the availability of operating capital. If operating capital is abundantly available, the ″best″ breeding method will be the one that maximizes the net present value (i.e., MAS), but if operating capital is constrained, the ″best″ breeding method will be the one that maximizes the internal rate of return (i.e., conventional selection). This insight may help to explain why private firms tend to invest more aggressively in biotechnology than public breeding programs, which are more likely to face budgetary constraints.

Abbreviations: BC – backcross, CIMMYT – *Centro Internacional de Mejoramiento de Maíz y Trigo* (International Maize and Wheat Improvement Center), IRR – internal rate of return, MAS – marker-assisted selection, NPV – net present value, PCR – polymerase chain reaction, QTLs – quantitative trait loci, SSR – simple sequence repeat

Introduction

Recent advances in biotechnology have led to the development of new research tools that could dramatically change the science of plant breeding. DNA-based molecular markers are one of these new tools. Among their many potential applications to plant breeding, DNA markers can be used to identify individual plants containing particular alleles of interest (Crouch 2000; Mohan et al. 1997; Ribaut and Hoisington 1998). This use of DNA markers has aroused considerable interest among plant breeders, because the ability to trace particular elite alleles with a high degree of precision could greatly facilitate many routine breeding tasks that up until now have been time-consuming, expensive, or both.

Many breeding programs have developed the capacity to carry out marker-assisted selection (MAS) more or less routinely. Managers of these programs must now decide whether it makes sense to put the technology to work on a large scale. The question is not an easy one. In describing the potential benefits

of MAS, proponents often overlook several important practical considerations. Even if markers can improve the precision of selection, they will not always be cost-effective. Depending on the nature of the target trait (quantitative or qualitative), the type of gene and the form of gene action that controls expression of the trait (e.g., major or minor gene, dominant or recessive effect), and the ease with which the target trait can be measured (detectable through visual inspection or only through more expensive field or laboratory analysis), conventional selection may be cheaper than MAS. The desirability of using DNA markers therefore depends in part on the cost of genotypic relative to phenotypic screening, which varies among applications. Furthermore, cost is not the only factor affecting the choice of screening method. Plant breeders must worry about controlling costs, but they also must be concerned about getting products out rapidly. Even in cases where MAS is more expensive than conventional selection, breeders who use MAS may be able to generate desired outputs more quickly. Since accelerated release of improved varieties often translates into economic benefits, time is an important consideration in addition to cost, and time requirements can vary widely depending on the choice of screening method.

This article and the preceding companion article (Dreher et al. 2003) present selected results of a study carried out at the International Maize and Wheat Improvement Center (CIMMYT) to compare the cost-effectiveness of conventional selection and MAS for different breeding applications. The results are based on research protocols used at CIMMYT and prices paid in Mexico for field and laboratory facilities, labor, and purchased inputs. In interpreting the findings of the CIMMYT case study, it is important to keep in mind that the objective of the two articles is not to describe novel breeding methods or present experimental results; rather, the objective is to provide empirical information, analysis, and discussion that will encourage more objective evaluation and foster better integration of conventional and biotechnology-assisted methods for crop genetic improvement. The companion article examined the cost of MAS relative to conventional phenotypic selection for a common application in maize breeding: detection of a particular allele at a single target locus. In that application, conventional selection and MAS are direct substitutes, because they generate the same information (presence or absence of the target allele). The article concluded that for that application, MAS may offer a cost-effective alternative to phenotypic selection. This second article presents results for a different breeding application: introgressing an elite dominant allele at a single target locus into an elite maize line (line conversion). In this application, conventional selection and MAS are not perfect substitutes, because the information generated using markers is different from that generated using conventional screening methods (specifically, markers are used to identify the allelic composition at many non-target loci throughout the genome). The additional information generated by markers can be used by breeders to alter selection strategies in ways that accelerate the line conversion process. Therefore, in comparing the cost-effectiveness of conventional selection and MAS in this second application, it is necessary to consider explicitly the value of the time savings made possible by MAS. The main purpose of analyzing this second breeding application is not to make a detailed technical comparison between conventional selection and MAS (which is why only a few basic breeding schemes are considered). Instead, the main purpose is to examine the tradeoff between time and money associated with the choice of breeding methods.

Research methods and data sources

Research methods

To assess the relative cost-effectiveness of conventional and MAS approaches for line conversion breeding, it is necessary to compare line conversion schemes that generate equivalent outputs. In theory, this is straightforward, assuming that the schemes have been designed expressly for the purpose of transferring an elite allele at a single target locus from a donor line to a recipient line, while recovering through successive backcross (BC) generations as much as possible of the recipient genome at the non-target loci (Frisch et al. 1999a). In practice, however, it is often difficult to identify conventional and MAS line conversion schemes that are directly comparable for at least two reasons. First, since conventional selection and MAS involve different techniques, the two methods are often used in different ways. Second, breeders rarely target individual traits controlled by single genes and work on them one at a time. Instead, breeders usually try to select for several traits simultaneously. Whenever multiple objectives are being pursued simultaneously, it is more difficult to quan-

tify genetic gains. Even if multiple breeding objectives can be combined into a single selection index, a given amount of progress measured in terms of the selection index may have been achieved in different ways.

