HARLOT plc: an amalgamation of the world's two oldest professions

David L Sackett, Andrew D Oxman on behalf of HARLOT plc

Tired of being good but poor, the authors have amalgamated the world's two oldest professions in a new niche company, HARLOT plc, specialising in How to Achieve positive Results without actually Lying to Overcome the Truth

Trout Research and Education Center, Markdale, ON, Canada N0C 1H0
David L Sackett
director

Department of Health Services Research, Norwegian Directorate for Health and Social Welfare, Oslo 0031, Norway
Andrew D Oxman
director

Correspondence to:
D L Sackett
sackett@bmts.com

BMJ 2003;327:1442–5

We've been good. DLS has prohibited sponsors' stockholders, much less employees, from seats on his data safety and monitoring boards and has enforced the banning of pharmaceutical reps from the medical wards at McMaster University. ADO has exposed problems with experts and has promulgated rigorous reviews of research to inform decisions about health care. In sum, we have established impeccable reputations for protecting the validity of randomised trials and systematic reviews, and for exposing lapses in methods, validity, therapeutic claims, and professional conduct.

We've also been poor. DLS drives a clapped out pick-up truck, and his rowing boat leaks. ADO wears worn out blue jeans and hasn't had a new pair of shoes for 10 years.

It has finally dawned on us that being good and being poor are causally related: being good doesn't pay. Accordingly, we have decided that it's time for us to find out whether being bad pays better. We're combining the world's oldest and second oldest professions, cashing in on our reputations, and distributing this confidential prospectus for our new company, HARLOT plc.

HARLOT services

HARLOT plc will provide a comprehensive package of services to discriminating trial sponsors who don't want to risk the acceptance and application of their products and policies amid the uncertainties of dispassionate science. Through a series of blind, wholly owned subsidiaries, we can guarantee positive results for the manufacturers of dodgy drugs and devices who are seeking to increase their market shares, for health professional guilds who want to increase the demand for their unnecessary diagnostic and therapeutic services, and for local and national health departments who are seeking to implement irrational and self serving health policies. The tables summarise our services: table 1 shows the ways we can cook the data in an individual randomised controlled trial; table 2 displays an array of aftercare services for keeping the truth from interfering with sales and implementation; and table 3 lists the services that we offer to our non-elite (that is, shallow pockets) customers. Limited space permits the individual description of only a few of our services. References for all of them can be obtained by subpoena from our legal department.

Defining medicine

Medicine is politics
"Politics is nothing more than medicine on a grand scale."
Rudolf Virchow, 1848[1]

Politics is money
"[Politics is] the conduct of public affairs for private advantage."
Ambrose Bierce, 1911[2]

Ergo, medicine is money
"Pliny says, in so many words, that the cerates and cataplasms, plasters, collyria, and antidotes, so abundant in his time, as in more recent days, were mere tricks to make money."
Oliver Wendell Holmes, 1860[3]

It's the money, dummy

This prospectus is addressed primarily to drug companies, with good reason. One of them now has 10 products with more than $1bn in sales each, and some 165 million people worldwide take its medicines. Its market capitalisation recently passed that of Microsoft Corporation and is second only to that of General Electric. In 2000, the top nine drug companies in the United States had over $155bn in revenue. The top executives in these companies were paid between $3m and $17m plus stock options valued between $11m and $73m. Drug companies have the cake, and they are eating it too. Put simply, we want a piece of that cake.

If you are not a member of this elite club, you may want to skip to table 3, where we list our bargain basement services. Once we have paid off our mortgages, we will consider pro bono work. Meanwhile, if you would like our help, please make sure to send us your credit card number and bank balance.

E-Zee-Me-Too Protocols

Our E-Zee-Me-Too Protocol team provides "stepped care" service for dodgy "me too" drugs or devices and useless screening tests. With our protocol strategies, such as those listed in table 1, as long as your "me too" drug isn't a lot worse than a sip of triple distilled water, we can guarantee you a positive trial. As you can see from the final column, the cost of this service depends on how many steps we must climb to generate a foolproof protocol.

