Supporting Information

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SI Text

S1. Proof of Theorem 1

The procedure that declares as replicated all features with r values $\le q$ is equivalent to the procedure in *Variations* in the main text, where the choice of emphasis between the studies is discussed, as proved in *Lemma S1.1*. We show that our proposal, in its most general form [i.e., with $c_2 \in (0,1)$], controls the FDR at a level at most

$$f_{00}c_1(q)c_2q^2 + f_{01}c_1(q)q + E\left(\frac{|I_{10}\cap\mathcal{R}_1|}{\max(|\mathcal{R}_1|,1)}\right)c_2q \qquad \textbf{[S1]}$$

under the conditions of *Theorem 1*, where $f_{0j} = |I_{0j}|/m, j \in \{0,1\}$, and $f_{10} = |I_{10}|/m$.

Before proving the above upper bound on the FDR, we show that if the above upper bound holds and $l_{00} \le f_{00}$, *Theorem 1* follows. Note that if the constants (l_{00}, c_2) satisfy the inequality

$$f_{00}c_1(q)c_2q + f_{01}c_1(q) + c_2 \le 1,$$

then the FDR for replicability analysis is controlled at level at most q. This inequality holds for any choice of (l_{00}, c_2) that satisfies the relationship

$$l_{00} \le \frac{1 - f_{01} - f_{00}c_2q}{1 - c_2q}.$$

Unfortunately, f_{00} and f_{01} are not known. If the guess for l_{00} is indeed conservative, i.e., $l_{00} \le f_{00}$, then the above inequality holds because $f_{00} \le 1 - f_{01}$. Thus, for any value $l_{00} \le f_{00}$ and $c_2 \in (0,1)$, the FDR for replicability analysis is controlled at level at most q.

Proof for the Upper Bound in [S1]. Let R_j be the indicator of whether feature j was declared replicated for $j = 1, \ldots, m$, and $R = \sum_{j=1}^m R_j$. The FDR for replicability analysis is

$$\mathrm{FDR} = E\left(\sum_{j\in I_{00}}\frac{R_j}{\max(R,1)}\right) + E\left(\sum_{j\in I_{01}}\frac{R_j}{\max(R,1)}\right) + E\left(\sum_{j\in I_{10}}\frac{R_j}{\max(R,1)}\right). \qquad \textbf{[S2]}$$

For items *i–iii* in *Theorem 1*, we find an upper bound for each of the three expectations in [S2]; specifically we show the following inequalities [S3]–[S5]:

$$E\left(\sum_{j\in I_{01}}\frac{R_j}{\max(R,1)}\right) \le |I_{01}|\frac{c_1(q)q}{m} = f_{01}c_1(q)q, \qquad \textbf{[S3]}$$

$$E\left(\sum_{j\in I_{10}}\frac{R_j}{\max(R,1)}\right) \le E\left(\frac{|I_{10}\cap\mathcal{R}_1|}{\max(|\mathcal{R}_1|,1)}\right)c_2q, \qquad \textbf{[S4]}$$

$$E\left(\sum_{j\in I_{00}}\frac{R_j}{\max(R,1)}\right) \le f_{00}c_1(q)c_2q^2. \qquad \textbf{[S5]}$$

Obviously the upper bounds in [S3]–[S5] and the equality in [S2] complete the proof for the upper bound in [S1]. The upper bounds in [S3] and [S4] follow directly from ref. 1. The key difference from ref. 1 is the fact that we consider a tighter upper bound for $E(\sum_{j\in I_{00}} R_j/\max(R,1))$ given in [S5]. We proceed to prove inequality [S5] for items *i–iii* in *Theorem 1*.

In all the derivations we refer to from ref. 1, we replace q_1 in ref. 1 with c_1q, $q - q_1$ in ref. 1 with c_2q, and $|I_0|$ in ref. 1 with $|I_{01}|$, unless stated otherwise. We start with the proof of item *i* of Theorem 1 for the case where the P values within the follow-up study are jointly independent. Inequality [S3] follows from the derivations leading to [A.3] in ref. 1. Inequality [S4] follows from the derivations leading to [A.7] in ref. 1, and by taking the expectation of the expression in [A.7] over the primary study P values. We now prove inequality [S5]. We recall the following definitions from ref. 1. Let $P_1^{(j)}$ and $P_2^{(j)}$ denote the vectors $P_1 = (P_{11}, \ldots, P_{1m})$ and $P_2 = (P_{21}, \ldots, P_{2m})$ with, respectively, P_{1j} and P_{2j} excluded. For $j \in \{1, \ldots, m\}$ arbitrarily fixed, let $\mathcal{R}_1^{(j)}(P_1^{(j)}) \subseteq \{1, \ldots, j-1, j+1, \ldots, m\}$ be the subset of indexes selected along with index j. Note that because the selection rule is stable, this subset is fixed as long as P_{1j} is such that j is selected based on $(P_1^{(j)}, P_{1j})$. For any $j \in \{1, \ldots, m\}$ and given $P_1^{(j)}$, for $i \in \{1, \ldots, j-1, j+1, \ldots, m\}$

$$e_i^{(j)} = \begin{cases} \max\left(\frac{P_{1i}}{c_1}, \frac{\left(\left|\mathcal{R}_1^{(j)}\left(P_1^{(j)}\right)\right|+1\right)P_{2i}}{mc_2}\right) & \text{if } i \in \mathcal{R}_1^{(j)}\left(P_1^{(j)}\right), \\ \infty & \text{otherwise.} \end{cases}$$

Let $e_{(1)}^{(j)} \le \ldots \le e_{(m-1)}^{(j)}$ be the sorted $e_i^{(j)}$ s, and $e_{(0)}^{(j)} = 0$. [The e values are closely related to T values defined in appendix A of ref. 1. Specifically, $e_i^{(j)} = T_i q/m$ for $j \in \{1, \ldots, m\}$ and $i \in \{1, \ldots, j-1, j+1, \ldots, m\}$.] For $r = 1, \ldots, m$, we define $C_r^{(j)}$ as the event in which if $j \in I_{00} \cup I_{01} \cup I_{10}$ is declared replicated, r hypotheses are declared replicated including j, which amounts to

$$C_r^{(j)} = \left\{\left(P_1^{(j)}, P_2^{(j)}\right) : e_{(r-1)}^{(j)} \le \frac{rq}{m}, e_{(r)}^{(j)} > \frac{(r+1)q}{m}, e_{(r+1)}^{(j)} > \frac{(r+2)q}{m}, \ldots, e_{(m-1)}^{(j)} > q\right\}.$$

Note that given P_1, for $r > |\mathcal{R}_1|$, $C_r^{(j)} = \varnothing$, because exactly $|\mathcal{R}_1| - 1$ $e_i^{(j)}$ s are finite. Obviously, $C_r^{(j)}$ and $C_{r'}^{(j)}$ are disjoint events for any $r \ne r'$, and $\cup_{r=1}^m C_r^{(j)}$ is the entire space of $(P_1^{(j)}, P_2^{(j)})$. Therefore, $\sum_{r=1}^m \Pr(C_r^{(j)}) = 1$.

Note that from the equivalent procedure in *Variations* in the main text, the following equality follows,

$$E\left(\sum_{j\in I_{00}}\frac{R_j}{\max(R,1)}\right) = \sum_{j\in I_{00}}\sum_{r=1}^m \frac{1}{r}\Pr\left(j \in \mathcal{R}_1, P_{1j} \le \frac{rc_1(q)q}{m}, P_{2j} \le \frac{rc_2q}{\max(|\mathcal{R}_1|,1)}, C_r^{(j)}\right) \le \sum_{j\in I_{00}}\sum_{r=1}^m \frac{1}{r}\Pr\left(P_{1j} \le \frac{rc_1(q)q}{m}, P_{2j} \le c_2q, C_r^{(j)}\right) \qquad \textbf{[S6]}$$

$$\le c_2q\frac{c_1(q)q}{m}\sum_{j\in I_{00}}\sum_{r=1}^m \Pr\left(C_r^{(j)}\right) = |I_{00}|c_2q\frac{c_1(q)q}{m} = f_{00}c_1(q)c_2q^2, \qquad \textbf{[S7]}$$

where the inequality in [S6] follows from the fact that for any given realization of $|\mathcal{R}_1|$ and value of r such that $r > |\mathcal{R}_1|$,

$C_r^{(j)} = \varnothing$, the inequality in [**S7**] follows from the independence of the P values and the fact that P_{1j} and P_{2j} are null-hypothesis P values, and the first equality in [**S7**] follows from the fact that $\sum_{r=1}^{m} \Pr(C_r^{(j)}) = 1$, thus completing the proof of item 1 for the case where the P values within the follow-up study are independent.

We now prove item *i* of *Theorem 1* for the case where the P values within the follow-up study have property PRDS. The inequalities [**S3**] and [**S4**] for this case follow from the results in the supplementary material of ref. 1. Specifically, inequality [**S3**] follows from the proof of theorem S3.1 in ref. 1 and inequality [**S4**] follows from the proof of item 2 in lemma S2.1 in ref. 1. For $j \in I_{00}$ and an arbitrary fixed $p_1 = (p_{11}, \ldots, p_{1m})$ such that $|\mathcal{R}_1(p_1)| > 0$,

$$
\begin{aligned}
E\left(\frac{R_j}{\max(R,1)}\middle| P_1 = p_1\right) &= \sum_{r=1}^{|\mathcal{R}_1(p_1)|} \frac{I\left(j \in \mathcal{R}_1(p_1), p_{1j} \le \frac{rc_1(q)q}{m}\right)}{r} \\
&\quad \times \Pr\left(P_{2j} \le \frac{rc_2 q}{|\mathcal{R}_1(p_1)|}, C_r^{(j)} | P_1 = p_1\right) \\
&\le I\left(p_{1j} \le \frac{|\mathcal{R}_1(p_1)| c_1(q) q}{m}, j \in \mathcal{R}_1(p_1)\right) \\
&\quad \times \sum_{r=1}^{|\mathcal{R}_1(p_1)|} \frac{1}{r} \Pr\left(P_{2j} \le \frac{rc_2 q}{|\mathcal{R}_1(p_1)|}, C_r^{(j)} | P_1 = p_1\right) \\
&= I\left(p_{1j} \le \frac{|\mathcal{R}_1(p_1)| c_1(q) q}{m}, j \in \mathcal{R}_1(p_1)\right) \\
&\quad \times \sum_{r=1}^{|\mathcal{R}_1(p_1)|} \frac{1}{r} \Pr\left(C_r^{(j)} | P_{2j} \le \frac{rc_2 q}{|\mathcal{R}_1(p_1)|}, P_1 = p_1\right) \\
&\quad \times \Pr\left(P_{2j} \le \frac{rc_2 q}{|\mathcal{R}_1(p_1)|}\middle| P_1 = p_1\right) \\
&\le \frac{c_2 q}{|\mathcal{R}_1(p_1)|} I\left(p_{1j} \le \frac{|\mathcal{R}_1(p_1)| c_1(q) q}{m}, j \in \mathcal{R}_1(p_1)\right) \\
&\quad \times \sum_{r=1}^{|\mathcal{R}_1(p_1)|} \Pr\left(C_r^{(j)} | P_{2j} \le \frac{rc_2 q}{|\mathcal{R}_1(p_1)|}, P_1 = p_1\right)
\end{aligned}
\qquad \textbf{[S8]}
$$