To avoid these complications, the case study used stylized breeding schemes that rely on classic BC procedures to transfer a trait controlled by a single dominant gene (for a textbook example, see Figure 1). It was assumed that the presence of the particular elite allele at the target locus can be detected by phenotypic selection, which in all the schemes analyzed for the case study is performed at every generation. In these stylized schemes, genetic gains can be estimated by considering the proportion of the recurrent parent genome that is recovered in each successive BC generation, assuming Mendelian segregation at all loci (Ragot et al. 1995; Tanksley et al. 1989).

Three inbred line conversion schemes were analyzed for the case study. The first scheme ("conventional") can be completed with phenotypic selection methods using only 20 plants screened in each generation. This scheme relies on a standard BC procedure and represents the minimum amount of resources needed for a traditional line conversion project. Theoretically, use of seven plants per generation provides a 99% chance of recovering the target allele in at least one backcross individual. In our representative selection schemes (conventional conversion and MAS with selection only at the target locus), we increased the number to 20 plants per generation to provide a margin of error for poor germination, lack of pollination, and other seed production problems that often occur during practical selection exercises. After six generations of backcrossing, theoretically 99.2% of the recipient genome will be fixed (homozygous) in the offspring (Ragot et al. 1995; Tanksley et al. 1989). The second scheme ("MAS-A") calls for MAS at non-target loci in every BC generation. With this scheme, three generations of backcrossing are needed to produce plants that are 99.3% identical to the desirable parent (Ribaut et al. 2002). The third scheme ("MAS-B") involves MAS at non-target loci only in the third generation of backcrossing and produces a genotype that is 97.8% identical to the desirable parent after three BC generations. In both of the MAS schemes, the level of conversion achieved after three BC generations considering one target locus was predicted through simulations based on the following parameters: (1) only the best genotype is selected in each generation, (2) MAS is conducted at non-target loci using 109 DNA markers distributed at intervals of 20 cM on 10 chromosomes (assuming a 2000 cM genome), and (3) flanking markers are located 20 cM apart from the target locus. In MAS-A, phenotypic and genotypic selections are carried out in all three BC generations using a two-step procedure. First, phenotypic selection at the target gene is performed on 200 plants to identify 100 plants that carry the desirable allele, and then MAS is used to identify the individual plant from among these 100 plants whose genotype contains the highest proportion of homozygous recipient alleles at non-target loci. In MAS-B, only phenotypic selection is carried out in the BC1 and BC2 generations using 20 plants in each generation; then MAS at non-target loci is carried out in the BC3 generation on 100 plants that contain the elite allele at the target locus. The genetic models used for the simulations, as well as additional details about the selection schemes, are presented in (Ribaut et al. 2002).*

In actual practice, the proportion of the recurrent parent genome that is finally recovered will tend to differ slightly from the predicted percentages. Particularly in the case of the conventional scheme, the 99.2% figure could be overestimated because of linkage drag (Tanksley et al. 1989). In the MAS schemes, linkage drag can be reduced with the help of markers, both flanking markers located on either side of the target locus as well as background markers (Frisch et al. 1999b).

In these stylized breeding schemes, it was assumed that selection at the target locus can be accomplished using conventional phenotypic screening methods. Obviously this type of application does not exploit the full potential of markers, since markers can be used to select for the presence of elite alleles at target loci for traits that are not easily identified via phenotypic screening. But since we are interested here in the relative efficiency of conventional selection vs. MAS, there would be no point in estimating the cost of using MAS to accomplish a task that could not be accomplished phenotypically (e.g., selecting for the

* In the case study described here, the percentage of the recurrent parent genome recovered at each generation was calculated assuming a diploid genome of 4,000 cM (20 chromosomes). The results reported in Ribaut et al. (2002) were calculated assuming a haploid genome of 2,000 cM (10 chromosomes). Therefore, while the results of the present study and those of Ribaut et al. (2002) are perfectly consistent, they are not directly comparable when expressed in percentage terms due to a difference of 2,000 cM in the absolute values of all data.

