# Lessons Learned from Carrier Screening: Cystic Fibrosis

# The Parent's Perspective

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Population-based Carrier Screening for Single Gene Disorders:
Lessons Learned and New Opportunities
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# Outline of Talk

1. Results from two California obstetrical provider surveys
   - October 2001 (before ACOG recommendation)
   - August 2003
2. “Parental” perspective on carrier screening for CF

# *Cystic Fibrosis Prenatal Screening in California: Results of a Statewide Practitioner Survey*

## *October 2001*

**Suman M. Paranjape, et al.**
Interdisciplinary Masters Program
University of California, Berkeley

# Survey Objectives and Methods

- Assess CF prenatal screening practices, attitudes and beliefs prior to ACOG recommendations in October 2001
- 17-item survey mailed to 10% random sample of non-Kaiser obstetrical providers in California

# 2001 Survey Population

- Response rate - 24% out of N=748
- MDs – 77%
- Patient demographics

| Race/Ethnicity | Survey | 1999 Births |
|---|---|---|
| Caucasian | 32% | 33% |
| Hispanic | 49% | 48% |
| Black | 8% | 7% |
| Other | 11% | 12% |

# 2001 Survey Results

- Practitioners offering CF screening 41%
- Patients offered CF screening x 42%
- CA patients offered CF screening = 17%

(compared to 96% for XAFP screening and 39% for 1st trimester Trisomy 21 screening)

# Patients to whom providers recommend CF screening

| | Respondents |
|---|---|
| • Family history | 44% |
| • Ethnicity (Caucasian, Jewish, French Canadian) | 16% |
| • At risk | 12% |

# Barriers to CF Screening

| | Respondents |
|---|---|
| • No information for patients/ providers | 39% |
| • Insurance coverage or cost | 22% |
| • Patient demographics | 22% |
| • Other factors/situations | 18% |

# Provider Concerns about CF Screening

Most cited no ethical dilemmas, but some indicated concerns about:

- Genotype/phenotype correlations between CF mutations and disease severity
- Problems identifying mutations in non-Caucasian populations
- Continual improvements in CF treatment

# *California Prenatal Care Genetic Screening Survey*

## *July 2003*

**Lisa Feuchtbaum, DrPH, et al.**
Genetic Disease Screening Program
California Department of Public Health

# Survey Objectives and Methods

- Assess views on, and experiences with, mandatory newborn screening, supplemental newborn screening for metabolic disorders, and carrier screening for cystic fibrosis in July 2003

