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Pediatrics 2004;114;1620-1626
DOI: 10.1542/peds.2004-0447

This information is current as of June 22, 2005

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End-of-Life After Birth: Death and Dying in a Neonatal Intensive Care Unit

Jaideep Singh, MD; John Lantos, MD; and William Meadow, MD PhD

ABSTRACT. Objective. In canonical modern bioethics, withholding and withdrawing medical interventions for dying patients are considered morally equivalent. However, electing not to administer cardiopulmonary resuscitation (CPR) struck us as easily distinguishable from withdrawing mechanical ventilation. Moreover, withdrawing mechanical ventilation from a moribund infant “feels” different from withdrawing mechanical ventilation from a hemodynamically stable child with a severe neurologic insult. Most previous descriptions of withdrawing and withholding intervention in the neonatal intensive care unit (NICU) have blurred many of these distinctions. We hypothesized that clarifying them would more accurately portray the process of end-of-life decision-making in the NICU.

Methods. We reviewed the charts of all newborn infants who had birth weight >400 g and died in our hospital in 1988, 1993, and 1998 and extracted potential ethical issues (resuscitation, withdrawal, withholding, CPR, do-not-resuscitate orders, neurologic prognosis, ethics consult) surrounding each infant’s death.

Results. Using traditional definitions, roughly half of all deaths in our NICU in 1993 and 1998 were associated with “withholding or withdrawing.” In addition, by 1998, >40% of our NICU deaths could be labeled “active withdrawal,” reflecting the extubation of infants regardless of their physiologic instability. This practice is growing over time. However, 2 important conclusions arise from our more richly elaborated descriptions of death in the NICU. First, when CPR was withheld, it most commonly occurred in the context of moribund infants who were already receiving ventilation and dopamine. Physiologically stable infants who were removed from mechanical ventilation for quality-of-life reasons accounted for only 3% of NICU deaths in 1988, 16% of NICU deaths in 1993, and 13% of NICU deaths in 1998. Moreover, virtually none of these active withdrawals took place in premature infants. Second, by 1998 infants, who died without CPR almost always had mechanical ventilation withdrawn. Finally, the median and average day of death for 100 nonsurvivors who received full intervention did not differ significantly from the 78 nonsurvivors for whom intervention was withheld.

Conclusions. In our unit, a greater and greater percentage of doomed infants die without ever receiving chest compressions or epinephrine boluses. Rather, we have adopted a nuanced approach to withdrawing/writholding NICU intervention, providing what we hope is a humane approach to end-of-life decisions for doomed NICU infants. We suggest that ethical descriptions that reflect these nuances, distinguishing between withholding and withdrawing interventions from physiologically moribund infants or physiologically stable infants with morbid neurologic prognoses, provide a more accurate reflection of the circumstances of dying in the NICU.

ABBREVIATIONS. NICU, neonatal intensive care unit; CPR, cardiopulmonary resuscitation; DR, delivery room; DNR, do not resuscitate.

Thirty years ago, Duff and Campbell described their experience in making end-of-life decisions in neonates. Their explicit purpose was to shed light on this presumably widespread, although underreported, behavior. Perhaps unexpected, a large segment of the general public was dismayed. Publications and legislation followed, for the most part disparaging doctors for “playing God in the nursery.”

Ethical complexities in neonatology have always been propelled by 2 distinct forces. Advances in technology and pharmacology have placed larger and larger numbers of newborns within the scope of neonatal intensive care unit (NICU) care, and more and more controversy has evolved over whether we are doing the right thing. The vast majority of infants in the NICU are admitted for a “trial of therapy,” tacitly or explicitly agreed on by their doctors and parents. If the infants do well, then it is all good. If they do poorly, then how do they die?