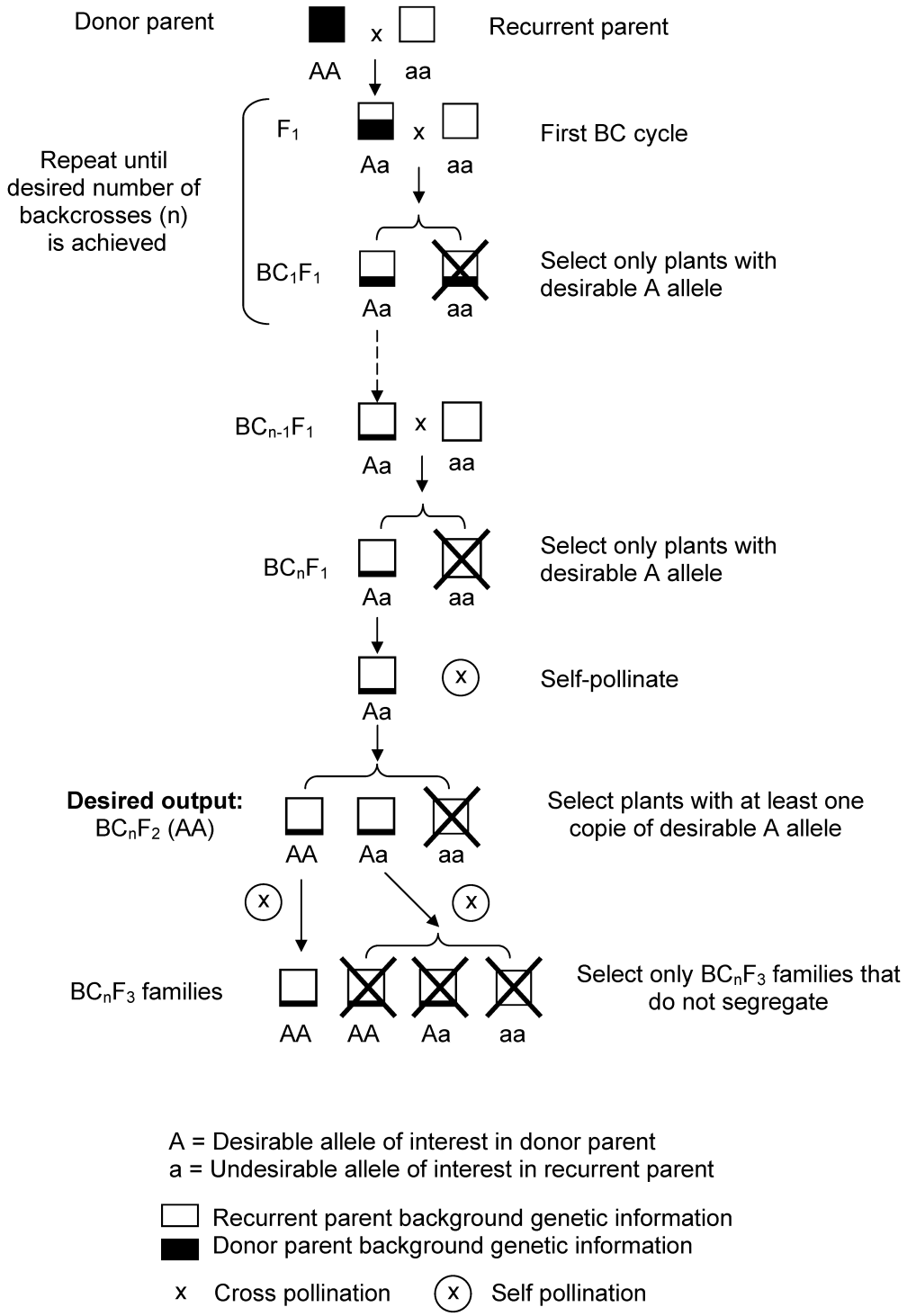

Figure 1. Backcrossing selection scheme for a dominant gene considering n successive backcross cycles. The reduction of the donor genetic contribution (represented in black at each cycle) was calculated assuming Mendelian segregation at all loci. The allelic composition at the target gene is presented at each cycle. Using phenotypic selection, it is not possible to distinguish between AA and Aa genotypes after the first cycle of self-pollination, so a second cycle of self-pollination is needed to identify BC_nF_3 families that do not segregate. This second cycle of self-pollination can be conducted in parallel to other cross-pollinations with target germplasm at minimum additional cost.

Table 1. Cost and time requirements of a conventional inbred line conversion scheme[a]

Season number	Pollination	Backcross number[b]	Recurrent parent recovered (%)	Generation cost (US$)[c]
1	Cross	–	–	16.36
2	Backcross	–	50.00	16.56
3	Backcross	1	75.00	15.45
4	Backcross	2	87.50	15.45
5	Backcross	3	93.75	15.45
6	Backcross	4	96.88	15.45
7	Backcross	5	98.44	15.45
8	Self	6	99.22	4.95
			Total cost:	115.12

[a]Calculated assuming that plants are grown under irrigation at CIMMYT's Tlaltizapán research station. In each season, one pollination bag and one glassine bag are required for each plant that is fertilized.
[b]Refers to the backcross generation that is planted in the field at the beginning of the season.
[c]Twenty plants grown in each generation. This is far fewer than would be grown in most commercial line conversion programs, as breeders rarely focus on a single target trait. Here the number was chosen to make the output of the conventional line conversion scheme (one completely converted line) more directly comparable with the output of the two MAS schemes.

presence of one copy of a recessive allele at a target locus). To keep the schemes as comparable as possible, we selected two breeding schemes that produce equivalent outputs, albeit at different costs and in different amounts of time (conventional and MAS-A). The need to produce equivalent outputs also explains why the conventional scheme includes six BC generations, which theoretically are needed to achieve ″complete line″ conversion (interpreted here to mean recovery of more than 99% of the recurrent parent genome). Most maize breeders involved in line conversion work would normally stop short of this level, since usually it is not necessary to recover such a large proportion of the recurrent parent genome. (An exception would be single-gene conversion of elite inbred lines being used as parents for successful commercial hybrids.) Reducing the number of BC cycles to obtain a ″more realistic″ conventional line conversion scheme would not significantly change the already very low cost of the scheme presented in Table 1 ($115.12).

MAS-B does not produce exactly the same output as the other two schemes, in the sense that lines converted using MAS-B have recovered only 97.8% of the recurrent parent genome, compared to 99.2% and 99.3% recovery rates for lines converted using the conventional and MAS-A schemes, respectively. Nevertheless, MAS-B was included in the study because it is the type of scheme that might be used by a breeder interested in using the power of DNA markers to accelerate the line conversion process while still containing costs.

Once the cost and time requirements had been calculated for each of the three breeding schemes, the relationship between time and money as it relates to crop improvement research was explored by developing a simple model of a plant breeding program and using it to compare the economic returns to each of the representative inbred line conversion schemes. Two different measures of project worth were used: the net present value (NPV) of the discounted streams of costs and benefits, and the internal rate of return (IRR) to the initial research investment.