$$
\le \frac{c_2 q}{|\mathcal{R}_1(p_1)|} I\left(p_{1j} \le \frac{|\mathcal{R}_1(p_1)| c_1(q) q}{m}, j \in \mathcal{R}_1(p_1)\right), \qquad \textbf{[S9]}
$$

where inequality [**S8**] follows from the independence of the P values across the studies and the fact that P_{2j} is a null-hypothesis P value. We now show that inequality [**S9**] holds. It follows from item 1 of lemma S2.1 in the supplementary material of ref. 1 that

$$
\sum_{r=1}^{|\mathcal{R}_1(p_1)|} \Pr\left(C_r^{(j)} | P_{2j} \le \frac{rc_2 q}{|\mathcal{R}_1(p_1)|}, P_1 = p_1\right) \le 1
$$

for any $p_1 = (p_{11}, \ldots, p_{1m})$ and $j \in I_{10} \cap \mathcal{R}_1(p_1)$. It is straightforward to verify that this result holds for $j \in I_{00} \cap \mathcal{R}_1(p_1)$ as well, yielding inequality [**S9**]. It follows that for $j \in I_{00}$,

$$
E\left(\frac{R_j}{\max(R,1)}\right) \le c_2 q E\left[\frac{I\left(P_{1j} \le |\mathcal{R}_1(P_1)| c_1(q) q / m, j \in \mathcal{R}_1(P_1)\right)}{\max\left(|\mathcal{R}_1(P_1)|, 1\right)}\right]. \qquad \textbf{[S10]}
$$

Note that for $j \in I_{00}$

$$
\begin{aligned}
&E\left[\frac{I\left(P_{1j} \le \frac{|\mathcal{R}_1(P_1)| c_1(q) q}{m}, j \in \mathcal{R}_1(P_1)\right)}{\max\left(|\mathcal{R}_1(P_1)|, 1\right)}\right] \\
&\quad = \sum_{r=1}^{m} \frac{1}{r} \Pr\left(P_{1j} \le \frac{rc_1(q)q}{m}, j \in \mathcal{R}_1(P_1), \left|\mathcal{R}_1^{(j)}\left(P_1^{(j)}\right)\right| = r - 1\right) \qquad \textbf{[S11]} \\
&\quad \le \sum_{r=1}^{m} \frac{1}{r} \Pr\left(P_{1j} \le \frac{rc_1(q)q}{m}, \left|\mathcal{R}_1^{(j)}\left(P_1^{(j)}\right)\right| = r - 1\right) \qquad \textbf{[S12]} \\
&\quad \le \frac{c_1(q)q}{m} \sum_{r=1}^{m} \Pr\left(\left|\mathcal{R}_1^{(j)}\left(P_1^{(j)}\right)\right| = r - 1\right) = \frac{c_1(q)q}{m}. \qquad \textbf{[S13]}
\end{aligned}
$$

The inequality in [**S13**] follows from the independence of the P values within the primary study and the fact that P_{1j} is a null-hypothesis P value. The equality in [**S13**] follows from the fact that $\cup_{r=1}^{m} \{|\mathcal{R}_1^{(j)}(P_1^{(j)})| = r - 1\}$ is the entire space of $P_1^{(j)}$, represented as a union of disjoint events. Combining [**S10**] with [**S13**], we obtain for $j \in I_{00}$

$$
E\left(\frac{R_j}{\max(R,1)}\right) \le c_2 q \frac{c_1(q)q}{m}. \qquad \textbf{[S14]}
$$

Summing this upper bound over all $j \in I_{00}$, we obtain the upper bound in [**S5**], thus completing the proof of item *i* of Theorem 1 for the case where the set of P values within the follow-up study has property PRDS.

We now prove item *ii* of Theorem 1. Inequalities [**S3**] and [**S4**] follow from the results in the supplementary material of ref. 1. Specifically, inequality [**S3**] follows from the derivations leading to [S2.8] in ref. 1 and inequality [**S4**] follows from the proof of item 2 and item 3 of Lemma S2.1 in ref. 1. We now prove inequality [**S5**]. Both for the case where the P values within the follow-up study are independent and for the case where the P values within the follow-up study have property PRDS, the derivations leading to [**S10**] and [**S12**] remain valid when m is replaced with m^* in the denominators of the fractions appearing in those derivations and in the terms defining $C_r^{(j)}$. Therefore

$$
\begin{aligned}
&\sum_{j \in I_{00}} E\left[\frac{I\left(P_{1j} \le |\mathcal{R}_1(P_1)| c_1(q) q / m^*, j \in \mathcal{R}_1(P_1)\right)}{\max\left(|\mathcal{R}_1(P_1)|, 1\right)}\right] \\
&\quad \le \sum_{j \in I_{00}} \sum_{r=1}^{m} \frac{1}{r} \Pr\left(P_{1j} \le \frac{rc_1(q)q}{m^*}, \left|\mathcal{R}_1^{(j)}\left(P_1^{(j)}\right)\right| = r - 1\right).
\end{aligned}
\qquad \textbf{[S15]}
$$

It follows from the derivations leading from [S2.3] to [S2.8] in the supplementary material of ref. 1, replacing I_0 with I_{00}, q_1 with $c_1(q)q$, and the event $C_r^{(j)}$ with the event $\left|\mathcal{R}_1^{(j)}(P_1^{(j)})\right| = r - 1$ both in the derivations and in the definition of p_{jrl}, that

$$
\sum_{j \in I_{00}} \sum_{r=1}^{m} \frac{1}{r} \Pr\left(P_{1j} \le \frac{rc_1(q)q}{m^*}, \left|\mathcal{R}_1^{(j)}\left(P_1^{(j)}\right)\right| = r - 1\right) \le |I_{00}| \frac{c_1(q)q}{m}. \qquad \textbf{[S16]}
$$

Combining [**S10**] with m replaced by m^*, [**S15**], and [**S16**], we obtain inequality [**S5**], which completes the proof of item *ii* of Theorem 1.

We now prove item *iii* of Theorem 1. If we replace $\tilde{q}_1$ with $\tilde{c}_1(q)q$ and $|I_0|$ with $|I_{01}|$ in the derivations leading to [S2.18] in the supplementary material in ref. 1, we obtain

$$E\left(\sum_{j\in I_{01}}\frac{R_j}{\max(R,1)}\right)\le |I_{01}|\frac{\tilde{c}_1(q)q}{m}=f_{01}\tilde{c}_1(q)q. \qquad \textbf{[S17]}$$

It follows from the definition of $\tilde{c}_1(x)$ that $\tilde{c}_1(x)\le c_1(x)$ for all $x\in(0,1)$, in particular $\tilde{c}_1(q)\le c_1(q)$. Inequality **[S3]** follows immediately from this inequality and inequality **[S17]**. Inequality **[S4]** is obtained using the derivations from the main text and the supplementary material of ref. 1, as detailed in the proof of inequality **[S4]** for item *i* of Theorem 1. For this item q_1 is replaced with $\tilde{c}_1(q)q$ in those derivations, and to obtain inequality **[S4]** we use the fact that $\tilde{c}_1(q)\le c_1(q)$. We now prove inequality **[S5]**. Both for the case where the P values within the follow-up study are independent and for the case where the P values within the follow-up study have property PRDS, the derivations leading to **[S10]** and **[S11]** remain valid when $c_1(q)$ is replaced with $\tilde{c}_1(q)$ in those derivations and in the terms defining $C_r^{(j)}$. Therefore

$$\sum_{j\in I_{00}}E\left(\frac{R_j}{\max(R,1)}\right)\le c_2 q\sum_{j\in I_{00}}\sum_{r=1}^{m}\frac{1}{r}\Pr\left(P_{1j}\le\frac{r\tilde{c}_1(q)q}{m},\, j\in\mathcal{R}_1(P_1),\left|\mathcal{R}_1^{(j)}\left(P_1^{(j)}\right)\right|=r-1\right). \qquad \textbf{[S18]}$$

It follows from the derivations leading from [S2.9] to [S2.18] in the supplementary material of ref. 1, replacing I_0 with I_{00}, $\tilde{q}_1$ with $\tilde{c}_1(q)q$, and the event $C_r^{(j)}$ with the event $|\mathcal{R}_1^{(j)}(P_1^{(j)})|=r-1$ both in the derivations and in the definition of $\tilde{p}_{jrl}$, that

$$\sum_{j\in I_{00}}\sum_{r=1}^{m}\frac{1}{r}\Pr\left(P_{1j}\le\frac{r\tilde{c}_1(q)q}{m},\, j\in\mathcal{R}_1(P_1),\left|\mathcal{R}_1^{(j)}\left(P_1^{(j)}\right)\right|=r-1\right)\le |I_{00}|\frac{\tilde{c}_1(q)q}{m}. \qquad \textbf{[S19]}$$

Combining **[S18]** with **[S19]**, and using the fact that $\tilde{c}_1(q)\le c_1(q)$, we obtain inequality **[S5]**, which completes the proof of item *iii* of Theorem 1.