In canonical modern bioethics, withholding and withdrawing medical interventions for dying patients are considered morally equivalent, yet in the context of the NICU, electing not to administer epinephrine and chest compressions to a progressively hypotensive, bradycardic infant who is already receiving dopamine and mechanical ventilation (nominal, an instance of withholding cardiopulmonary resuscitation [CPR]) struck us (and, in our experience, strikes most parents as well) as easily distinguishable from withdrawing the endotracheal tube from the same child. Moreover, we could envision ethically important distinctions between withdrawing mechanical ventilation from a moribund premature infant (on the grounds that the intervention would not stave off imminent death; ie, “futility”)
compared with withdrawing mechanical ventilation from a hemodynamically stable child of similar size with a severe neurologic insult (on the grounds that the benefits of continued intervention and ultimate survival would not be worth the burden of the eventual life to be lived, ie, “quality of life”).

Most previous descriptions of withdrawing and withholding intervention in the NICU have blurred many of these distinctions. We hypothesized that clarifying them would more accurately portray the process of end-of-life decision making in the NICU. Moreover, we were interested in determining how advances in neonatology in the past decade (surfactant, antenatal steroids, extracorporeal membrane oxygenation, and antenatal ultrasound screening) has had an impact on the process of dying in the NICU. We report here our experience with deaths in our NICU, using both traditional bioethical definitions of withdrawing and withholding and our own, more richly elaborated, categories.

METHODS

Demographics
We reviewed the charts of all newborn infants who had birth weight >400 g and died in our hospital in 1988, 1993, and 1998. We chose 400 g as an arbitrary birth weight cutoff on the basis of the observation that in our institution, we have not had any survivor with birth weight <400 g. We determined demographics: place of death (NICU vs delivery room [DR]), birth weight, gestational age (using a combination of antenatal obstetric evaluation and physical examination), day of death, diagnoses (using both clinical and autopsy material when available), and neurologic condition (using imaging studies and neurology or neurosurgery consultations).

During the study period, the average daily census in our NICU was 50 patients, accounting for roughly 18000 NICU patient-days per year. Approximately 800 infants were admitted in each study year, three fourths of whom were inborn and one fourth of whom were transported from outlying nurseries.

In 1988, surfactant, antenatal corticosteroids, and antenatal ultrasound were not commonly used in our NICU population. In 1993, surfactant was used routinely, but antenatal steroids were still rare. By 1998, antenatal corticosteroids were routinely administered to mothers with expected premature deliveries, and antenatal level II ultrasounds were routine. Subspecialty pediatric surgery and extracorporeal membrane oxygenation were available in our NICU during each of the study years.

Assignment of Ethical Categories

Using an extensive chart review, we extracted potential ethical issues (resuscitation, withdrawal, withholding, CPR, do-not-resuscitate [DNR] orders, neurologic prognosis, and ethics consult) surrounding each infant’s death. We then categorized the child’s death in 2 ways: first, encompassing all cases of withdrawing/withholding independent of cause and, second, in more detail, distinguishing cases of physiologic futility from those of presumed quality-of-life concerns.

Definitions of Withholding and Withdrawing

For the sake of internal consistency and to facilitate generalizability to other NICUs, withholding NICU intervention was taken to be equivalent to withholding CPR. We recognize that this definition provides a lower limit to the number of cases of withholding, as there may have been more episodes of withholding (eg, not providing additional catecholamine infusions despite hypotension, not making additional ventilator changes despite hypoxia or hypercarbia). Nonetheless, all cases in which an infant died without CPR represent cases of withholding a medical intervention, and in these more subtle cases, CPR was also likely withheld.

For similar reasons, withdrawing intervention was taken to be equivalent to withdrawing mechanical ventilation. Again, we recognize that this definition provides only a lower bound to the number of instances of withdrawing.

Statistical Analyses

Comparisons of variables across 3 study years were performed by analysis of variance (for continuous variables) and χ² contingency tables (for categorical variables). Statistical significance was accepted at the level of P < .05. All retrospective chart reviews were approved by the institutional review board at the University of Chicago.

RESULTS

Demographics of Nonsurvivors

A total of 178 infants with birth weight >400 g died in our hospital during the 3 study years. Twenty-three were deemed not viable in the DR and died there. Four of these children had congenital anomalies incompatible with life, diagnosed prenatally. Nineteen were considered not viable because of extreme prematurity and were not resuscitated. A total of 155 children were admitted to the NICU and subsequently died there.