NPVs were calculated by summing the stream of net benefits associated with each breeding scheme over the life of a commercially successful variety developed by the breeding scheme:

$$NPV = \sum_{t=1}^{n} (GB_t - VR_t - RC_t)$$

where:

GB = gross benefits (calculated as area planted to the variety x incremental benefits associated with adoption),

VR = varietal release expenses (cost of evaluation trials, registration procedures, seed multiplication, advertising and promotion, etc.),

RC = research investment costs, and

t = years (where n = the total number of years that elapse during the research stage, release stage, and adoption stage).

The following plausible values were used for key parameters:

Research stage
Investment costs and time requirements for the three line conversion schemes were taken from the CIMMYT case study.

Release stage
The varietal release lag was assumed to be two years. Varietal release costs were assumed to be $10,000 per year.

Adoption stage
Adoption and disadoption were assumed to follow a smooth path, with peak adoption occurring after four years and complete disadoption after 10 years. The maximum area planted to the variety was assumed to be 10,000 ha, and the net benefits associated with adoption were assumed to be $25 per hectare (which could be due to an increase in yield, an increase in crop quality, or a decrease in input use). These values can be considered typical of those faced by a medium-sized breeding program working with maize or other common field crops (e.g., wheat, barley, rice, sorghum).

The IRR for each breeding scheme was conventionally calculated by determining the discount rate that drives the NPV to zero. The IRR can be interpreted as the maximum interest that an investment project (in this case, a breeding scheme) could pay for the resources used if the project is to recover its investment and operating costs and still break even (Gittinger 1980). More simply, the IRR can be thought of as the rate of return on the capital invested in each breeding scheme (Gittinger 1980).

Data sources

Data sources and methods used to calculate costs of field operations and laboratory procedures are described in Dreher et al. (2003). The cost estimates, which are based on prices prevailing during the 1999/2000 winter breeding cycle, relate to field operations carried out at CIMMYT's research station in Tlaltizapán, Mexico, and to simple sequence repeat (SSR) DNA marker analysis carried out in the Applied Biotechnology Center located at CIMMYT headquarters in El Batán, Mexico.

Results

Breeding costs

Tables 1, 2 and 3 show the costs of the three inbred line conversion schemes. Unit costs for field operations and laboratory procedures were estimated using methods described in Dreher et al. (2003). For the present exercise, it was assumed that all field work is performed at the Tlaltizapán research station during the irrigated winter cycle. Phenotypic screening (performed in all of the breeding schemes) was assumed to be costless. This assumption is reasonable for applications in which the trait of interest can be evaluated through simple visual inspection of plants, since the cost of visual inspection is negligible. It is less reasonable for applications in which the trait of interest can be detected only through elaborate field screening procedures or by subjecting plant tissue samples to expensive laboratory analysis. Here the assumption is justified because at CIMMYT the cost-effectiveness of conventional selection relative to MAS is very insensitive to changes in field production costs, including phenotypic screening costs. (Sensitivity analysis revealed that even if field production costs are doubled, the basic economic results reported below would remain unaffected.)**

When phenotypic screening is costless, conventional breeding is inexpensive. At CIMMYT, the conventional scheme costs only $115. This scheme, it should be recalled, involves six generations of backcrossing and produces plants that theoretically have 99.2% of their genome fixed with alleles from the recurrent parent. In comparison, marker-assisted breeding is expensive. The cost of MAS-A, which involves three generations of backcrossing and in which DNA markers are used at every backcross generation, comes to $20,076. This scheme closely resembles the conventional scheme in that at least one plant in the final generation of plants theoretically will have recovered 99.3% of the recurrent parent genome. In the simulation exercise described in Ribaut et al. (2002), it was assumed that 109 markers are used to screen at

** The assumption of zero phenotypic screening costs was made because phenotypic screening costs vary greatly depending on the trait of interest. Since the objective of this paper is to compare the costs of phenotypic versus genotypic selection, we deliberately decided not to bias the analysis against conventional selection by including extremely high phenotypic selection costs. It is important to keep in mind, however, that depending on the application, phenotypic selection costs can in fact be significant.

Table 2. Cost and time requirements of MAS-A inbred line conversion scheme[a]

Season number	Pollination	Backcross number[b]	Number of plants analyzed	Number of DNA markers	Recurrent parent recovered (%)	Generation cost (US$)
1	cross	–	2[c]	300[c]	–	834.06
2	backcross	–	–	–	50.0	16.56
3	backcross	1	100	109	84.9	13,693.87
4	backcross	2	100	33	96.6	4,290.85
5	Self	3	100	8	99.3	1,240.99
					Total cost:	20,076.33

[a]Calculated assuming that plants are grown under irrigation at CIMMYT's Tlaltizapán research station. In each season, one pollen bag and one glassine bag are required for each plant that is fertilized. SSR DNA marker analyses are performed after leaf samples are harvested and DNA is extracted using a sap extractor. DNA is quantified using a spectrophotometer, PCR amplified using 22 base-pair custom primers, and separated on an agarose gel (2% Metaphor, 1% Seakem).
[b]Refers to the backcross generation that is planted in the field at the beginning of the season.
[c]Markers used to screen only the DNA extracted from the two parental lines to identify polymorphisms.