Lemma S1.1. For Steps i–iv in the computation of r values:

i) *For feature $i\in\mathcal{R}_1$, if a solution $r_i\in(0,1)$ to $f_i(r_i)=r_i$ exists, then this solution is unique; i.e., the r value in step iv is well defined.*
ii) *Item i holds when the function $f_i(x)$ is computed with the modification in item ii of Theorem 1.*
iii) *Declaring the features with r values at most q is equivalent to the procedure given in Variations, second paragraph, in the main text.*
iv) *For r values computed with the modification in item ii of Theorem 1, declaring the features with r values at most q is equivalent to the procedure given in Variations, where m is replaced by $m^*=m\sum_{i=1}^{m}1/i$.*
v) *The function $\tilde{c}_1(x)$ in item iii of Theorem 1 is well defined. For r values computed with the modification in item iii of Theorem 1, declaring the features with r values at most q is equivalent to the procedure given in Variations, where $c_1(q)$ is replaced by $\tilde{c}_1(q)$.*

Proof of Lemma S1.1.

Proof of items i and ii of Lemma S1.1. Simple calculations show that $g(x)=xc_1(x)$ is a strictly increasing function of x for $x>0$. Therefore, for each feature $j\in\mathcal{R}_1$, $e_j(x)/x$ is a strictly decreasing function of x. Despite the fact that $e_j(x)/[x\cdot\mathrm{rank}(e_j(x))]$ may not be monotone decreasing functions for $j\in\mathcal{R}_1$, it is guaranteed that $f_i(x)/x=\min_{\{j:e_j(x)\ge e_i(x),j\in\mathcal{R}_1\}}e_j(x)/[x\cdot\mathrm{rank}(e_j(x))]$ is a strictly decreasing function of x for each feature $i\in\mathcal{R}_1$. [The proof that $f_i(x)/x$ is a strictly decreasing function is quite involved and is omitted for brevity.] Therefore, if a solution $r_i\in(0,1)$ to $f_i(x)/x=1$ exists, then it is unique, because for all $x<r_i$, $f_i(x)/x>1$ and for all $x>r_i$, $f_i(x)/x<1$. When the function $f_i(x)$ is computed with the modification in item *ii* of *Theorem 1*, the proof remains the same, because m^* does not depend on x.

Proof of items iii–v of Lemma S1.1. It is easy to see that for the procedure given in *Variations*, second paragraph, in the main text, $\mathcal{R}_2=\{i\in\mathcal{R}_1: f_i(q)\le q\}$. The same result holds for the function $f_i(x)$ with the modification of items *ii* and *iii* of *Theorem 1* and the modified procedures in items *iv* and *v* of *Lemma S1.1*, respectively. Therefore, it is enough to prove that for $i\in\mathcal{R}_1$, $f_i(q)\le q$ if and only if $r_i\le q$ for items *iii*–*v* of *Lemma S1.1*.

Proof of item iii. Assume $f_i(q)\le q$. Note that $f_i(x)$ can be defined on $[0,1)$ and $f_i(0)>0$ because the P values are positive. It can be shown that $f_i(x)$ is a continuous function on $[0,1)$ and therefore $h_i(x)=f_i(x)-x$ is a continuous function as well. [It is easy to see that $f_i(x)$ is continuous at each x_0 where e values are unique. Note that for each $j\in\mathcal{R}_1$ the numerator of $e_j(x)m/\mathrm{rank}(e_j(x))$ is continuous and there is a small neighborhood of x_0 where $\mathrm{rank}(e_j(x))$ does not change, yielding that $e_j(x)m/\mathrm{rank}(e_j(x))$ is continuous at x_0. Because the minimum of continuous functions is also continuous, $f_i(x)$ is a continuous function as well. For x_0 where e values are not unique, the proof is more involved. In these points the functions $e_j(x)m/\mathrm{rank}(e_j(x))$ may be not continuous; however, $f_i(x)$ is continuous.] Using the facts that $h_i(0)=f_i(0)-0>0$ and $h_i(q)=f_i(q)-q\le 0$, we obtain from the intermediate value theorem that a value $0<x_i\le q$, satisfying $f_i(x_i)=x_i$, exists. Using item *i*, we obtain that this solution is unique and $r_i=x_i$. Thus, we have proved $r_i\le q$. Let us now assume that $r_i\le q$ and prove that $f_i(q)\le q$. Because $r_i\le q$, $r_i\ne 1$, and therefore r_i is the unique solution in $(0,1)$ to $f_i(x)=x$. It follows from the fact that $f_i(x)/x$ is monotone decreasing (see proof of item *i*) that $f_i(q)/q\le f_i(r_i)/r_i=1$, and therefore $f_i(q)\le q$.

Proof of item iv. We need to prove that when we replace m with $m^*=m\sum_{i=1}^{m}1/i$ in the computation of $f_i(x)$ and r_i for $i\in\mathcal{R}_1$, $r_i\le q$ if and only if feature i is rejected by the procedure in *Variations*, where m is replaced by $m=m^*$. It is easy to see that for this modified procedure, $\mathcal{R}_2=\{i\in\mathcal{R}_1: f_i(q)\le q\}$, where $f_i(q)$ is computed with the modification above. It remains to prove that $\{i\in\mathcal{R}_1: f_i(q)\le q\}=\{i\in\mathcal{R}_1: r_i\le q\}$. Because $f_i(x)$ is continuous, it is obvious that the modified function $f_i(x)$ is continuous as well. Moreover, $f_i(x)/x$ is monotone decreasing in x; thus using arguments similar to the proof of item *iii*, the result follows.

Proof of item v. The proof that the function $\tilde{c}_1(x)$ is well defined, i.e., that for all $x\in(0,1)$ a solution a to $a\sum_{i=1}^{\lceil tm/(ax)-1\rceil}1/i=c_1(x)$ exists, is technical and therefore is omitted. Similarly to the items above, we need to prove that $\{i\in\mathcal{R}_1:\tilde{f}_i(q)\le q\}=\{i\in\mathcal{R}_1:\tilde{r}_i\le q\}$, where $\tilde{f}_i(x)$ and $\tilde{r}_i$ are the modified functions and r values, respectively, given in item *iii* of *Theorem 1*. We first show that if $\tilde{f}_i(q)\le q$, then $\tilde{r}_i=\min\{x:\tilde{f}_i(x)\le x\}\in(0,1)$ exists. It can be shown that $\tilde{c}_1(x)$ is right continuous, and therefore $\tilde{f}_i(x)$ is right continuous. [The proof that $\tilde{c}_1(x)$ is right continuous is based on the facts that $\lceil tm/(ax)-1\rceil$ is a right continuous function of x and $c_1(x)$ is a continuous function. Since the proof is technical, it is omitted.] If $\tilde{f}_i(q)\le q$, then $\inf\{x:\tilde{f}_i(x)\le x\}<1$. It remains to show that $\inf\{x:\tilde{f}_i(x)\le x\}\ne 0$, because $\tilde{f}_i(x)$ is right continuous for all $x\in(0,1)$; therefore if $\inf\{x:\tilde{f}_i(x)\le x\}\in(0,1)$, then $\inf\{x:\tilde{f}_i(x)\le x\}=\min\{x:\tilde{f}_i(x)\le x\}$. We now prove that $\inf\{x:\tilde{f}_i(x)\le x\}\ne 0$. Note that $\tilde{c}_1(x)\le c_1(x)$ for all $x\in(0,1)$, and therefore it can be shown that $\tilde{f}_i(x)\ge f_i(x)$ for all $x\in(0,1)$. As we noted in the proof of item *iii* of *Lemma S1.1*, $f_i(x)$ can be defined for $x\in[0,1)$, it is a continuous function on $[0,1)$, and $f_i(0)>0$. Therefore, $\delta>0$ exists such that $f_i(x)>x$ for $x\in[0,\delta)$. It follows that $\tilde{f}_i(x)>x$ for $x\in(0,\delta)$, and therefore

$\inf\{x : \tilde{f}_i(x) \le x\} \neq 0$. Thus, we have proved that if $\tilde{f}_i(q) \le q$, then $\tilde{r}_i = \min\{x : \tilde{f}_i(x) \le x\} \in (0,1)$ exists. From the definition of $\tilde{r}_i$ we obtain $\tilde{r}_i \le q$. Assume now that $\tilde{r}_i \le q$; i.e., $\min\{x : \tilde{f}_i(x) \le x\} \le q$. It can be shown that $\tilde{f}_i(x)/x$ is a monotone decreasing function, and therefore $\tilde{f}_i(q)/q \le \tilde{f}_i(r_i)/r_i \le 1$; i.e., $\tilde{f}_i(q) \le q$. [The proof that $\tilde{f}_i(x)/x$ is a monotone decreasing function is quite involved and is omitted for brevity. It is based on the facts that $\tilde{c}_1(x)x$ is monotone increasing, and therefore $e_j(x)/x$ is monotone decreasing for all $j \in \mathcal{R}_1$.]

S2. GWAS Real Data Examples

Tables S1, S2, and S5 show the results of the replicability analysis for the SNPs followed up based on the results of the primary study (or studies). Columns 1–3 in Tables S1 and S2 and columns 1 and 2 in Table S5 contain the position of each SNP. Columns 4 and 5 in Tables S1 and S2 and columns 3 and 4 in Table S5 show the primary and follow-up P values. Columns 6–8 in Tables S1 and S2 and column 6 in Table S5 show the r values for different choices of l_{00}. Column 9 in Tables S1 and S2 and column 5 in Table S5 show the metaanalysis P values, which are the unadjusted P values computed using the data from the primary and follow-up studies for testing the global null hypothesis of no association in any of the studies. In Tables S1 and S2 the rows are sorted by the metaanalysis P values, and the handful of findings with most significant metaanalysis P values that were reported as interesting in the published works are marked with an asterisk in the last column.

S3. Choice of Selection Rule for Replicability Analysis

Although any stable selection rule can be used, some selection rules may be more efficient than others. For a given FDR level q, the promising hypotheses for replicability analysis are the set of hypotheses rejected with the BH procedure at level $c_1(q)q$ on the primary study P values. Therefore, for the purpose of replicability analysis, the set of hypotheses to be considered should be only this set or a subset thereof. This means that if R_1 hypotheses are followed up, not all R_1 features need to be selected for a replicability analysis at a predetermined level q. The advantage of selecting only the relevant subset is that the power of the procedure will be greater because the problem of multiplicity among the selected hypotheses will be smaller, without compromising any potential replicability claims. Specifically, for the r value to be below q, only the subset of R_1 hypotheses selected for follow-up with primary study P values that are small enough needs to be considered, where our requirement for small enough is as follows: When applying the BH procedure at level $c_1(q)q$ on $p_{11},\ldots,p_{1m}$, these hypotheses will be among the rejected. Computing the r values for the subset of $\mathcal{R}_1$ with small enough primary study P values, we receive smaller r values than if all R_1 SNPs are considered for replicability analysis.