- 12-item survey mailed to prenatal care providers in California (N=6,197)*

**American Journal of Obstetrics & Gynecology* 194:131-137, January 2006.

# 2003 Survey Population

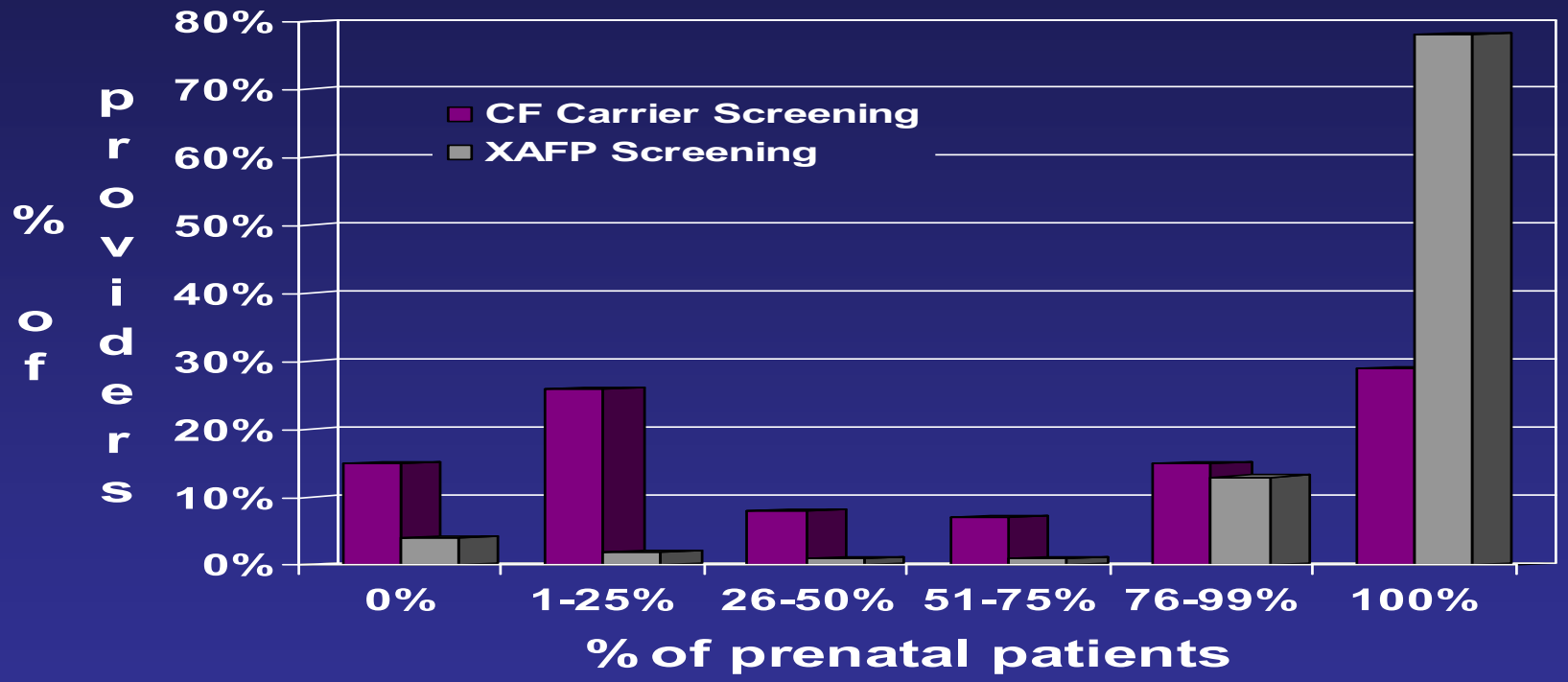
## Type of Providers

| | Response Rate | Respondents |
|---|---|---|
| Overall | 11% | 669 (100%) |
| MD/DO | 9% | 470 (70%) |
| Nurses/Midwives/ Others | 18% | 199 (30%) |