Table 3. Cost and time requirements of MAS-B inbred line conversion scheme[a]

Season number	Pollination	Backcross number[b]	Number of plants analyzed	Number of DNA markers	Recurrent parent recovered (%)	Generation cost (US$)
1	cross	–	2[c]	300[c]	–	834.06
2	backcross	–	–	–	50.0	16.56
3	backcross	1	20	–	75.0	15.45
4	backcross	2	20	–	87.5	15.45
5	Self	3	100	109	97.8	13,681.75
					Total cost:	14,563.27

[a]Calculated assuming that plants are grown under irrigation at CIMMYT's Tlaltizapán research station. In each season, one pollen bag and one glassine bag are required for each plant that is fertilized. SSR DNA marker analyses are performed after leaf samples are harvested and DNA is extracted using a sap extractor. DNA is quantified using a spectrophotometer, PCR amplified using 22 base-pair custom primers, and separated on an agarose gel (2% Metaphor, 1% Seakem).
[b]Refers to the backcross generation that is planted in the field at the beginning of the season.
[c]Markers used to screen only the DNA extracted from the two parental lines to identify polymorphisms.

non-target loci in all three BC generations. Practically speaking, however, the number of markers that must be used decreases in each successive BC generation, because once the recipient allele has been fixed at any given non-target locus, it is not necessary to continue screening at that locus in subsequent generations—the locus will remain homozygous for the rest of the selection process. Therefore, in the MAS-A scheme 109 markers are used in the first BC generation, 33 markers in the second BC generation, and 8 markers in the third and final BC generation. The declining number of markers reflects the increasing percentage of the recipient genome that is fixed at each BC generation. The cost of MAS-B, which involves three generations of backcrossing, but in which DNA markers are used only in the third generation, comes to $14,563. Theoretically this scheme produces at least one plant that will have recovered 97.8% of the recurrent parent genome.

Time requirements

Tables 1, 2 and 3 also show the time required to complete the three line conversion schemes. With the conventional scheme, eight generations (including six generations of backcrossing) are needed to perform a complete line conversion. Since the information provided by the background markers can be used to identify individual plants that contain more of the recurrent parent genome, using MAS-A, the time needed to complete the same level of line conversion can be reduced to only five generations (including three generations of backcrossing). The data presented in Tables 1, 2 and 3 indicate that for maize inbred line

conversion projects such as the one analyzed here, the choice between conventional and marker-assisted selection technology involves a tradeoff between time and money. Comparing the two schemes that generate the most similar outputs, the conventional scheme costs US $115 and requires eight growing generations, while MAS-A costs US $20,076 but requires only five growing generations. For this particular application, the inbred line conversion scheme based exclusively on phenotypic selection methods costs much less than do the schemes based on MAS methods. However, the lower cost of the conventional breeding scheme comes at a price: more time is needed to produce the final product.

Economic profitability

The choice of breeding method can be viewed as an investment decision that can be evaluated using conventional investment criteria (Sanders and Lynam 1982). Standard project appraisal techniques can be used to assess the relative attractiveness of alternative mutually exclusive investment opportunities whose costs and benefits are spread out through time (Gittinger 1980). Figure 2 depicts the ″variety life cycle″ assumed by the model. The stream of costs and benefits associated with the development, release, and adoption by farmers of a modern maize variety can be divided into three stages: (1) a *research stage* during which the variety is developed, (2) a *release stage* during which the variety is evaluated and registered for release, and during which commercial seed is produced, and (3) an *adoption stage* during which the variety is taken up and grown by farmers. During the first two stages, net benefits are negative, because costs are incurred without any benefits being realized. During the third stage, net benefits turn positive as the variety is taken up and grown by farmers; net benefits increase until the peak adoption level is achieved and then decline when the variety is replaced by newer varieties. Depending on the context, the benefits generated by an improved maize variety can be expressed in different ways. For a private seed company, the benefits are likely to consist of profits from seed sales. For a public breeding program, the benefits might be measured as the value-added associated with use of the new variety due to increases in the quantity and or quality of production, decreases in input use, or both.

Figure 3 illustrates the streams of net benefits generated by the conventional and the MAS-A line conversion schemes. (Results for the MAS-B scheme are very similar and consequently have not been included in the figure.) The conventional scheme features low costs during the research stage, but it takes longer to complete. The MAS-A scheme features high costs during the research stage, but it takes less time to complete. Since the two schemes generate very similar outputs, for purposes of this exercise the release stage and adoption stages are assumed to be identical in terms of cost as well as duration. From an economic point of view, the advantage of MAS thus derives from the fact that the release and adoption stages are moved forward in time.

Table 4 shows the NPVs generated by the three line conversion schemes under the baseline assumptions.*** The two MAS schemes generate larger NPVs than the conventional scheme. MAS-A, which results in ″complete″ line conversion and therefore is more directly comparable with the conventional scheme, generates $133,623 more in discounted benefits than the phenotypic scheme. This figure, which can be interpreted as the economic benefits associated with the accelerated release of a maize variety, is large and positive. This suggests that even though MAS costs much more than conventional selection methods for inbred line conversion projects carried out at CIMMYT, the additional investment is worthwhile because by accelerating the rate of varietal release, MAS generates large additional economic benefits.

One drawback of using NPV as a measure of project worth is that it does not take into account the size of the initial investment. In the case of the maize inbred line conversion schemes examined for our case study, while it is true that the two MAS schemes generate larger NPVs, it is also true that they are more expensive. What if the resources needed to carry out the MAS schemes are not available? The question is relevant, especially for breeding programs that face constraints on their operating budgets. When research

*** The NPVs and IRRs reported in Table 4 should be interpreted with care. As described in Dreher et al. (2003), in the CIMMYT case study the costs of field operations and laboratory procedures were estimated assuming that the breeding program already exists and that DNA markers are available for the allele(s) of interest. The NPVs and IRRs thus were calculated based on marginal costs incurred by an established breeding program operating at full capacity. Including the initial capital investment costs associated with establishing field and laboratory research facilities, training researchers, and/or identifying DNA markers would increase the costs and lower the NPV and IRR of all three line conversion schemes.