For the example of GWAS of IgA nephropathy, for an FDR level of 0.05, only 14 SNPs of the 61 followed up had primary study P values small enough to be considered for replicability analysis. The number of r values below 0.05 was still seven with this modified selection rule, but these seven r values were smaller than the r values for the 7 SNPs in Table 1 of the main text. Specifically, with parameters $(l_{00}, c_2) = (0.8, 0.5)$ for this superior selection rule that selected 14 SNPs for follow-up, the r values were 0.005, 0.008, 0.005, 0.008, 0.005, 0.041, and 0.017, whereas the r values computed using all 61 SNPs selected were, respectively, 0.007, 0.009, 0.006, 0.009, 0.009, 0.041, and 0.017.

S4. Power Comparison for Different Values of (l_{00}, c_2)

We conducted simulations to investigate how the power and FDR of our proposal depend on $c_2 \in (0,1)$ and $l_{00} \in \{0, 0.5, 0.8, 0.9\}$ for $q = 0.05$. The P values were generated independently as follows. Let P_{1j} and P_{2j} be the P values in the primary and in the follow-up study, respectively, for feature j. We set $P_{1j} = 1 - \Phi(X_{1j})$ and $P_{2j} = 1 - \Phi(X_{2j})$, where $X_{1j} \sim N(\mu_{1j}, 1)$, $X_{2j} \sim N(\mu_{2j}, 1)$. For $i \in \{1,2\}$, we set $\mu_{ij} = 0$ if feature j comes from a true null hypothesis in study i and $\mu_{ij} = \mu_i > 0$ if feature j comes from a false null hypothesis in study i. The values of μ_1 and μ_2 were set according to the requirement that the power of the Bonferroni procedure at level 0.05 in the primary study is π_1 and that in the follow-up study is π_2, for $\pi_1 = 0.1$ and $\pi_2 \in \{0.2, 0.5, 0.8\}$. Specifically, we set $\mu_1 = \Phi^{-1}(1 - 0.05/m) - \Phi^{-1}(1 - \pi_1)$ and $\mu_2 = \Phi^{-1}(1 - 0.05/R_1) - \Phi^{-1}(1 - \pi_2)$, where Φ^{-1} is the inverse of the cumulative distribution function of a standard normal variable and R_1 is the number of rejected hypotheses by the BH procedure at level $c_1 \times 0.05$ applied on the primary study P values. In addition, $m = 1{,}000$, $f_{00} = 0.9$, $f_{01} = f_{10} = 0.025$, and $f_{11} = 0.05$.

The simulation results were based on 10,000 repetitions. The FDR was estimated by averaging the false discovery proportion. The average power was estimated by the average number of true replicability claims, divided by mf_{11}. We also estimated the probability that our proposal makes at least one true replicability claim (which we refer to as "power for at least one") by the proportion of repetitions in which at least one true replicability claim was made. The SEs of the estimators were of the order of 10^{-3} or 10^{-4} for all of the sets of parameters.

A comparison of columns 8 and 9 with columns 3, 5, and 7 in Table S4 shows that the gain in power of using $l_{00} > 0$ over $l_{00} = 0$ can be large. Fig. S1 shows the average power and the power for at least one as a function of $c_2 \in \{0.05, 0.1, \ldots, 0.95\}$ for our proposal with $l_{00} \in \{0, 0.5, 0.8, 0.9\}$ and $q = 0.05$. As expected, both measures of power increase as l_{00} increases. For fixed l_{00} and (π_1, π_2), the highest average power among all of the choices of c_2 is close to the average power when $c_2 = 0.5$ (Fig. S1 *A*, *C*, and *E*), also shown in Table S4. The power curve for at least one as a function of c_2 is flat around $c_2 = 0.5$ (Fig. S1 *B*, *D*, and *F*), suggesting as well that $c_2 = 0.5$ is an appropriate choice.

Fig. S2 shows the FDR as a function of $c_2 \in \{0.05, 0.1, \ldots, 0.95\}$, for our proposal with $l_{00} \in \{0, 0.5, 0.8, 0.9\}$ and $q = 0.05$. It can be seen that the FDR is far below 0.05 for all of the sets of parameters considered. This follows from the fact that our data generation may result in FDR much lower than the upper bound given in [**S1**]. To see this, note that it follows from the proof of *Theorem 1* that the FDR of our proposal achieves the upper bound in [**S1**] when the P values under the alternative are practically zero. In our simulation setting, this condition would hold if μ_i for $i \in \{1,2\}$ were always extremely large compared with $N(0,1)$ random variables; e.g., $\mu_i \ge 4$. Obviously this does not hold for our data generation process. Therefore, we could get higher FDR values for another data generation process; however, we still would not expect to achieve 0.05 because of using conservative upper bounds for f_{01} and $E(|I_{10} \cap \mathcal{R}_1|/(\max|\mathcal{R}_1|, 1))$ in expression [**S1**].

S5. GWAS Simulation Example

The goal of the simulation was threefold: first, to verify that the FDR is controlled below the nominal level for realistic simulations with GWAS-type dependency, even if hypotheses with primary study P values above $c_1(q)q/m$ are followed up; second, to compare the performance of our suggested proposal with the BH procedure on maximum P values; and third, to examine the effect of l_{00} on the power of the two procedures.

The information on l_{00} is incorporated into the BH procedure on maximum P values, to make the comparison fair, by performing the BH procedure at level $q/(1 - l_{00})$. It is straightforward to show that the FDR is controlled at level at most q for the BH procedure on the maximum P values at level $q/(1 - l_{00})$, when the P values within each study are independent.

We simulated two GWAS from the simulator HAPGEN2 (2). The two studies were generated from two samples of the HapMap project (3), a sample of 165 Utah residents with Northern

and Western European ancestry (CEU) and a sample of 109 Chinese in Metropolitan Denver, Colorado (CHD). In the CEU and CHD populations, respectively, 34 and 38 SNPs were set as disease SNPs with an increased multiplicative relative risk of 1.2, and 18 of the disease SNPs were common to both populations. Each study contained 4,500 cases and 4,500 referents. The linkage disequilibrium (LD) across SNPs, as measured for the samples in the HapMap project, was retained. Due to LD, the number of SNPs associated with the phenotype in each study was larger than the number of disease SNPs. See ref. 1 for the details of this simulation.

The CHD study was the primary study, and the CEU study was the follow-up study. SNPs were selected for follow-up only if they were discovered by the BH procedure at level $c_1(0.05)\times 0.05$. Table S3 presents the average number of replicated findings, as well as the average false discovery proportion (FDP), for our proposal with $c_2 = 0.5$ and $q = 0.05$, and the BH procedure on maximum P values at level $0.05/(1-l_{00})$, for different values of l_{00}. From columns 4 and 7 it is clear that the FDR is controlled and that our proposal is actually conservative, for all values of l_{00}. From a comparison of columns 2 and 5 it is clear that our proposal is more powerful than the BH procedure on maximum P values. Finally, from comparisons of the rows it is clear that the power increases as l_{00} increases.

S6. Procedure for FWER Control

Theorem S6.1. *A procedure that declares findings with Bonferroni r values at most α as replicated controls the FWER for replicability analysis at level at most α if $l_{00} \le f_{00}$ and the follow-up study P values are independent of the primary study P values.*

Proof of Theorem S6.1. It is easy to show that the procedure that declares findings with Bonferroni r values at most α as replicated is equivalent to that of declaring as replicated all features with $f_j^{\mathrm{Bonf}}(\alpha) \le \alpha$. The equivalence follows from the facts that $f_j^{\mathrm{Bonf}}(x)$ is a continuous function of x and $f_j^{\mathrm{Bonf}}(x)/x$ is strictly monotone decreasing. We prove that the above procedure controls the FWER at a level that is smaller than or equal to

$$c_1c_2f_{00}\alpha^2 + f_{01}c_1\alpha + c_2\alpha E\left(\frac{|\mathcal{R}_1\cap I_{10}|}{\max(|\mathcal{R}_1|,1)}\right), \qquad \textbf{[S20]}$$

where $c_1 = (1-c_2)/(1-l_{00}(1-c_2\alpha))$. Note that this upper bound is equal to the upper bound given in expression [**S1**] with $q=\alpha$. We showed in the proof of *Theorem 1* that the expression in [**S1**] is at most q if $l_{00} \le f_{00}$. Therefore, if the upper bound in [**S20**] holds and $l_{00} \le f_{00}$, then *Theorem S6.1* follows.

We now prove that the expression in [**S20**] is an upper bound for the FWER for replicability analysis, which is $\Pr(R_{00}+R_{10}+R_{01}>0)$. Note that

$$\Pr(R_{00}+R_{10}+R_{01}>0) \le E(R_{00}+R_{10}+R_{01}) = \sum_{x\in\{00,01,10\}}\sum_{j\in I_x} E(R_j).$$

For the procedure that declares as replicated all features with $f_j^{\mathrm{Bonf}}(\alpha)\le\alpha$, which is equivalent to the procedure that declares findings with Bonferroni r values at most α as replicated (as discussed above),

$$E(R_j) = \Pr\left(j\in\mathcal{R}_1, P_{1j}\le\frac{c_1\alpha}{m}, P_{2j}\le\frac{c_2\alpha}{\max(|\mathcal{R}_1|,1)}\right). \qquad \textbf{[S21]}$$

We give an upper bound for expression [**S21**] for $j\in I_{01}$, $j\in I_{10}$, and $j\in I_{00}$. For $j\in I_{01}$,

$$\Pr\left(j\in\mathcal{R}_1, P_{1j}\le\frac{c_1\alpha}{m}, P_{2j}\le\frac{c_2\alpha}{\max(|\mathcal{R}_1|,1)}\right) \le \Pr\left(P_{1j}\le\frac{c_1\alpha}{m}\right) \le \frac{c_1\alpha}{m}, \qquad \textbf{[S22]}$$

where the last inequality follows from the fact that P_{1j} is a null-hypothesis P value.