Ethics-R-Us

If you purchase our "seamless service" option, your completed protocol will be immediately presented to one of our Ethics-R-Us outlets (situated in all major shopping malls), where, for a fee, we can guarantee its approval within 45 minutes. As a Christmas special, we'll toss in our pre-approved, generic consent forms in which study patients waive their right to receive any information whatsoever about the risks or side effects of the study treatments. Furthermore, in light of all the fuss about paying exorbitant bounties and bonuses to

Table 1 Stepped care for "me too" drugs or devices and useless screening tests

Step	Bias to be exploited	Strategies for applying this bias (while hiding your intentions and actions)	Payment
E—Zee-me-Too Protocols			
1	Selective, non-systematic reviews	Cite just those reports that support your product, proposal, or policy (and slag all your competitors)	£
2	Substituting placebos for established effective treatment	Invoke fallacious "placebo effects" and "assay-sensitivity" arguments in order to avoid head to head comparisons	$
3	Unconcealed allocation to ensure better prognoses in "experimental" patients	Provide updatable wall posters for displaying the group to which the next patient will be allocated, see-through allocation envelope systems, etc	€
4	"Mini-max" manipulation of your competitor's product	Give insufficient ("mini") doses of your competitor's product, accompanied by scary ("max") warnings about its (but not yours) side effects and toxicity	Ocean-front property in New Jersey
5	Incorporating irrelevant surrogate and composite end points	Concoct an invalid inflation of event rates (especially among control patients)	Lapis lazuli
6	"Shifting the goal posts" for "superiority" and "non-inferiority"	Require trivially better outcomes for "superiority" but massively worse outcomes for "inferiority"	Diamonds
Ethics-R-Us			
7	Uninformed consent	Create consent forms in which study patients sign a "waiver of right to receive information" about the nature of, risks of, or alternatives to your product	¥
RATs (Research Administration Teams)			
8	Adding efficacious co-interventions to (just) your product	Give (just) the experimental patients additional treatments of known efficacy, find and treat their comorbidity, etc	Ocean-front property in California
9	Unblinded outcome assessment	Provide encouragement of (only) experimental patients' functional capacity performance or symptom scores, and ignore their minor strokes, heart failure, and side effects	Insider trading before publication
10	Repeated interim analyses	Scan repeated early analyses for spurious but favourable trends that justify terminating the trial in your favour	Rubies
FPSU (Find the Pony Statistical Unit)			
11	Munchausen's statistical grid (looking for the pony)	Execute sub^0-group analysis where n=keep going until you find a statistically significant effect in your favour	n×10^3 shares of stock
12	Overinterpretation of a positive trial	Report just the (impressive) relative risk reduction while suppressing the (unimpressive) absolute risk reduction and number needed to treat	0.5% of net sales
13	Overinterpretation of an indeterminate trial	Report a too small trial with a huge 95% confidence interval (that includes 0) as "negative," thereby "proving" that there is "no difference" between your product and the (better) one produced by your competitor	0.5% of gross sales

clinicians for sticking patients into trials, every Ethics-R-Us outlet provides (through our wholly owned subsidiary in Zurich) numbered bank accounts for hiding each collaborator's payments.

RATs (Research Administration Teams)

To be sure that your E-Z-Me-Too protocol is executed to your advantage, you need only hire our RATs (Research Administration Teams) to take over the conduct of your trial. Depending on the trial result you require, we will reveal randomisation codes and implement contamination, co-intervention, and biased outcome assessment to meet your every need.