Table 1 presents the causes of death for the 178 nonsurvivors during the 3 study years divided into 3 diagnostic categories: prematurity, congenital anomalies incompatible with life, and asphyxia/sepsis in term infants. Several points are apparent. Despite a stable birth population (~3000 births per year), fewer infants died in 1998 compared with 1993 or 1988. The reduction in NICU mortality was completely accounted for by the improved survival of premature infants. There was also an increase in the percentage of deaths accounted for by infants with congenital anomalies in 1998 versus 1988. Deaths of term infants from asphyxia/sepsis were rare (<10% of all deaths in any study year) and displayed no trend during the study period.

Withholding Intervention: DNR Orders and Withholding CPR for Dying Infants

Figure 1 displays the frequency of all deaths associated with DNR orders for the 155 infants who died after having been admitted to the NICU. The frequency of DNR orders for infants who died in 1998 (56%) was significantly higher than the percentage of DNR orders that were written for infants who died in 1988/1993 (39% and 29%, respectively; P = .01).

What were the circumstances surrounding these DNR orders? Specifically, were the DNR orders writ-

<table>
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<th>TABLE 1. Demographics of Nonsurviving Infants</th>
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<td>Diagnoses</td>
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<td>Diagnoses</td>
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<tr>
<td>1988                                     1993    1998    Total</td>
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<tr>
<td>Extreme prematurity (% nonsurvivors)</td>
</tr>
<tr>
<td>Anomalies (% nonsurvivors)</td>
</tr>
<tr>
<td>Asphyxia/sepsis at term (% nonsurvivors)</td>
</tr>
<tr>
<td>Total no. of deaths</td>
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ten before or after an episode of CPR? Figure 2 reveals that 85% of all DNR orders that were written in 1993 and 1998 were written before any CPR was administered—significantly higher than in 1988, when only 36% of the DNR orders preceded an episode of CPR (P < .001). Viewed from another perspective, 64% of the infants who died with DNR orders in 1988 had already experienced at least 1 episode of CPR, whereas by 1998, this number had fallen to 15%.

How many infants died without ever receiving CPR, regardless of whether a DNR order was explicitly entered? Figure 3 reveals that in 1988, only 16% of infants died in the NICU without any episode of CPR, significantly less than in later years 1993 (63%) and 1998 (69%; P < .001). Did this trend to withhold resuscitation extend to the DR? No. As Fig 4 reveals, there was no significant increase in withholding DR resuscitation over the study years. In 1998, only 2 (4%) of 48 of nonsurviving infants died in the DR without an initial attempt at resuscitation.

Withdrawing Intervention: Futility Versus Quality-of-Life Considerations

Figure 5 reveals the frequency of active withdrawal of intensive intervention (defined as withdrawal of mechanical ventilation) for the 155 infants who died in the NICU. Not surprising, all of the infants for whom mechanical ventilation was withdrawn had CPR withheld. Consequently, the infants who had NICU intervention withdrawn represent a strict subset of those who had NICU intervention withheld.

As Fig 5 displays, the percentage of infants for whom NICU intervention was withdrawn rose from 10% in 1988 to 35% in 1993 and 42% in 1998 (P < .001). Consequently, using traditional categories, by 1998, 42% of our NICU deaths would be considered active withdrawal, reflecting the extubation of infants regardless of their physiologic instability. However, a more detailed description of ethically relevant categories again provides more insight into these practices.
All extubations were performed with the concurrence of both the physicians and the parents. Under what circumstances did the active withdrawal of ventilation take place? Two distinct scenarios dominated our data. One subset of infants were deteriorating hemodynamically despite maximal NICU intervention—in these cases, the futility of continued invasive treatment was apparent, and the ventilator was removed so that the mother could hold her infant in her arms without tapes and tubes while the infant died. Another subset of infants was hemodynamically stable but had devastating neurologic injury—either congenital (eg, holoprosencephaly, trisomy 13) or acquired (eg, asphyxia, severe intraventricular hemorrhage). In these infants, the ventilator was removed because both the parents and the physicians agreed that the burdens of continuing medical interventions outweighed the benefits of prolonging life.