For $j\in I_{00}\cup I_{10}$ and an arbitrary fixed $p_1 = (p_{11},\ldots,p_{1m})$ such that $|\mathcal{R}_1(p_1)|>0$,

$$\begin{aligned} E(R_j|P_1=p_1) &= I\left(p_{1j}\le\frac{c_1\alpha}{m}, j\in\mathcal{R}_1(p_1)\right)\Pr\left(P_{2j}\le\frac{c_2\alpha}{|\mathcal{R}_1(p_1)|}\middle| P_1=p_1\right) \\ &\le \frac{c_2\alpha}{|\mathcal{R}_1(p_1)|} I\left(p_{1j}\le\frac{c_1\alpha}{m}, j\in\mathcal{R}_1(p_1)\right), \end{aligned} \qquad \textbf{[S23]}$$

where inequality [**S23**] follows from the independence of the P values across the studies and the fact that P_{2j} is a null-hypothesis P value. Using [**S23**] we obtain the upper bounds on expression [**S21**] for $j\in I_{10}$ and for $j\in I_{00}$. For $j\in I_{10}$, it follows that

$$E(R_j|P_1=p_1) \le \frac{c_2\alpha}{|\mathcal{R}_1(p_1)|} I(j\in\mathcal{R}_1(p_1)),$$

and therefore

$$E(R_j) \le c_2\alpha E\left(\frac{I(j\in\mathcal{R}_1)}{\max(|\mathcal{R}_1|,1)}\right). \qquad \textbf{[S24]}$$

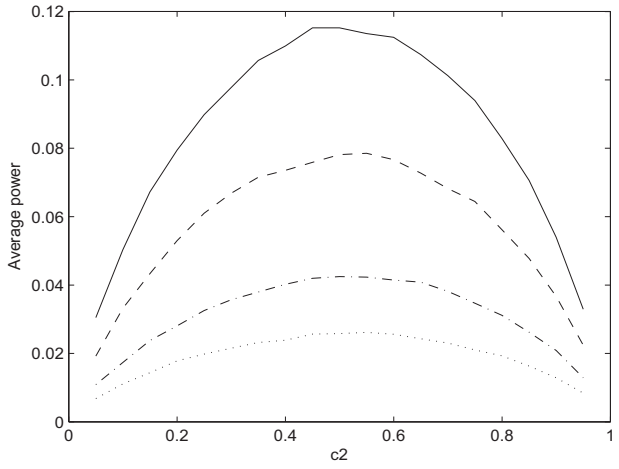
For $j\in I_{00}$, it follows that

$$\begin{aligned} E(R_j) &\le c_2\alpha E\left[\frac{I(P_{1j}\le c_1\alpha/m, j\in\mathcal{R}_1(P_1))}{\max(|\mathcal{R}_1(P_1)|,1)}\right] \\ &\le c_2\alpha E\left[I\left(P_{1j}\le\frac{c_1\alpha}{m}\right)\right] \le c_2\alpha\frac{c_1\alpha}{m}, \end{aligned} \qquad \textbf{[S25]}$$

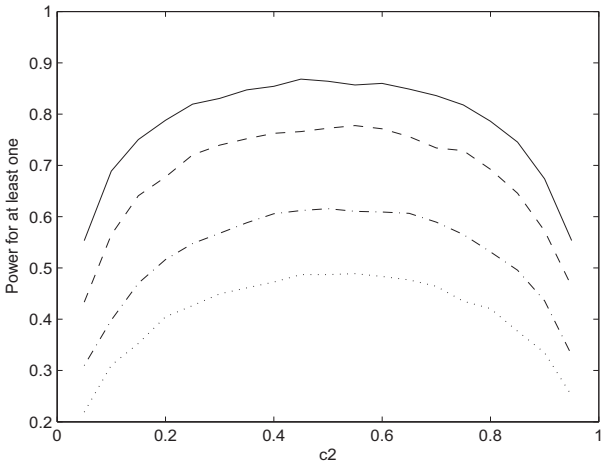
where the last inequality follows from the fact that P_{1j} is a null-hypothesis P value. From summing over the upper bounds [**S22**], [**S24**], and [**S25**] it thus follows that

$$\begin{aligned} \mathrm{FWER} &\le E(R_{00}+R_{10}+R_{01}) \le c_1c_2f_{00}\alpha^2 + f_{01}c_1\alpha \\ &\quad + c_2\alpha E\left(\frac{|\mathcal{R}_1\cap I_{10}|}{\max(|\mathcal{R}_1|,1)}\right). \end{aligned}$$

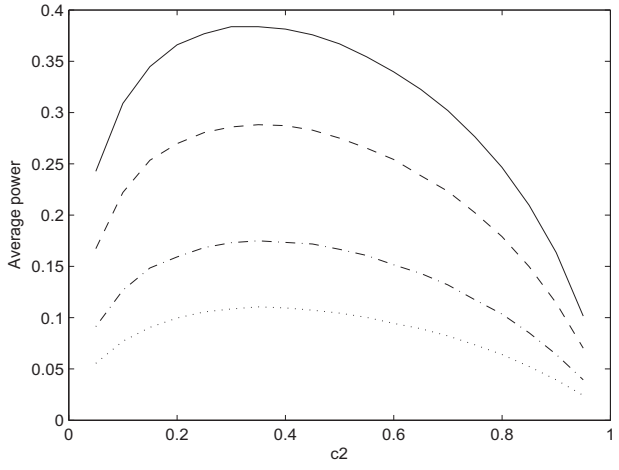
1. Bogomolov M, Heller R (2013) Discovering findings that replicate from a primary study of high dimension to a follow-up study. *J Am Stat Assoc* 108(504):1480–1492.
2. Su Z, Marchini J, Donnelly P (2011) HAPGEN2: Simulation of multiple disease SNPs. *Bioinformatics* 27(16):2304–2305.
3. International HapMap Consortium (2003) The International HapMap Project. *Nature* 426(6968):789–796.



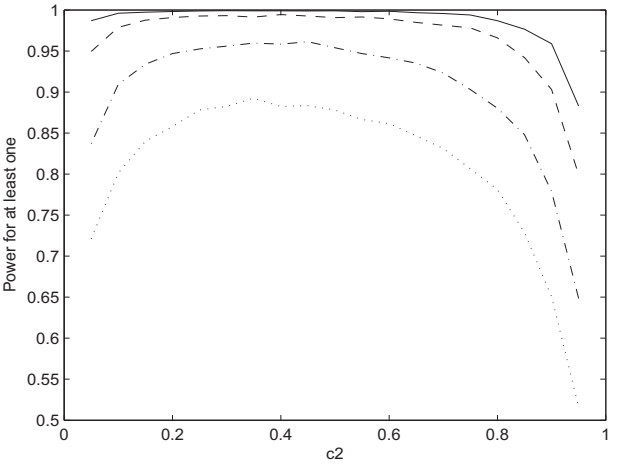
(a) Average power, $(\pi_1, \pi_2) = (0.1, 0.2)$.



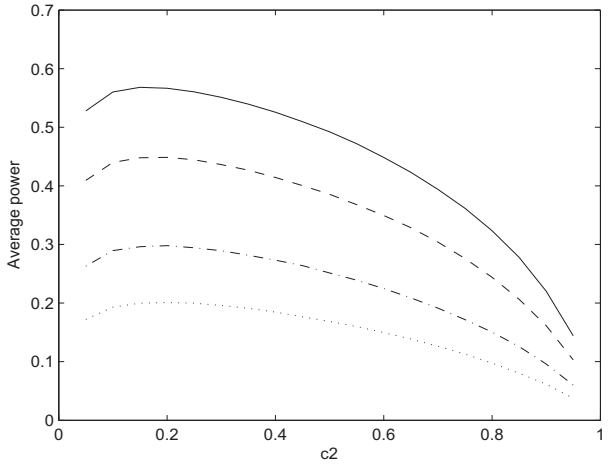
(b) Power for at least one, $(\pi_1, \pi_2) = (0.1, 0.2)$.



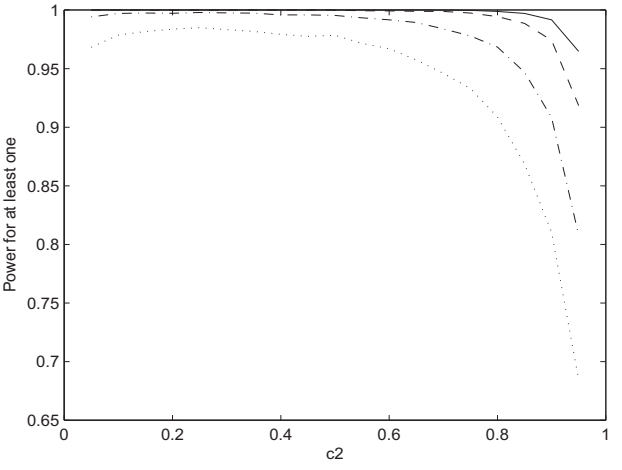
(c) Average power, $(\pi_1, \pi_2) = (0.1, 0.5)$.



(d) Power for at least one, $(\pi_1, \pi_2) = (0.1, 0.5)$.



(e) Average power, $(\pi_1, \pi_2) = (0.1, 0.8)$.



(f) Power for at least one, $(\pi_1, \pi_2) = (0.1, 0.8)$.

Fig. S1. The estimated average power (*A*, *C*, and *E*) and the probability of at least one true replicability claim (power for at least one) (*B*, *D*, and *F*) of our proposal with parameters $(l_{00}, c_2, 0.05)$ as a function of c_2 in a simulation where $f_{00} = 0.9$, $f_{01} = f_{10} = 0.025$, $f_{11} = 0.05$; the number of hypotheses examined in the

Legend continued on following page

primary study is 1,000; and the signal-to-noise ratios for the primary study and the follow-up study, respectively, are taken according to the requirement that the power of the Bonferroni procedure at level 0.05 in the primary study is π_1 and that in the follow-up study is π_2 for $(\pi_1,\pi_2)=(0.1,0.2)$ (*A* and *B*), $(\pi_1,\pi_2)=(0.1,0.5)$ (*C* and *D*), $(\pi_1,\pi_2)=(0.1,0.8)$ (*E* and *F*). $l_{00}=0.9$ (solid curve), $l_{00}=0.8$ (dashed surve), $l_{00}=0.5$ (dashed-dotted curve), and $l_{00}=0$ (dotted curve). The SEs of the estimators were of the order of 10^{-3} or 10^{-4} for all of the sets of parameters.