Our RATs also can provide four extraordinary services. Firstly, we will establish criteria that study patients have to meet before they are "available for follow up." In brief, these criteria require that they must survive the immediate toxicity of your drug before they are included in any analyses. Secondly, we have devised a clever subversion of the "back the winner" strategy, which we call "lose the loser." Once a suitable number of patients taking your drug seem to be heading for trouble, we will move the study clinic to a new, secret (to them) location and, when they miss their next appointment, censor them from all subsequent analyses. Thirdly, we will fax you unblinded interim analyses after every event, to assist you in stopping the trial as

Table 2 Aftercare programme

Designation	Strategy	Tactic
SAFE (Say Anything For a Euro) panel of "experts"	Provide generous research grants, first class travel, luxurious accommodations, exorbitant honorariums, and gargantuan ongoing "consultant" fees to "experts" who (surprise) favour your product, screening test, or programme	Get SAFE experts to generate the guidelines, write the editorials, pick the keynote speakers, referee for the key journals, etc
SCUM (Sick Celebrities to Use in the Media)	Hire stars of stage and screen, famous athletes, and washed up politicians who will "disease monger" and tout your product or screening test	Get them on to talk shows, into gossip magazines, and into the front lines of parades on any issue
PPCT (Pay the Piper and Call the Tune)	Give generous "journalism" awards for articles that monger your disease or praise your product in the lay media	Continue to feed media new diseases and products to push
RCAF (Rabid Citizens Against Facts)	Secretly fund "patients' action" groups to attack any counter-evidence that shows your product, programme, or screening test is useless or harmful	Denounce detractors with testimonials and threats
DISARM (DIScourage Arguments with Research Money)	Disarm your critics by funding an evaluation of your new screening test or health programme	Then stop the funding, ignore the results as out of date, or abandon the test or programme for a new, equally untested one
FYP (Foundation in Your Pocket)	Build beautiful headquarters and conference centres for health foundations	Smooth the way for infiltrating SAFE experts into their leadership and programme development
MTM (Move the Ministry)	Lobby to shift responsibility for the approval of new drugs and devices from the Ministry of Health to the Ministry of Industry	Shift the objective from healthy patients to healthy national economies
GFGC (Get the Fox to Guard the Chicken house)	Purchase a pharmaceutical benefits management organisation	Control the selection and purchasing of drugs while preserving the illusion of a market
BOSS (Bureau Of Secret Surveillance)	Buy confidential information from pharmacists as to exactly who is prescribing exactly what	Tailor drug reps' visits to focus on just the prescribing habits that need to be changed to your benefit
SOW (Save/Sacrifice Our Workers)	Threaten to move your product development and manufacture to another country	Launch media and lobbying blitzes that exaggerate how many jobs will be lost if you leave (see cigarette manufacturers' ploys)
SHARKS (Striking Horror And Retreat through Killer Solicitors)	Hire all the really good lawyers	Use them to threaten nay-sayers, members of drug review boards, etc with frivolous but expensive libel lawsuits. Suppress negative health technology assessment reports until you've met your sales targets

Table 3 Non-elite services

Customers	Services	What we can do for you
Governments, health insurance companies, and health maintenance organisations	OUR (Opportunistic Use of Research) support	We can find whatever research there is that supports your views and trash any research that is in conflict with your views. (Note: if you change your views, there will be an additional charge for this service.) We can also help you to design evaluations that will take as long as you want. In the rare event that one of our studies does not give you the answers you want, we will give you ample warning so that you can cut the study's funding and suppress its findings
Professional organisations	POMP (Professional Opportunities to Maximise Profit)	We can find whatever research there is to support aggressive use of your guild's services and trash any research that suggests that your services are not highly effective
Clinicians and hospitals who might get sued	TIT (Trials in the Interest of Treating) for clinicians and hospitals	Our package of preventive services includes our generic informed consent forms, modelled after the forms we use to get study patients to waive their right to receive information. When you are sued, we can provide you with the evidence you need to defend yourself and your staff, regardless of whether you were right or wrong, and we can trash the plaintiff's evidence
Patients and patient organisations who might want to sue	TAT (Trials for Advocating Treatments) for patients and patient organisations	If you want to sue your care giver, we can provide you with the evidence you need and trash the defendants' evidence. If your organisation wants to demand a treatment, no matter how useless it might be, we can provide you with the evidence you need to support your claims
Lawyers	EWOCs (Expert Witnesses On Call)	We can provide you with expert witnesses and the research to back their testimony, and we can attack the credibility of the other side's experts. (Note: if we are asked to provide witnesses for both sides, we guarantee results only for the side that offers us the largest fee)
Academics	SALAMI (our how to Succeed in Academic Life Advice and Mentoring Institute)	We can teach you how to pad your curriculum vitae, raise your profile, exploit your trainees, and slice your research results into a minimum of one article per enrolled patient