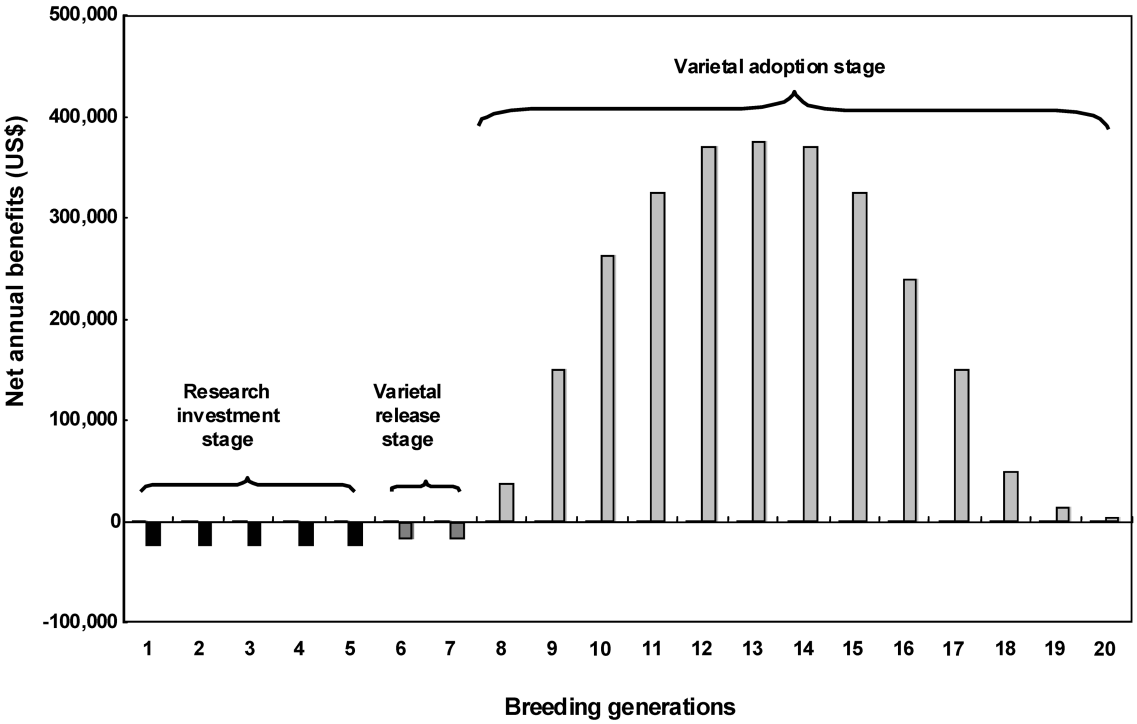

Figure 2. Stylized economic model of a plant breeding program showing flow of annual research net benefits associated with the development and release of an improved plant variety. Annual net benefits are initially negative during the research investment period. They remain negative during the varietal release period when varietal testing and varietal registration costs are being incurred. Following the commercial release of the variety, annual net benefits turn positive as the variety is adopted by farmers. Annual net benefits increase until peak adoption is achieved and then decrease with disadoption as the area planted to the variety declines.

resources are limited, managers must become more conscious of opportunity costs, because as they well know, resources committed to one breeding project cannot be devoted to other breeding projects.

In the presence of a budget constraint, a better measure for comparing mutually exclusive alternative investment projects is the IRR (Gittinger 1980). Table 4 shows the IRRs to the resources invested in each of the three line conversion schemes under the baseline assumptions. Even though the conventional scheme has a smaller NPV than the MAS schemes, it generates a larger IRR. In interpreting the IRRs presented in Table 4, what should be noted are the relative sizes, not the absolute sizes. The current analysis does not include capital investment costs associated with establishment of CIMMYT's breeding stations and laboratory facilities, costs of training researchers and technicians, or costs of research activities that are not directly related to line conversion (for example, initial development of elite inbred lines, test crossing, evaluation of experimental hybrids). The returns to inbred line conversion therefore are not as high as suggested by the IRRs shown in Table 4. Including these other costs would drive down the IRRs for all three line conversion schemes by approximately equal amounts. Based on conventional investment principles, investment in inbred line conversion would be considered attractive as long as the returns to this activity exceed the returns that could be obtained by alternative investments.

In interpreting these findings, three caveats should be noted:

First, our analysis considered only variable costs. Fixed costs, particularly the capital investment needed to establish conventional field breeding stations and biotechnology research facilities, were considered already invested and consequently were ignored. The economic question being addressed therefore is one that might be asked by a manager of an established plant breeding program that already has the capacity to carry out both conventional selection and MAS; the manager is trying to decide whether a particular breeding project should be undertaken using conventional selection or MAS.