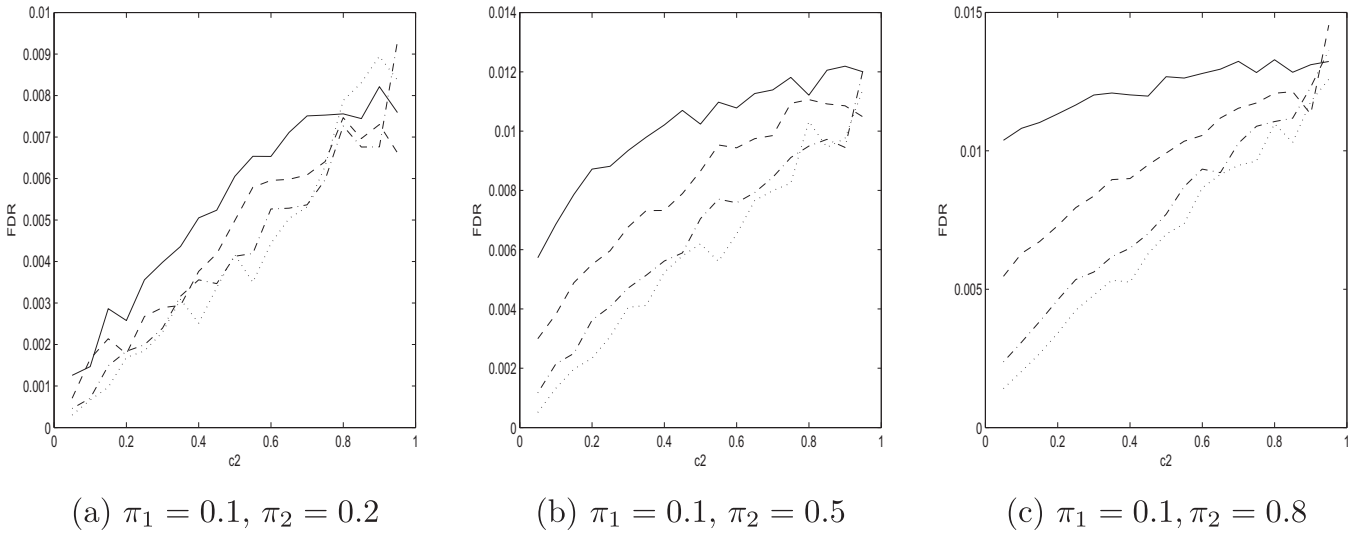


Fig. S2. The estimated FDR of our proposal with parameters $(l_{00},c_2,0.05)$ as a function of c_2 in a simulation where $f_{00}=0.9$, $f_{01}=f_{10}=0.025$, $f_{11}=0.05$; the number of hypotheses examined in the primary study is 1,000; and the signal-to-noise ratios for the primary study and the follow-up study, μ_1/σ_1 and μ_2/σ_2, respectively, are taken according to the requirement that the power of the Bonferroni procedure at level 0.05 in the primary study is π_1 and that in the follow-up study is π_2 for $(\pi_1,\pi_2)=(0.1,0.2)$ (*A*), $(\pi_1,\pi_2)=(0.1,0.5)$ (*B*), and $(\pi_1,\pi_2)=(0.1,0.8)$ (*C*). $l_{00}=0.9$ (solid curve), $l_{00}=0.8$ (dashed curve), $l_{00}=0.5$ (dashed-dotted curve), and $l_{00}=0$ (dotted curve). The SEs were of the order of 10^{-3} or 10^{-4} for all of the sets of parameters.

Table S1. Replicability analysis for the study of ref. 1

Chr.	Position	Gene	p1	p2	$I_{00} = 0$	$I_{00} = 0.5$	$I_{00} = 0.8$	p_meta
6	32,685,358	HLA-DRB1	8.19e-08	8.57e-14	0.0243	0.0150	0.0074	4.13e-20*
8	6,810,195	DEFAs	2.04e-07	1.25e-07	0.0409	0.0207	0.0090	3.18e-14*
6	32,779,226	HLA-DQA/B	3.28e-08	3.57e-06	0.0224	0.0147	0.0059	3.43e-13*
22	28,753,460	MTMR3	2.30e-07	2.02e-05	0.0409	0.0207	0.0090	1.17e-11*
6	30,049,922	HLA-A	4.05e-09	3.68e-04	0.0224	0.0150	0.0090	1.74e-11*
17	7,403,693	TNFSF13	1.50e-06	2.52e-05	0.1907	0.1001	0.0413	9.40e-11*
17	7,431,901	MPDU1	5.52e-07	3.16e-04	0.0819	0.0418	0.0169	4.31e-10*
2	111,315,937	ACOXL	6.83e-05	3.41e-03	1	1	1	4.08e-07
16	31,255,249	x	6.67e-05	7.41e-03	1	1	1	4.64e-06
4	78,121,177	x	3.14e-10	8.16e-01	1	1	1	2.23e-05
11	113,369,319	x	1.82e-09	9.74e-01	1	1	1	5.42e-05
7	33,386,800	BBS9	2.75e-05	1.67e-01	1	1	1	1.17e-04
11	44,042,263	x	1.74e-05	2.72e-01	1	1	1	1.24e-04
4	40,144,579	x	9.95e-07	6.72e-01	1	1	1	1.85e-04
12	13,229,380	x	1.23e-05	4.41e-01	1	1	1	3.09e-04
14	69,116,920	x	4.60e-05	3.72e-01	1	1	1	3.71e-04
8	30,305,114	x	3.19e-05	4.73e-01	1	1	1	5.38e-04
12	129,587,780	x	4.59e-05	5.53e-01	1	1	1	6.84e-04
6	31,382,359	x	8.20e-08	9.53e-01	1	1	1	7.64e-04
16	77,632,003	WWOX	7.20e-05	4.57e-01	1	1	1	1.04e-03
8	97,393,458	PTDSS1	5.67e-05	6.12e-01	1	1	1	1.09e-03
6	26,384,629	x	4.32e-06	2.79e-01	1	1	1	1.25e-03
13	62,434,248	x	3.77e-05	5.39e-01	1	1	1	1.70e-03
11	109,836,841	FDX1	7.15e-05	7.19e-01	1	1	1	2.03e-03
18	35,923,102	x	4.35e-05	2.85e-01	1	1	1	2.32e-03
6	13,733,392	RANBP9	1.70e-05	8.45e-01	1	1	1	2.55e-03
9	78,162,069	PSAT1	5.98e-05	8.01e-01	1	1	1	2.71e-03
10	55,006,847	x	7.93e-05	6.87e-01	1	1	1	3.16e-03
6	33,163,516	x	1.46e-04	7.74e-01	1	1	1	4.56e-03
7	158,006,056	x	9.26e-05	7.50e-01	1	1	1	4.99e-03
6	106,231,017	x	6.19e-05	8.59e-01	1	1	1	6.41e-03
21	19,339,830	x	7.81e-05	5.34e-01	1	1	1	6.58e-03
12	19,488,937	AEBP2	4.95e-05	4.77e-01	1	1	1	6.92e-03
18	57,221,085	x	8.62e-06	5.48e-01	1	1	1	7.96e-03
10	76,538,473	DUSP13	7.84e-05	8.54e-01	1	1	1	9.18e-03
8	1,307,131	x	4.95e-05	7.52e-01	1	1	1	1.14e-02
16	72,315,398	x	4.92e-05	9.92e-01	1	1	1	1.24e-02
3	130,747,968	H1FOO	1.85e-05	8.90e-01	1	1	1	1.65e-02
12	39,245,441	x	1.21e-07	4.38e-01	1	1	1	1.66e-02
7	92,588,411	CCDC132	1.28e-07	4.09e-01	1	1	1	1.77e-02
1	110,389,963	x	1.46e-07	2.59e-01	1	1	1	1.99e-02
9	21,342,862	x	7.95e-05	9.45e-01	1	1	1	2.18e-02
2	46,170,592	PRKCE	1.78e-05	3.40e-01	1	1	1	2.21e-02
17	52,636,364	x	3.45e-05	5.20e-01	1	1	1	2.26e-02
1	82,547,439	x	5.51e-05	8.89e-01	1	1	1	2.72e-02
6	156,238,397	x	4.73e-05	1.43e-01	1	1	1	2.80e-02
11	61,956,393	x	2.16e-06	5.37e-01	1	1	1	4.10e-02
10	135,319,919	x	3.90e-05	6.76e-01	1	1	1	4.33e-02
12	66,026,196	x	2.57e-06	5.08e-01	1	1	1	4.42e-02
8	25,535,212	x	2.46e-05	3.44e-01	1	1	1	5.31e-02
15	88,817,746	IQGAP1	8.64e-05	2.22e-01	1	1	1	5.76e-02
6	13,707,282	SIRT5	3.98e-05	3.66e-01	1	1	1	6.84e-02
1	70,907,559	x	3.96e-05	4.71e-01	1	1	1	7.24e-02
1	176,696,794	CEP350	7.14e-05	4.50e-01	1	1	1	1.04e-01
12	8,955,888	x	7.85e-06	2.07e-01	1	1	1	1.10e-01
11	94,090,071	x	5.22e-05	3.08e-01	1	1	1	1.29e-01
2	4,641,380	x	9.57e-05	3.68e-01	1	1	1	1.39e-01
1	23,749,819	x	8.10e-05	2.08e-01	1	1	1	1.58e-01
7	105,466,371	x	4.61e-05	9.90e-02	1	1	1	2.32e-01
5	4,489,013	x	8.96e-05	3.83e-02	1	1	1	4.40e-01
1	215,993,345	x	2.67e-05	1.32e-02	1	1	1	4.90e-01

Chr., chromosome.

1. Yu XQ, et al. (2012) A genome-wide association study in Han Chinese identifies multiple susceptibility loci for IgA nephropathy. *Nat Genet* 44(2):178–182.