soon as random variation is leaning in your direction. Finally, if interim analyses just don't look good, we will show you how to change the study question and end points to rescue your useless product. Our charges for all this depend on the number of strategies we have to apply and the depth of your pockets.

FPSU (Find the Pony Statistical Unit)

Our FPSU (Find the Pony Statistical Unit) services include back-stepwise sample size calculation software (just tell us how many patients you can get, and we'll instantly tell you the relative risk reduction claims you'll need to fabricate to justify your trial). We can provide unblinded analyses after every event, so that you will learn of impressive but irrelevant trends in the data long before your Data Safety and Monitoring Board does.

Our speciality is data dependent subgroup analysis through the use of the "Munchausen statistical grid." This strategy exploits the happy fact that the number of potential ponies in a muck of trial data is 2^n where n = the number of dichotomised subgroups. Even if your intervention is totally worthless, we'll keep doubling the number of subgroups until we can emerge from the muck with at least one pony subgroup in which it seems to work. What is more, we'll then turn that phoney result over to our BS (Biology and Sociology) brain trust, which will supply a minimum of three highly plausible theories to support our otherwise patently unbelievable subgroup result. We reconcile statistical significance in the face of multiple analyses by simply ignoring this meddlesome issue.

Ghost Writers in the Sky

Once your data are sufficiently cooked, it is time for us to help you write them up. Our "Ghost Writers in the Sky" have perfected the "Johnny Mercer strategy" for reporting indeterminate trials:

1. We "accentuate the positive" by reporting only favourable subgroup analyses. Moreover, you don't have to settle for just one paper in just one journal. For no extra charge, we will randomise the sentences in the original article and submit the suitably camouflaged duplicate publication to a second, unsuspecting journal. Additional publications (our current record is 42) are available for correspondingly higher fees, but we warn you at the outset that these fees will be multiplied by a DVF (déjà vu factor).

2. We "eliminate the negative" by omitting or burying all unfavourable results where nobody can ever find and report them. After all, what they (patients, clinicians, regulators, and the public) don't know can't hurt you. We have a contact in the Wieliczka salt mine who can guarantee burial of negative results 200 metres underground.

3. And we definitely "don't mess with Mr In-Between." We stay out of the DMZ (disappointing, minimally important zone) by suppressing equivocal results and bothersome confidence intervals. We report only relative risk reductions when absolute risk reductions and numbers needed to treat (NNTs) reveal that your drug really isn't worth a bean.

Aftercare

See table 2 for our aftercare programme. To maintain the positive spin on indeterminate results, we have created three useful pressure groups whose financial ties to HARLOT plc are carefully concealed.

Our SAFE (Say Anything For a Euro) panel of experts is ready, at the drop of a banknote, to appear on television, chummy up to reporters, or write favourable commentaries in leading clinical journals. When prudish editorial policies restrict their honoraria to $10 000 a year, we can arrange lifelong annuities, interest-free loans, or tuition-free Oxbridge or Ivy League education for their offspring. Our SAFE panel will be especially useful as members of committees writing guidelines for professional societies, where they will ensure recommendations that will please you and your stockholders.

Our stable of SCUM (Sick Celebrities to Use in the Media) will appear on talk shows and, apparently by chance, describe their life threatening illnesses and how your drug saved them. Coupled with saturation campaigns of direct to consumer advertisements, we can fill doctors' offices with patients who demand your drug by name or colour.