## Prenatal Patients

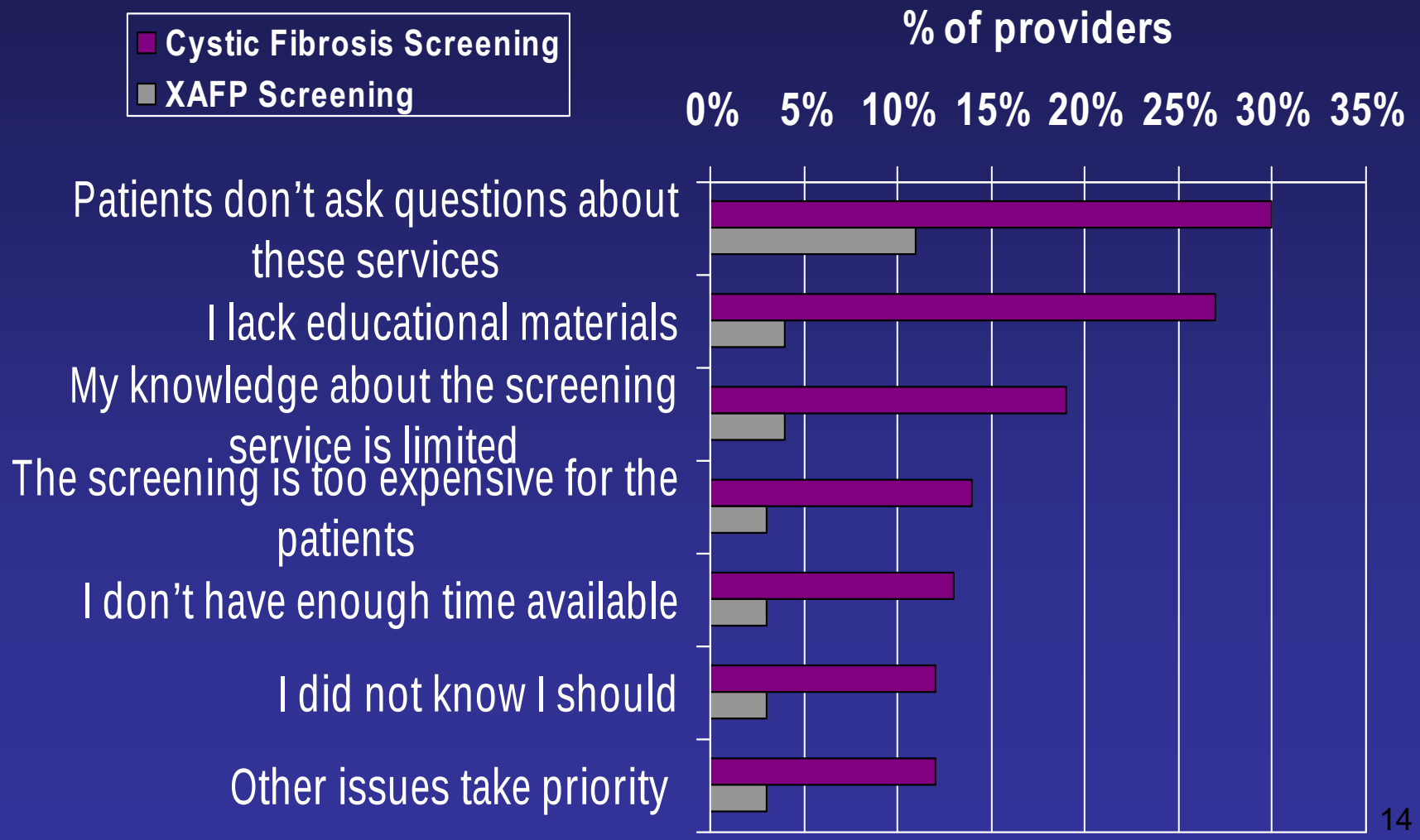
| | % on Medicaid |
|---|---|
| Patients of respondents | 39% (min, max = 31%, 47%) |
| CA Live Births | 42% |

## Q: Please estimate the percentage of prenatal patients with whom you and your staff discussed each of these screening services. (Please select only one for each)