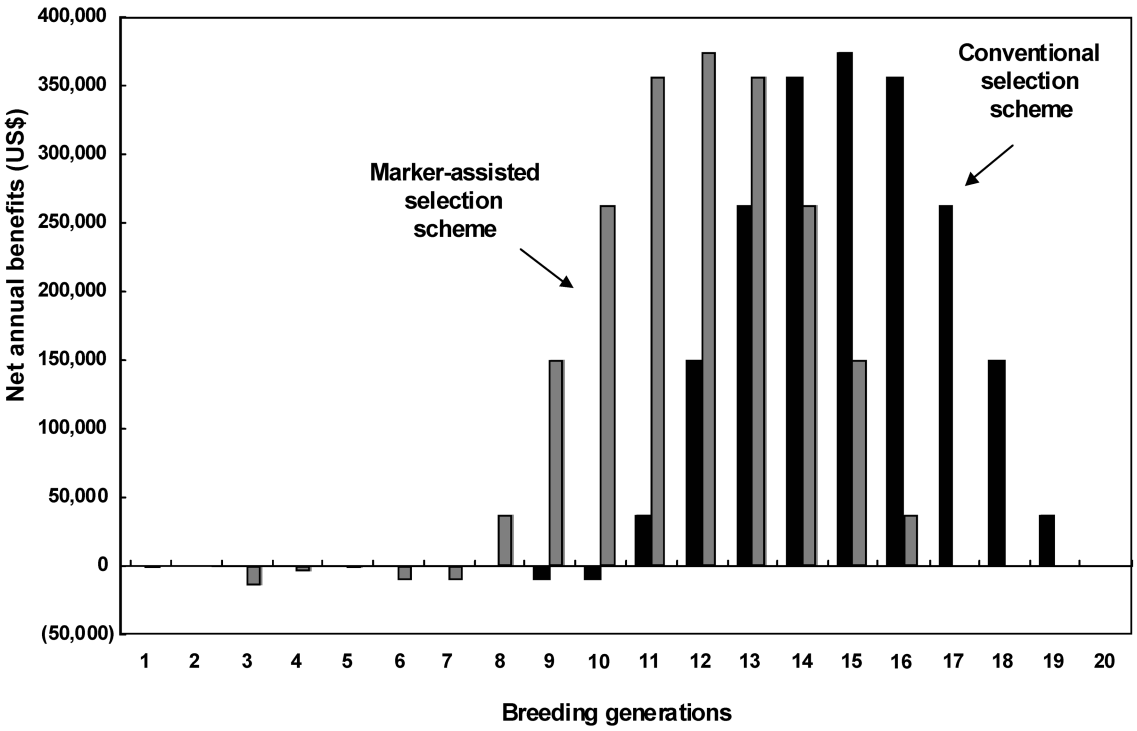

Figure 3. Comparison of the flow of annual research net benefits generated by conventional and marker-assisted inbred line conversion schemes. The marker-assisted scheme (MAS-A) features larger up-front investment costs (larger negative annual net benefits in years 1–6), but because marker-assisted selection accelerates the line conversion process, varieties based on the converted line are released earlier and adoption by farmers occurs sooner. Positive annual net benefits generated by the marker-assisted line conversion scheme are therefore moved forward in time.

Table 4. Measures of project worth, conventional and MAS line conversion schemes.

	Conventional	MAS-A	MAS-B
Net present value (NPV)	$364,150	$497,773	$503,167
NPV-based rank	3	2	1
Internal rate of return (IRR)	131%	74%	98%
IRR based rank	1	3	2

Second, our analysis assumed that the technology required to carry out conventional selection and MAS is already available. Costs of basic research activities were ignored, for example, costs associated with the initial development of phenotypic screening procedures, construction of linkage maps, identification of target genes or quantitative trait loci (QTLs) for traits of interest, development of reliable DNA markers, etc. Basic research costs are often very large, so their inclusion would almost certainly influence the optimal choice of breeding method. It is difficult to say *a priori*, however, whether basic research costs are likely to be larger for conventional or MAS breeding.

Third, our analysis focused on a very specific application—introgression of an elite allele at a single dominant gene into an elite maize line. In assessing the relative cost-effectiveness of conventional and MAS methods in line conversion breeding, we did not try to quantify economic benefits that are not directly related to the line conversion objective. Breeders will quickly point out that field phenotypic evaluation almost always generates information about many traits other than the trait being converted, and that this information often has value. This suggests that even though MAS may be more cost-effective for narrowly-defined projects (such as the line conversion project considered here), conventional phenotypic selection may be preferable when multiple traits are being improved simultaneously.

Discussion

DNA markers are one of many new biotechnology-based tools that have the potential to increase the

technical efficiency of plant breeding. But are MAS methods cost-effective? Since DNA markers can be used in many different ways for many different purposes, obviously it is very difficult to generalize. As most plant breeders well know, the cost of using DNA markers can vary greatly depending on the crop, the breeding application, the trait(s) being targeted, the availability of suitable marker technology, and other factors. This application-specificity complicates economic analysis, but it does not invalidate it completely. Well-designed case studies can help plant breeders make better decisions about choice of breeding strategy by generating detailed empirical information about the costs and time requirements of alternative selection methods.

The results of the CIMMYT study show that for a common application in maize breeding (line conversion), the choice between conventional selection and MAS involves a tradeoff between time and money. MAS is more expensive than conventional selection, but by using MAS, breeders can accomplish the line conversion in less time. In cases where neither breeding method shows clear superiority in terms of cost and speed, the relative attractiveness of the two breeding methods can be evaluated using conventional investment criteria.