Table S2. Replicability analysis for the study of ref. 1, with 635,547 SNPs in the primary study and with 126 SNPs followed up

Row no.	Chr.	Position	p1	p2	$I_{00} = 0$	$I_{00} = 0.5$	$I_{00} = 0.8$	p_meta
1	1	67,417,979	3.19e-34	1.50e-36	4.05e-28	2.03e-28	8.11e-29	2.15e-68
2	1	67,414,547	5.05e-36	3.10e-29	3.91e-27	3.91e-27	3.91e-27	3.33e-63*
3	1	67,387,537	1.35e-24	5.62e-17	4.72e-15	4.72e-15	4.72e-15	1.82e-39
4	2	233,962,410	5.66e-21	7.67e-14	4.83e-12	4.83e-12	4.83e-12	1.18e-32*
5	5	40,428,485	2.51e-22	2.79e-08	1.34e-06	1.14e-06	1.14e-06	3.09e-27*
6	5	40,437,266	2.26e-22	3.18e-08	1.34e-06	1.14e-06	1.14e-06	3.41e-27
7	2	233,965,368	1.28e-21	3.66e-05	5.76e-04	5.76e-04	5.76e-04	4.61e-25
8	10	64,108,492	9.51e-12	1.61e-10	1.73e-06	1.14e-06	4.84e-07	2.23e-20*
9	5	131,798,704	2.29e-09	3.52e-11	2.08e-04	1.04e-04	4.16e-05	1.16e-18*
10	18	12,769,947	5.95e-12	2.41e-07	7.20e-06	6.48e-06	6.48e-06	2.55e-17*
11	10	101,281,583	8.53e-11	1.69e-07	1.05e-05	6.48e-06	5.32e-06	1.53e-16*
12	5	150,239,060	3.18e-11	2.57e-07	7.20e-06	6.48e-06	6.48e-06	1.70e-16*
13	10	101,282,445	9.09e-11	3.10e-07	1.05e-05	7.10e-06	7.10e-06	3.05e-16
14	18	12,799,340	3.27e-11	1.23e-06	2.38e-05	2.38e-05	2.38e-05	7.05e-16
15	5	150,203,580	4.09e-11	7.47e-07	1.57e-05	1.57e-05	1.57e-05	7.33e-16
16	13	43,355,925	8.04e-08	1.33e-07	5.68e-03	2.84e-03	1.21e-03	1.04e-13*
17	5	158,747,111	4.40e-09	3.66e-06	3.73e-04	1.86e-04	7.46e-05	1.93e-13*
18	6	167,408,399	1.65e-07	3.26e-07	8.74e-03	4.57e-03	1.91e-03	5.22e-13*
19	3	49,696,536	1.08e-07	5.64e-07	6.54e-03	3.27e-03	1.38e-03	5.76e-13*
20	17	37,767,727	2.97e-06	9.15e-08	8.58e-02	4.60e-02	2.07e-02	3.41e-12*
21	3	49,676,987	9.47e-08	2.24e-06	6.02e-03	3.01e-03	1.27e-03	3.55e-12
22	1	197,667,523	3.41e-07	2.34e-06	1.44e-02	7.50e-03	3.36e-03	7.17e-12*
23	12	39,104,262	8.95e-08	6.55e-05	5.99e-03	3.00e-03	1.27e-03	6.36e-11
24	6	106,541,962	1.85e-06	7.70e-06	6.03e-02	3.23e-02	1.42e-02	1.22e-10*
25	9	114,645,994	1.96e-07	6.58e-05	9.46e-03	4.93e-03	2.18e-03	1.30e-10*
26	12	38,888,207	6.64e-08	1.65e-04	4.96e-03	2.49e-03	1.91e-03	1.54e-10*
27	6	20,836,710	1.26e-07	2.78e-04	7.28e-03	3.65e-03	2.92e-03	4.48e-10*
28	11	75,978,964	7.16e-08	7.32e-04	8.02e-03	6.83e-03	6.36e-03	6.60e-10*
29	21	44,439,989	5.41e-06	1.59e-05	1.32e-01	7.27e-02	3.18e-02	7.04e-10*
30	1	157,665,119	1.75e-07	4.81e-04	8.90e-03	4.93e-03	4.33e-03	7.30e-10*
31	1	169,593,891	2.01e-07	3.21e-04	9.46e-03	4.93e-03	3.24e-03	7.66e-10*
32	1	197,691,964	9.69e-07	1.00e-04	3.52e-02	1.94e-02	8.07e-03	8.10e-10
33	10	35,327,656	4.24e-06	2.53e-05	1.10e-01	6.03e-02	2.64e-02	8.93e-10*
34	19	1,074,378	5.80e-09	3.47e-03	2.82e-02	2.57e-02	2.19e-02	1.06e-09
35	19	1,075,031	6.48e-09	2.10e-02	1.10e-01	9.80e-02	8.97e-02	1.18e-09
36	20	61,798,026	7.60e-07	1.38e-04	2.93e-02	1.57e-02	6.52e-03	1.30e-09
37	7	50,081,722	1.58e-05	9.41e-06	2.73e-01	1.67e-01	8.20e-02	1.39e-09
38	6	167,405,736	1.65e-07	1.21e-03	1.09e-02	1.02e-02	9.24e-03	1.58e-09
39	9	4,971,602	3.40e-07	4.30e-04	1.44e-02	7.50e-03	4.01e-03	1.73e-09*
40	6	32,789,255	1.53e-08	3.82e-03	2.93e-02	2.75e-02	2.35e-02	2.17e-09
41	8	126,609,233	2.45e-06	1.09e-04	7.41e-02	3.87e-02	1.74e-02	2.25e-09*
42	7	50,046,933	2.46e-05	1.10e-05	3.68e-01	2.36e-01	1.24e-01	2.30e-09*
43	17	35,294,289	1.06e-06	2.92e-04	3.74e-02	2.06e-02	8.57e-03	2.50e-09*
44	6	32,484,449	7.23e-09	6.02e-03	4.10e-02	3.79e-02	3.23e-02	2.60e-09
45	8	126,603,853	1.90e-06	1.82e-04	6.04e-02	3.23e-02	1.42e-02	2.78e-09
46	9	114,648,320	1.31e-07	4.22e-03	3.13e-02	2.95e-02	2.53e-02	3.67e-09
47	21	15,727,091	1.03e-05	4.58e-05	2.02e-01	1.16e-01	5.37e-02	3.70e-09*
48	1	114,015,850	7.75e-06	8.25e-05	1.67e-01	9.75e-02	4.28e-02	4.95e-09
49	1	114,089,610	9.05e-06	1.01e-04	1.89e-01	1.10e-01	4.85e-02	7.30e-09*
50	10	35,589,263	6.05e-06	1.76e-04	1.40e-01	8.00e-02	3.42e-02	8.04e-09
51	21	44,436,378	5.21e-06	3.61e-04	1.30e-01	7.14e-02	3.16e-02	1.43e-08
52	21	15,734,423	1.00e-05	4.44e-04	2.02e-01	1.16e-01	5.31e-02	3.36e-08
53	3	49,499,240	2.42e-08	1.94e-01	5.28e-01	5.28e-01	5.28e-01	3.56e-08
54	9	4,978,761	1.96e-06	1.62e-03	6.08e-02	3.25e-02	1.42e-02	4.34e-08
55	2	61,129,193	3.07e-06	2.80e-03	8.67e-02	4.64e-02	2.08e-02	6.36e-08
56	1	169,594,596	1.90e-07	2.60e-02	1.30e-01	1.16e-01	1.09e-01	9.01e-08
57	3	49,425,868	2.84e-08	1.07e-01	3.28e-01	3.16e-01	3.16e-01	1.20e-07
58	13	43,497,789	6.90e-07	8.82e-03	5.85e-02	5.05e-02	4.36e-02	1.44e-07
59	2	61,098,480	3.82e-06	5.65e-03	1.03e-01	5.54e-02	3.16e-02	1.57e-07
60	6	20,797,924	1.83e-07	2.88e-02	1.34e-01	1.19e-01	1.17e-01	1.64e-07

Table S2. Cont.