Figure 6 reveals that ~40% of all withdrawals of mechanical ventilation occurred in hemodynamically stable infants. There was no significant change in this percentage over the study years. Recall, however, that the absolute number of active withdrawals increased significantly comparing 1988 with 1993/1998 (Figure 5). Consequently, the absolute number of active withdrawals for quality-of-life reasons increased significantly in our nursery comparing 1988 with 1993/1998 ($P < .05$).

It is interesting, as Fig 7 reveals, that the overwhelming preponderance of these instances of active withdrawal from hemodynamically stable infants occurred in term infants with congenital anomalies or asphyxia, and not in premature infants with intraventricular hemorrhage or periventricular leukomalacia. In no year did even 5% of all active withdrawals occur in extremely low birth weight infants with devastating neurologic injury.

Table 2 summarizes the data presented in Figs 5, 6, and 7. In both 1993 and 1998, roughly half of all NICU deaths were associated with withdrawing/withholding, and by 1998, almost all NICU deaths were characterized by active withdrawal of mechanical ventilation.

**Demographics of Nonsurvivors Whose Interventions Were Withdrawn/Withheld**

Table 3 presents a more detailed analysis of the 78 infants whose deaths were associated with either withholding or withdrawing NICU interventions, comparing them with the 100 nonsurviving infants whose NICU interventions were not either withdrawn or withheld as they died (these infants died on a ventilator, while receiving CPR). The juxtaposition allows comparison of the impact of providing or refraining from NICU interventions at the end of life.

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<tr>
<td>No. of deaths</td>
<td>68</td>
<td>62</td>
<td>48</td>
</tr>
<tr>
<td>No. of withdraw/stable (%)</td>
<td>2 (3)*</td>
<td>10 (16)</td>
<td>6 (13)</td>
</tr>
<tr>
<td>No. withdraw/moribund (%)</td>
<td>5 (7)†</td>
<td>12 (19)</td>
<td>14 (29)</td>
</tr>
<tr>
<td>No. CPR withheld without withdrawal (%)</td>
<td>10 (15)</td>
<td>17 (27)</td>
<td>2 (4)†</td>
</tr>
<tr>
<td>No. died/full intervention (%)</td>
<td>51 (75)†</td>
<td>24 (39)</td>
<td>26 (54)</td>
</tr>
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* $P < .05$; † $P < .01$. 

Fig 5. Percentage of nonsurvivors who died after withdrawal of mechanical ventilation. There was a significant increase comparing 1998 and 1993 versus 1988; $P < .05$.

Fig 6. Percentage of nonsurvivors who had mechanical ventilation withdrawn for quality-of-life concerns in 1988, 1993, and 1998. There was no significant trend over time.

Fig 7. Percentage of extremely low birth weight nonsurvivors who had mechanical ventilation withdrawn for quality-of-life concerns in 1988, 1993, and 1998. There was no significant trend over time.
TABLE 3. Comparison of Nonsurviving Infants: Withdraw/Withhold Versus Full Support

<table>
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<tr>
<th>Gestational Age, wk</th>
<th>Birth Weight, g</th>
<th>Day of Death, d</th>
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<tbody>
<tr>
<td><strong>Withdraw/withhold (n = 78)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average</td>
<td>29</td>
<td>1380</td>
</tr>
<tr>
<td>SD</td>
<td>6.9</td>
<td>1068</td>
</tr>
<tr>
<td>Median</td>
<td>26</td>
<td>774</td>
</tr>
<tr>
<td><strong>Full support (n = 100)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average</td>
<td>29</td>
<td>1247</td>
</tr>
<tr>
<td>SD</td>
<td>5.6</td>
<td>970</td>
</tr>
<tr>
<td>Median</td>
<td>26</td>
<td>800</td>
</tr>
</tbody>
</table>

There are no significant differences in birth weight, gestational age, or day of death comparing infants who received continued ventilation and CPR and those for whom these interventions were withheld or withdrawn. These observations reveal that continuing to provide NICU intervention (or not) had little impact on the duration of life for these doomed infants.