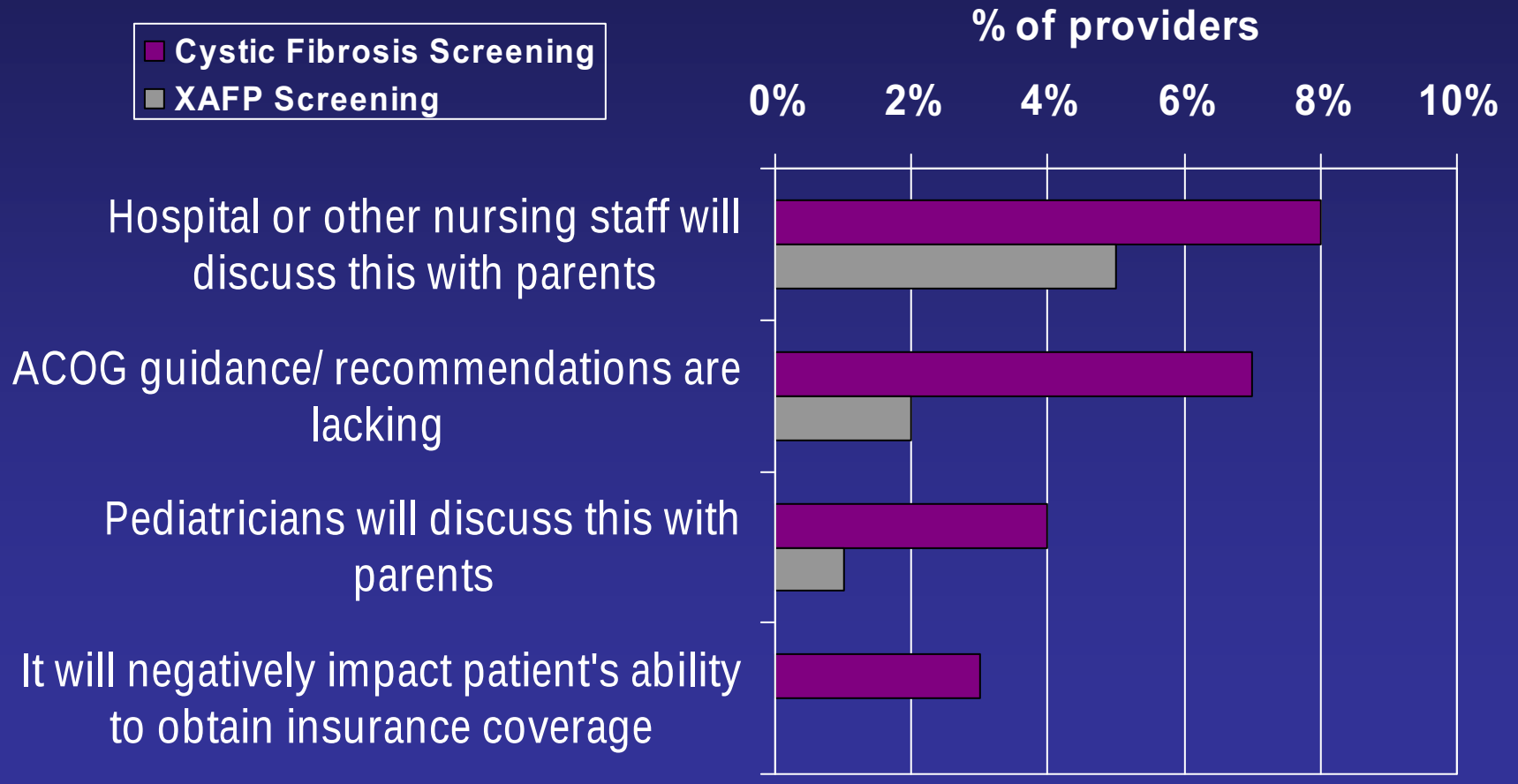



| Type of screening | % of prenatal patients |
|---|---|
| CF Carrier | 53% (min 46%, max 60%) |
| XAFP | 91% (min 89%, max 93%) |

# Q: Which of the following 11 factors, if any, limit your ability or willingness to discuss screening with your prenatal patients? (Please select all that apply) – top seven factors (>10%)



# Q: Which of the following 11 factors, if any, limit your ability or willingness to discuss screening with your prenatal patients? (Please select all that apply) – bottom four factors (<10%)



# Conclusions: 2001 & 2003 Surveys

- Penetration of prenatal CF carrier screening increased from ~17% in 2001 to ~53% in 2003
- In 2003, barriers included:
  - Inadequate provider knowledge and time
  - Lack of patient knowledge to ask
  - Lack of CF screening educational materials
  - Screening test costs too high for some patients

# Other Changes since October 2001

- Availability of CF newborn screening has increased dramatically from 8 state programs in 2001 to over 40 currently
- CF clinical care has improved and predicted median age of survival has risen from 32 years in 2001 to 37 years in 2006
- Knowledge about CFTR mutation frequencies and genotype-phenotype correlations has improved
- Over one dozen different commercial CFTR multiple mutation panel tests available (ACMG-23 or more)
- Six years of experience gained conducting CF carrier screening