Row no.	Chr.	Position	p1	p2	$I_{00} = 0$	$I_{00} = 0.5$	$I_{00} = 0.8$	p_meta
61	6	5,096,246	3.54e-07	1.92e-02	1.03e-01	9.49e-02	8.34e-02	3.48e-07
62	1	157,691,986	2.98e-07	2.77e-02	1.32e-01	1.16e-01	1.14e-01	3.82e-07
63	17	29,611,838	2.01e-06	1.35e-02	7.91e-02	7.14e-02	6.19e-02	5.34e-07
64	17	37,824,128	7.42e-06	7.40e-03	1.65e-01	9.50e-02	4.17e-02	7.10e-07
65	19	18,300,383	5.43e-08	5.26e-02	2.02e-01	1.92e-01	1.84e-01	7.54e-07
66	2	27,652,888	3.62e-05	3.81e-03	5.06e-01	3.16e-01	1.75e-01	1.15e-06
67	6	3,378,317	1.04e-06	3.91e-02	1.67e-01	1.54e-01	1.49e-01	1.37e-06
68	2	102,521,887	1.02e-05	1.60e-02	2.02e-01	1.16e-01	7.20e-02	1.45e-06
69	2	27,642,591	3.44e-05	1.08e-02	4.86e-01	3.14e-01	1.70e-01	2.30e-06
70	2	230,934,834	7.59e-06	5.44e-02	2.02e-01	1.93e-01	1.85e-01	2.48e-06
71	20	61,820,069	2.04e-07	3.30e-01	7.58e-01	7.58e-01	7.58e-01	2.66e-06
72	6	3,379,241	1.15e-06	5.82e-02	2.13e-01	2.04e-01	1.96e-01	2.83e-06
73	10	75,302,766	1.23e-05	3.14e-02	2.23e-01	1.32e-01	1.24e-01	3.03e-06
74	1	7,840,274	1.47e-06	5.41e-02	2.02e-01	1.93e-01	1.85e-01	3.63e-06
75	6	149,618,772	3.64e-06	4.40e-02	1.85e-01	1.67e-01	1.64e-01	4.39e-06
76	6	21,578,398	4.97e-06	6.78e-02	2.41e-01	2.34e-01	2.25e-01	5.02e-06
77	22	20,264,229	1.25e-06	3.25e-01	7.58e-01	7.58e-01	7.58e-01	6.26e-06
78	11	63,906,946	4.74e-06	2.45e-01	6.30e-01	6.30e-01	6.30e-01	7.44e-06
79	4	187,576,360	1.35e-06	8.65e-02	2.87e-01	2.83e-01	2.76e-01	7.81e-06
80	2	230,916,728	8.93e-06	8.43e-02	2.83e-01	2.80e-01	2.72e-01	9.04e-06
81	17	29,849,794	1.25e-05	9.61e-02	3.10e-01	3.07e-01	2.99e-01	1.01e-05
82	2	102,529,086	1.08e-05	4.93e-02	2.02e-01	1.83e-01	1.75e-01	1.11e-05
83	20	57,351,084	1.73e-06	1.01e-01	3.22e-01	3.14e-01	3.10e-01	1.18e-05
84	4	187,585,769	1.34e-06	1.07e-01	3.28e-01	3.16e-01	3.16e-01	1.33e-05
85	16	84,545,499	4.74e-06	2.26e-01	5.87e-01	5.87e-01	5.87e-01	1.40e-05
86	18	17,927,329	1.59e-05	4.43e-02	2.73e-01	1.67e-01	1.64e-01	1.44e-05
87	18	54,054,001	5.56e-06	2.07e-01	5.55e-01	5.55e-01	5.55e-01	1.97e-05
88	14	75,071,147	4.71e-06	1.52e-01	4.35e-01	4.26e-01	4.26e-01	2.25e-05
89	5	37,949,301	1.74e-06	2.73e-01	6.68e-01	6.68e-01	6.68e-01	2.41e-05
90	10	75,324,937	1.12e-05	1.04e-01	3.28e-01	3.16e-01	3.16e-01	3.32e-05
91	6	21,565,929	1.09e-05	1.23e-01	3.68e-01	3.56e-01	3.56e-01	3.40e-05
92	11	63,967,228	1.60e-05	8.82e-02	2.89e-01	2.85e-01	2.78e-01	3.45e-05
93	12	58,059,725	2.84e-05	1.49e-01	4.32e-01	4.22e-01	4.22e-01	3.97e-05
94	22	20,281,207	8.65e-07	4.93e-01	1.00e+00	1.00e+00	1.00e+00	4.55e-05
95	4	106,463,957	6.25e-06	2.71e-01	6.68e-01	6.68e-01	6.68e-01	5.03e-05
96	1	222,692,358	2.73e-06	3.93e-01	8.46e-01	8.46e-01	8.46e-01	5.08e-05
97	4	7,649,390	3.24e-06	3.52e-01	7.99e-01	7.99e-01	7.99e-01	5.27e-05
98	17	35,315,722	3.41e-06	4.19e-01	8.95e-01	8.95e-01	8.95e-01	5.45e-05
99	3	13,3674,827	6.84e-06	1.61e-01	4.56e-01	4.46e-01	4.46e-01	6.21e-05
100	1	7,766,478	1.45e-05	2.11e-01	5.60e-01	5.60e-01	5.60e-01	6.82e-05
101	8	83,235,127	1.32e-05	2.23e-01	5.85e-01	5.85e-01	5.85e-01	1.28e-04
102	21	39,215,894	8.73e-06	2.63e-01	6.63e-01	6.63e-01	6.63e-01	1.65e-04
103	10	122,495,603	2.08e-05	3.63e-01	8.10e-01	8.10e-01	8.10e-01	1.98e-04
104	14	75,056,332	1.28e-05	3.31e-01	7.58e-01	7.58e-01	7.58e-01	2.22e-04
105	13	80,961,793	1.61e-07	3.72e-01	8.22e-01	8.22e-01	8.22e-01	2.23e-04
106	18	75,866,208	1.38e-06	2.56e-01	6.52e-01	6.52e-01	6.52e-01	2.80e-04
107	12	13,070,503	8.89e-06	4.35e-01	9.18e-01	9.18e-01	9.18e-01	3.27e-04
108	10	132,842,492	2.65e-05	4.41e-01	9.18e-01	9.18e-01	9.18e-01	3.88e-04
109	5	37,948,752	1.06e-05	4.41e-01	9.18e-01	9.18e-01	9.18e-01	4.78e-04
110	13	80,973,593	2.64e-07	3.29e-02	1.48e-01	1.32e-01	1.28e-01	5.54e-04
111	12	13,046,606	4.05e-05	4.55e-01	9.40e-01	9.40e-01	9.40e-01	7.51e-04
112	10	1,453,158	7.72e-06	2.90e-01	6.96e-01	6.96e-01	6.96e-01	7.56e-04
113	1	181,883,035	1.04e-05	3.88e-01	8.43e-01	8.43e-01	8.43e-01	9.32e-04
114	18	59,311,578	1.01e-05	4.98e-01	1.00e+00	1.00e+00	1.00e+00	9.48e-04
115	7	130,385,443	1.24e-05	3.81e-01	8.35e-01	8.35e-01	8.35e-01	9.64e-04
116	18	55,030,807	1.75e-05	3.04e-01	7.23e-01	7.23e-01	7.23e-01	1.06e-03
117	19	50,999,246	1.95e-05	4.60e-01	9.42e-01	9.42e-01	9.42e-01	1.32e-03
118	15	72,660,732	7.44e-06	2.73e-01	6.68e-01	6.68e-01	6.68e-01	1.33e-03
119	18	55,028,896	8.34e-06	3.56e-01	8.01e-01	8.01e-01	8.01e-01	1.80e-03
120	16	84,542,932	3.44e-04	2.78e-01	1.00e+00	1.00e+00	1.00e+00	2.39e-03
121	8	107,779,719	2.92e-05	3.14e-01	7.40e-01	7.40e-01	7.40e-01	2.78e-03
122	12	58,052,436	1.14e-05	2.89e-01	6.96e-01	6.96e-01	6.96e-01	3.45e-03

Table S2. Cont.

Row no.	Chr.	Position	p1	p2	$l_{00}=0$	$l_{00}=0.5$	$l_{00}=0.8$	p_meta
123	18	54,054,701	9.40e-06	1.95e-01	5.28e-01	5.28e-01	5.28e-01	5.28e-03
124	18	75,865,061	2.11e-06	1.08e-01	3.28e-01	3.16e-01	3.16e-01	6.92e-03
125	15	72,685,472	5.81e-06	7.71e-02	2.70e-01	2.59e-01	2.52e-01	1.27e-02
126	8	107,743,073	2.59e-05	1.43e-01	4.19e-01	4.09e-01	4.09e-01	1.36e-02

The last column marks the 30 SNPs that were highlighted as "convincingly (Bonferroni $P<0.05$) replicated CD risk loci," based on the follow-up study P values, in table 2 of the main text of ref. 1.

1. Barrett JC, et al.; NIDDK IBD Genetics Consortium; Belgian-French IBD Consortium; Wellcome Trust Case Control Consortium (2008) Genome-wide association defines more than 30 distinct susceptibility loci for Crohn's disease. *Nat Genet* 40(8):955–962.

Table S3. For 4,500 cases and 4,500 referents in both studies, the average number of associated and disease SNPs discovered (SE) and the average FDP (SE), for different values of l_{00}

	FDR r values ≤ 0.05			BH procedure on maximum P values at level $0.05/(1-l_{00})$		
	No. replicated findings			No. replicated findings		
l_{00}	Associated SNPs (SE)	Disease SNPs (SE)	FDP (SE)	Associated SNPs (SE)	Disease SNPs (SE)	FDP (SE)
0	41.5 (5.3)	8.3 (0.5)	0.011 (0.011)	29.2 (3.2)	7.4 (0.4)	0.000 (0.000)
0.8	55.4 (5.3)	9.3 (0.4)	0.013 (0.013)	39.0 (3.5)	8.5 (0.5)	0.000 (0.000)
0.9	58.4 (4.9)	9.6 (0.3)	0.014 (0.014)	42.8 (3.3)	9.1 (0.4)	0.000 (0.000)
0.95	59.9 (4.5)	9.7 (0.3)	0.015 (0.014)	46.1 (3.5)	9.3 (0.3)	0.000 (0.000)
0.99	60.0 (4.6)	9.7 (0.3)	0.015 (0.014)	50.8 (3.9)	9.4 (0.3)	0.000 (0.000)

The actual value of f_{00} was above 0.999. Results are given for our proposal with $c_2=0.05$ and $q=0.05$ in columns 2–4 and for the BH procedure on maximum P values at level $0.05/(1-l_{00})$ in columns 5–7. SNPs were selected for follow-up only if they were discovered by the BH procedure at level $c_1(0.05)\times 0.05$.

Table S4. The estimated average power of our proposal with parameters $(l_{00},c_2,0.05)$, where c_2 is the optimal choice among the values in $\{0.05,0.1,\ldots,0.95\}$ for $l_{00}=0.5$ (column 2), $l_{00}=0.8$ (column 4), $l_{00}=0.9$ (column 6), and $l_{00}=0$ (column 8), and the optimal value of c_2 is given in the row below; $c_2=0.5$, for $l_{00}\in\{0.5,0.8,0.9,0\}$ (columns 3, 5, 7, 9) in a configuration $f_{00}=0.9$, $f_{01}=f_{10}=0.025$, $f_{11}=0.05$

(π_1,π_2)	Optimal for $l_{00}=0.5$	$l_{00}=0.5$, $c_2=0.5$	Optimal for $l_{00}=0.8$	$l_{00}=0.8$, $c_2=0.5$	Optimal for $l_{00}=0.9$	$l_{00}=0.9$, $c_2=0.5$	Optimal for $l_{00}=0$	$l_{00}=0$, $c_2=0.5$
(0.1, 0.8)	0.2980	0.2515	0.4486	0.3858	0.5681	0.4921	0.2009	0.1686
	$c_2=0.2$		$c_2=0.2$		$c_2=0.15$		$c_2=0.2$	
(0.1, 0.5)	0.1749	0.1666	0.2881	0.2750	0.3837	0.3669	0.1105	0.1044
	$c_2=0.35$		$c_2=0.35$		$c_2=0.35$		$c_2=0.35$	
(0.1, 0.2)	0.0425	0.0425	0.0786	0.0781	0.1152	0.1152	0.0261	0.0258
	$c_2=0.5$		$c_2=0.55$		$c_2=0.5$		$c_2=0.55$	

The number of hypotheses examined in the primary study is 1,000. The signal-to-noise ratios for the primary study and the follow-up study, μ_1/σ_1 and μ_2/σ_2, respectively, are taken according to the requirement that the power of the Bonferroni procedure at level 0.05 in the primary study is π_1 and that in the follow-up study is π_2 (given in the first column). The SEs were of the order of 10^{-3} or 10^{-4} for all of the estimates.

Table S5. Replicability analysis for FWER control for the study of ref. 1 on GWAS of TPP

Chr.	Position	p1	p2	p_meta	r value
17	65,837,933	6.28e-10	1.49e-05	7.69e-14	0.00012
17	65,818,432	1.39e-09	7.36e-05	1.59e-12	0.00059
17	65,799,923	2.27e-09	7.25e-05	1.09e-12	0.00058
17	65,778,654	1.84e-08	0.000116	1.6e-11	0.00360

The number of SNPs in the primary study was 486,782, and 4 SNPs were followed up. The lower bound for f_{00} was $l_{00}=0.8$ for the r-value computation.

1. Cheung CL, et al. (2012) Genome-wide association study identifies a susceptibility locus for thyrotoxic periodic paralysis at 17q24.3. *Nat Genet* 44(9):1026–1029.