**DISCUSSION**

Inevitably, some infants will die in the NICU. The history of neonatology suggests that as neonatologists become better and better at saving infants at a particular limit of viability, the limit is rolled back to reveal another population at risk to die. This behavior is neither startling nor unethical. Infants are admitted to the NICU for therapeutic interventions agreed to by both their parents and their doctors. If the therapy does not work, then the infants will die. How do they die? Specifically, what role, if any, do neonatologists have in facilitating their deaths?

Withdrawing and withholding NICU interventions are easily understood and, for nonethicists, easily distinguishable. “Pulling the plug” on a ventilated patient (withdrawing) feels to most people more problematic than not intubating a patient in the first place (withholding). The impetus for postulating a seemingly counterintuitive moral equivalence between the 2 conditions derives directly from the importance of “trials of therapy.” If, having started down a therapeutic path (eg, placing a patient on a ventilator), one could never withdraw no matter how dismal the prospects for eventual recovery became (because it would be tantamount to “murder”), then many potentially successful treatments might be withheld from all patients for fear of the protracted burden of failure for some.

Granting the utilitarian rationale for placing withholding and withdrawn on a common ethical plateau, distinctions among and within withdrawals(withholdings in individual cases are readily made. At one extreme is withdrawing/intervention that are no longer working, eg, failing to stabilize cardiopulmonary function in patients who have become physiologically moribund. These are futile therapies, using the narrowest definition of futility. Few people object to withdrawing/intervention in these cases. Indeed, some (cf 25) argue that no one (neither the state nor the parent) has requisite standing to make such an objection.

Alternatively, there are interventions (usually mechanical ventilation) that do successfully stabilize the cardiopulmonary physiology of some infants, but for those infants, the ultimate neurologic outlook is so dismal that the burdens of continued medical intervention outweigh the benefits of continued life. These therapies would then be withheld/withdrawn for quality-of-life concerns. We undertook this study in an attempt to catalog the way infants actually died in our NICU. We made several observations.

First, fewer patients die now. It is widely appreciated that birth weight–specific mortality has fallen and that rates of premature birth are fairly constant. What is perhaps underappreciated is the consequence of these 2 demographic trends—namely, dying in the NICU is very rare (currently <10% of our NICU admissions; <20% of our ventilated admissions) and very predictable (roughly two thirds of all deaths occur in very premature infants; the other third are larger infants with anomalies or asphyxia).

Second, withdrawing/withdrawing intervention is common in the NICU. Using traditional definitions, roughly half of all deaths in our NICU in 1993 and 1998 were associated with withdrawing or withdrawing. Wall and Partridge described a similar figure in their study of death in another tertiary NICU between 1989 and 1992. In addition, by 1998, >40% of our NICU deaths could be labeled “active withdrawal,” reflecting the extubation of infants regardless of their physiologic instability. This practice is growing over time.

However, in our view, these statistics provide too thin a description of how life really ends in the NICU. In our view, 2 important conclusions arise from the descriptions of NICU deaths provided here. First, when CPR was withheld, it most occurred in the context of moribund infants who were already receiving ventilation and dopamine. Physiologically stable infants who were removed from mechanical ventilation for quality-of-life reasons accounted for only 3% of NICU deaths in 1988, 16% of NICU deaths in 1993, and 13% of NICU deaths in 1998. Moreover, virtually none of these active withdrawals took place in premature infants, in whom, arguably, the ultimate neurologic prognosis is more uncertain than in term infants with clearly defined anomalies. Second, by 1998, infants who died without CPR almost always had mechanical ventilation withdrawn.

Many might ask the ethical question in reverse: not why is withdrawing/withholding so frequent in our NICU, but why are our instances of withdrawing/withholding so rare? We think that these frequencies reflect the wishes of our relatively homogeneous parent population: single, black, matriarchal, religious, poor, distrustful. Most of our parents do not want to stop intensive care if there is a chance of survival, and most are willing to continue medical intervention even in the face of a high probabilistic prediction of morbidity. All of the clinical decisions documented here were undertaken after a consensus between physicians and caregivers had been achieved. Only when the doctors and parents together accepted the moribund state of the infant did we withdraw. Compared with many centers, it is
likely that we continue longer with NICU care for mortally ill infants.