# Prenatal Couples Need:

- Clear education about CF prior to testing
- Safe & accurate screening test
- Low cost test, couple covered by insurance
- Safe & accurate fetal diagnostic testing
- Interpretable test results
- Available and clear genetic counseling
- All follow up options available

# Problems with Education

- Medical providers educate parents differently about CF depending on their specialty area
  - Obstetrical providers: CF = fatal childhood disease
  - Pediatric providers: CF = treatable, chronic disorder
- Lack of clear educational message leads to parental confusion and distrust of medical profession
- **Possible Solutions:**

  Medical providers should give parents a similar message about CF across specialty areas. Education should start early and enlist the assistance of other preconception educators.

# Problems with Mutation Panel

- ACMG-23 CFTR mutation testing panel is:
  - based largely on carrier mutation frequencies, not case frequencies
  - includes mutations with varying degrees of severity
  - not equitable across geographic subgroups
  - not comprehensive for the non-White population

# Challenges posed by presence of CF Newborn Screening

- CF case detection rates are lower for prenatal carrier screening than for newborn screening

| | *% of California cases detectable* | |
|---|---|---|
| | Prenatal Screening | Newborn Screening |
| Whites | 88% | 95% |
| Blacks | 64% | 88% |
| Hispanics | 57% | 84% |

- Parental confusion occurs when prenatal screen negative goes on to have a newborn screen positive test result

# Possible Solutions to Mutation Panel Problems

- Continue to strive for a more sensitive and specific CFTR mutation panel
  - add mutations to improve sensitivity and equity across race/ethnic and geographic subgroups
  - remove mutations that are not severe yet prevalent to improve specificity
  - screen for variant combinations that result in severe disease, eg, R117H and (TG12-5T or TG13-5T)
  - consider using a more comprehensive mutation panel for male partner when sequential screening is used

# Conclusions about CF Carrier Screening

- Needs to be seen in a new context
  - Improved care for persons with CF
  - Earlier detection of CF with near universal newborn screening
- Need for earlier, more consistent, and clearer patient education about CF
- Need for a less costly yet more simple, sensitive, specific and equitable screening test
- Needs to be offered to more patients

# Thank you!

# CA Panel Selection Process

Mutations were selected to achieve an overall case detection rate of 90% or more in each race group

| Race | Min. mutation frequency to detect 78% of all chromosomes | # mutations selected |
|---|---|---|
| White | 1.0% | 8 |
| Black | 1.9% | 6 |
| Hispanic | 0.5% | 23 |
| Total | | 38* |

*CFTRdele2,3(21kb) was also added to the panel

# California 38 Panel vs. ACMG 23

1. delF508 *
2. delI507 *
3. G542X *
4. G551D *
5. G85E *
6. N1303K *
7. R1162X *
8. R334W *
9. R553X *
10. W1282X *
11. 1717-1G>A *
12. 3120+1G>A *
13. 3849+10kbC>T *
14. 621+1G>T *
15. 711+1G>T *
16. delF311 ^
17. A559T ^
18. R75X ^
19. R1066C ^
20. S549N ^
21. W1089X ^
22. 1812-1G>A ^
23. 2055del9>A ^
24. 2307insA ^
25. 3876delA ^
26. 935delA ^
27. 406-1G>A ^
28. 1288insTA ^
29. 2105-2117del13insAGAAA^
30. 296+2T>A ^
31. 3272-26A>G ^
32. 663delT ^
33. H199Y ^
34. P205S ^
35. Q98R ^
36. S492F ^
37. W1204X ^
38. CFTRdele2,3(21kb)^
39. A455E **
40. R117H **
41. R347P **
42. R560T **
43. 1898+1G>A **
44. 2184delA **
45. 2789+5G>A **
46. 3659delC **



*Cal 38 and ACMG 23 ^Cal 38 only **ACMG 23 only