Under what circumstances is the high investment cost of MAS relative to conventional breeding justified? Previous studies have not provided much guidance on this important practical question. In a sense, the lack of guidelines is not surprising. As Ragot and Hoisington (1993) point out, ″Because genotyping costs are determined by numerous factors, some of which are very case-specific, any general statement about the relative costs of DNA marker protocols is prone to be untrue″ (p. 982). Although these authors were comparing the costs of RFLP and RAPD protocols, rather than the cost of MAS based on SSR markers to the cost of conventional screening methods as we have done, their conclusion is equally valid for both types of comparisons.

Even if it is acknowledged that the cost of using DNA markers is highly application-specific, breeders still need some basis for deciding whether the use of markers is likely to be cost-effective for particular applications. In the absence of well-defined empirical guidelines or even general rules of thumb, many breeders rely on subjective ″gut instinct″ in selecting a screening method. For example, Beckman and Soller (1983) write, ″Costs for screening segregating resource populations for useful QTL...*seem* high, except when screening for a single quantitative trait. Thus this *could be* economically useful if the eventual recipient population were at a selection plateau and the economic value of the trait under improvement was high″ (p. 42, italics added).

Using a simple model of a plant breeding program, we have shown that the optimal choice of breeding technology depends critically on the availability of operating capital. If operating capital is freely available, the ″best″ breeding method will be the one that maximizes NPV (MAS), but if operating capital is constrained, the ″best″ breeding method will be the one that maximizes IRR (conventional selection). This finding is consistent with what has been happening in the plant breeding industry. Private firms, which can raise operating capital by drawing on corporate cash reserves, floating shares in the stock market, or borrowing in commercial credit markets, have been actively implementing biotechnology-assisted breeding schemes, including schemes that use DNA marker technologies. Private firms can maximize the net benefits generated by their breeding programs (also profits) by opting for technologies that allow them to bring new products into the market faster, even if these technologies are more costly to implement. In contrast, public plant breeding programs, which are more likely to face capital constraints in the sense that they are usually required to operate within their budget allocation, have been much slower to implement biotechnology-assisted breeding schemes, including schemes that use MAS. Public breeding programs can maximize the returns to their limited resources by sticking to lower-cost conventional selection methods, even though this means that breeding projects will take longer to complete.****,*****

**** The preceding discussion should not be interpreted to imply that the benefits of accelerated varietal release are necessarily trivial for breeders working in the public sector. For example, Pandey and Rajatasereekul (1999) estimated the returns to public rice breeding research in Thailand and concluded that a two-year reduction in the time needed to develop a successful rice variety translates into US $18 million dollars of additional social benefits. Similarly, based on a study of public wheat breeding programs in Australia, Brennan (1999) estimated that accelerating the release of a commercially successful wheat variety by one year generates about US $125,000 in additional benefits.

***** These results are not affected by the fact that the returns to investment in plant breeding are realized by different entities, depending on whether the investment is made by a public organization or a private company. Even though most public organizations expect to capture little or no return to their investment, this should not influence their choice of breeding strategy. Assuming that public organizations are interested in maximizing (social) benefits from

In interpreting these conclusions, it should, however, be remembered that spending on biotechnology is influenced by economic considerations other than those reflected in a conventional investment model. For example, the first firm to introduce a new germplasm product may be able to capture a larger share of the market than firms that introduce similar products later (in our stylized model of a plant breeding program, the adoption curve would rise faster and peak at a higher level). In some cases, the first firm to introduce a new germplasm product may be able to claim intellectual property rights and prevent competitors from marketing the product at all (the ″winner takes all″ scenario). Considerations such as these are not captured in our analysis, but they could also help explain the recent surge in private investment in biotechnology.

It should be kept in mind also that the desire to maximize returns to operating capital is not the only determinant of spending on biotechnology. As mentioned earlier, our analysis relates only to variable costs; the investment made by CIMMYT to establish capacity to carry out conventional and marker-assisted line conversion projects was treated as a sunk cost and ignored. Much of the spending on biotechnology that has occurred in the past decade has consisted of up-front capital investment made by breeding organizations seeking to get into biotechnology on an appropriate scale, which is a different investment decision from the one considered here. As with operating capital, however, it is likely that private firms have an easier time raising capital to finance the up-front investments needed to establish biotechnology research capacity.

For many plant breeding projects, the relative attractiveness of conventional selection vs. MAS will not be in doubt. Whenever phenotypic evaluation is faster and cheaper than genotypic screening, conventional selection will be preferable to MAS. Conversely, whenever genotypic screening is faster and cheaper than phenotypic evaluation, MAS will be preferable to conventional selection. The CIMMYT case study presented in this paper focused on a type of breeding project that does not fall into either of these two categories: breeding projects in which neither conventional selection nor MAS shows a clear advantage in terms of both speed and cost. For projects such as these, the optimal choice of breeding method is not obvious. As our analysis has shown, when switching between conventional selection and MAS implies a tradeoff between time and money, the cost-effectiveness of DNA markers depends critically on four parameters: (1) the relative cost of phenotypic vs. genotypic screening, (2) the time savings achieved using MAS, (3) the size and temporal distribution of benefits associated with accelerated release of improved germplasm, and (4) the availability to the breeding program of operating capital. All four of these parameters can vary significantly between breeding projects, suggesting that detailed economic analysis may be needed to predict in advance which selection technology will be optimal for a given breeding project.

their work, they will select the most economically attractive strategy regardless of how the returns are distributed. At the same time, since public organizations do not experience the financial ″bottom line″ with the same degree of immediacy as do private companies, they have to put more effort into calculating how their choice of breeding strategy affects the size and distribution through time of benefits.

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