How much does this potential prolongation cost? Surprisingly little, our data suggest. The median and average day of death for 100 nonsurvivors who received full intervention did not differ significantly from the 78 nonsurvivors for whom intervention was withheld. These observations reflect and confirm that the vast majority of nonsurvivors were dying despite NICU intervention—and for these infants, NICU intervention does not matter.

In this manner, we support and extend previously published work on the nonefficacy of CPR in selected NICU populations, where absent an acute mechanical catastrophe (eg, pneumothorax, extubation, plugged endotracheal tube), CPR is ineffective in preventing the death of moribund NICU patients.26–28 Nonetheless, given our infrequent use of withdrawing/withholding for quality-of-life reasons, we may well discharge a larger proportion of infants from our NICU with a future probability of impairment. This also reflects the wishes of our parent population.

Several methodologic caveats deserve explicit mention. First, the increased use of level II ultrasound during pregnancy may lead to an increase in the frequency of in utero diagnosis of anomalies, leading in turn either to more nonresuscitation in the DR or to more selective termination of gestation. We did not note an increase in nonresuscitation of infants with anomalies but have no information on selective termination.

What about the practice of “limitation contracts,” whereby physicians and parents agree to continue NICU intervention at the same level but not escalate? How should these be categorized in light of the “experimental” nature of much NICU care? Is choosing not to increase dopamine above 20 µg/kg per min “withholding”? What about not adding a vasopressin drip for the same patient, or not offering a fourth antibiotic to a septic patient who is doing poorly, or not raising the mean airway pressure from 28 to 32 cm H2O for a hypoxic child who is on an oscillator? These delicate negotiations are subtle instances of withholding and would likely fall below the radar for most of our reviews except insofar as they tend to be accompanied by a formal DNR order and no CPR as part of the bargain.

We can extend this caveat to active withdrawal of interventions other than ventilation. It is arguable whether discontinuing a catecholamine drip in the face of refractory hypotension is an active withdrawal or a medical decision based on medical indications (no apparent benefit/some potential harm). In either case, these decisions were beyond the scope of our analysis here and, we would argue, ethically irrelevant for parents. The only ethically important withdrawal in our NICU is extubation.

In sum, we have described the circumstances of death and dying in the NICU over a decade in 1 large tertiary NICU. What might be gained by such a project? We note in our unit that a progressively larger percentage of doomed infants die in their mothers’ arms, extubated, without ever having received chest compressions or epinephrine boluses. Ostensibly, instances of withholding/withdrawing these decisions derive from an increasingly nuanced view of the benefits and burdens of NICU intervention, providing what we hope is a more humane approach to critically ill NICU infants than we had previously offered. We suggest that revision of ethical categories to reflect distinctions between withholding and withdrawing interventions from physiologically moribund infants or physiologically stable infants with severely morbid neurologic prognoses would allow a richer, more accurate description of the circumstances of end-of-life decision making in the NICU.

REFERENCES

“The economist J. D. Klienke points out that if all physicians followed the treatment guidelines laid down by the National Institutes of Health the number of Americans being treated for hypertension would rise from 20 million to 43 million, the use of asthma medications would increase somewhere between 2-fold and 10-fold, and the number of Americans on 1 of the so-called ‘statin’ class of cholesterol-lowering medications would increase by at least a factor of 10. By these measures, it doesn’t seem that we are spending too much on prescription drugs. If the federal government’s own medical researchers are to be believed, we’re spending too little. . . . The fact that volume matters more than price also means that the emphasis of the prescription-drug debate is all wrong. We’ve been focused on the drug manufacturers, but decisions about prevalence, therapeutic mix, and intensity aren’t made by the producers of drugs, they’re made by the consumers of drugs. This is why increasing numbers of employers have in recent years made use of what are known as pharmacy benefit managers, or PBMs. The PBMs draw up drug formularies—lists of preferred medications. They analyze clinical-trials data to find out which drugs are the most cost-effective.”

Gladwell M. New Yorker. October 25, 2004

Noted by JFL, MD