If the media unearth some authoritative upstart who argues convincingly against the value of your

Summary points

We, the authors, are tired of being good but poor, and have decided to sacrifice the former to overcome the latter

We are therefore amalgamating the world's two oldest professions in a new company, HARLOT plc, that provides "cradle to (the patient's) grave" services that will maximise the profits of manufacturers of dodgy drugs and devices

Cashing in on our years of clinical research experience and as yet untarnished reputations, we can protect your worthless product as we shepherd it through the minefields sewn by objective scientists, fussy ethics committees, conscientious journal editors, writers of evidence based guidelines, and licensing bodies

As we work together to create shining examples of the seduction of science through HARLOTry, your gloss will be our gain

drug, we can activate our third pressure group, the RCAF (Rabid Citizens Against Facts). They can swamp switchboards and letters columns with testimonials favouring your drug, discredit naysayers with accusations of ulterior motives and unnatural practices, and, if all else fails, send anonymous death threats.

Unfortunately, however, there is always the danger that someone may reveal that the data simply do not support your claims. This situation calls for our most extreme (and costly) service, the SHARKS (Striking Horror And Retreat through Killer Solicitors) squad. They are masters at sending terrifying letters, threatening damage suits should the recipient continue to slander your drug's good (if undeserved) name (and cautioning against showing the letter to any professional body or the media). If all else fails, our SHARKS squad will obtain an injunction prohibiting the release and activation of offending recommendations or other damaging reports. The objective here is not to win the case, but simply to keep everybody from learning that your drug doesn't possess any real advantages until you've sold tonnes of it.

Contingency agreement

If you faithfully follow our advice, your drug should sell like hot cakes. In this happy situation, we reserve the right to refund all the fees you've paid us in return for 0.5% of gross sales in perpetuity. If we reach this mutually advantageous agreement, we'll throw in, at no extra charge, a safety net for your lead authors, should they be caught and exposed. Given our worldwide academic contacts, and for as long as our diminishing reputations survive, we should have no trouble getting them professorships at prestigious North American universities.

SALAMI (our how to Succeed in Academic Life Advice and Mentoring Institute) and other services

Although this prospectus focuses on our primary programme of services for firms with "me too" drugs and devices or useless screening tests, we also offer parallel services to others. For example, lazy but ambitious academics can subscribe to SALAMI's services. These include how to instantly size up a roomful of research celebrities and determine which one you want to be seen talking with (see figure), and how to get a paper into the Christmas issue of the *BMJ*.

We offered Iain Chalmers stock options in HARLOT plc and co-authorship of this manuscript. He refused the latter.

Contributors and sources: For potential customers, DLS and ADO both contributed these brilliant ideas and will fight each other for the credit (and profit). For libel lawyers, Chalmers did it.

Funding: We paid for the generation of this prospectus out of our own offshore "DD" bank accounts (generated through "double dipping" by requesting reimbursement for the same trip from at least two sources).

Competing interest: DLS's competing interests are so great as to warrant an entire page on the *BMJ*'s website (http://bmj.com/cgi/content/full/324/7336/539/DC1). They also are on file at several disciplinary bodies on both sides of the Atlantic. ADO has received an exorbitant fee (almost as much as a high priced lawyer earns in an hour) from two pharmaceutical firms on two occasions for showing up. He has benefited from generous funding from two pharmaceutical firms that have supported his work and has attended conferences that have been partially supported by pharmaceutical firms. He would be thrilled to receive more money from the drug industry to support his research and that of his colleagues, and to pay off his mortgage, but is afraid that his involvement with DLS may put an end to any chances of that happening.

1 Virchow R. Die offentliche Gesundheitspflege. *Medizinische Reform* 1848;5:21-21.
2 Bierce A. *The devil's dictionary*. 1911.
3 Holmes OW. Currents and counter-currents in medical science. In: Huth E, Murray TJ, eds. *Medicine in quotations*. Philadelphia: American College of Physicians, 2000:291.

The HARLOT team together with some of our satisfied customers on the road to riches. We can fabricate the results you need and, for a small extra fee, we can fabricate the photos you need too, showing you chumming with selected stars of science and cinema. The truth is in the eye of the beholder, and we can plaster whatever you want them to see directly on their retinas